

## Research

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# Diagnostic Yield of Flexible Sigmoidoscopy in Symptomatic Population: An Insight to Rapid Access Sigmoidoscopy Clinic

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## ABSTRACT

**Aim:** The study aim was to investigate the correlations between suspicious lower GI symptoms and endoscopic findings in symptomatic population using flexible sigmoidoscopy.

**Methods:** Retrospective review of all rapid access sigmoidoscopy clinic referrals was performed. Clinical, sigmoidoscopy findings and outcome were reviewed. Patients were further monitored for over five years for new cancers.

**Results:** A total of 445 patients met the inclusion criteria. Most patients (87.2%) had a flexible sigmoidoscopy in their first visit; 41.2% had barium enema to investigate proximal bowel. Polyp detection rate was 12.6% with an average distance of 23.1±18.9 cm from the anal verge. Passing mucus ( $p=0.05$ ) and incontinence ( $p=0.035$ ) were the only predictive symptoms for polyps. Cancer detection rate was 7%. Almost 93% of cancers were detected with the flexible sigmoidoscope alone with an average distance of 23.1±16.6 cm with majority being advanced as 17.9% had Duke's A. Weight loss ( $p=0.005$ ), tenesmus ( $p=0.006$ ) and passing mucus per rectum ( $p=0.008$ ) were three predictive symptoms on univariate and multivariate analysis. One patient developed a primary cancer 5 years from his index sigmoidoscopy. Substantial savings were achieved using this model of investigation.

**Conclusion:** Flexible sigmoidoscopy is easy, safe, sensitive and cost effective investigation for patients with suspicious lower colonic symptoms.

**KEYWORDS:** Symptomatic; Sigmoidoscopy; Cancer.

## INTRODUCTION

Worldwide the incidence of Colorectal Cancers (CRC) is approximately one million per year with an annual mortality approaching 5,00,000.<sup>1</sup> Despite medical advances and the high quality primary health care in Europe, the annual incidence is around 4,12,000 with an annual mortality reaching 50 percent.<sup>2</sup> The Republic of Ireland has a similar trend with an annual incident rate of close to 1,900 with an annual mortality of approximately 930 patients. In the report published by GLOBOCAN in 2002, Ireland had the highest mortality rates in Western European and the fourth worldwide.<sup>3</sup> Furthermore, the World Health Organisation has estimated that the number of newly diagnosed colorectal cancers will increase by 79% in males and 56% in females by 2020.<sup>4</sup> In response to these figures, the launch of a national colorectal screening program is anticipated to start this year targeting patients between the age of 60-69 in its first phase until it finally involves a screening population between 55-74 years old.<sup>4</sup>

Despite the high incidence of colorectal cancers and the intensive studies of the disease,

the early symptoms remain very vague resulting in 19-44% of patients presenting with advanced disease and requiring emergency surgery.<sup>5</sup> Part of the delay in the diagnosis can be linked to the reluctance of patients and primary care physicians to refer for endoscopy in secondary care centres.<sup>6</sup> The problem is further complicated by the universal delay to the index outpatient review and colonoscopy.<sup>7</sup>

The early stages of cancer are asymptomatic but clinically detectable. Cancer screening programmes target this stage as the cancer is still at an early stage and is believed to be curable. The advanced stages are symptomatic and will logically have a poorer outcome.<sup>8</sup> Although many studies recommend colonoscopy as a preferred investigation, most colorectal studies have been performed in asymptomatic cohorts with limited data in symptomatic population.<sup>9</sup>

Flexible sigmoidoscopy has been shown to reduce cancer related mortality.<sup>10</sup> Once-off flexible Sigmoidoscopy screening test for bowel cancer can reduce mortality from the disease by 43% (31% on a population basis) and reduce the incidence of bowel cancer by 33%.<sup>11</sup> Furthermore, sigmoidoscopy is more convenient for patients to evaluate their bowel compared to colonoscopy as it does not require an intense bowel preparation and it is a less stressful procedure.<sup>12</sup>

What is important is that despite all available diagnostic modalities, the vast majority of patients present only after developing worrying symptoms.<sup>13</sup> Therefore, the main objective of this study was to provide an evaluation of symptomatic patients presenting with suspicious symptoms of colorectal cancer to our rapid access colorectal clinic where they had flexible sigmoidoscopy in their index visit. Diagnostic yield, polyps and cancer detection rates, histological grade, anatomical location, presenting symptoms and economic viability were analysed. A secondary outcome was to look at new cancers diagnosed within the first five years following negative sigmoidoscopy.

## METHODS

The Rapid access colorectal clinic in Cork University Hospital was established in June 2001. The main objective of this clinic was to identify patients with symptoms suggestive of colorectal cancer and to review them within two weeks from referral. General Practitioners (GPs) in the hospital capture area were invited to refer all patients using a standardised referral form. The referral symptoms included in the form were rectal bleeding, passing mucus per rectum, Faecal Occult Blood (FOB) positive stool samples, and change in bowel habits, episodes of faecal incontinence, weight loss, anorexia, tenesmus and family history. GPs had to specify the duration of the symptom or symptoms and if there was a family history; age, sex, relationship to patient and the type of cancer should be included. All physical findings including per rectal examination had to be clearly highlighted.

Rapid access patients were seen as part of the general outpatient clinic. Upon arrival to the clinic, patients were reviewed with a full history and clinical examination. Half an hour before the flexible sigmoidoscopy, a phosphate enema was given by the endoscopy nurse. All sigmoidoscopies were performed by a consultant or a specialist registrar with a full sigmoidoscopy report written immediately after the procedure and before reviewing the next patient. No sedation was administered and banding of haemorrhoids was performed in the same visit if indicated. Patients with high risk polyps (multiple or high grade) or with symptoms suggestive of neoplasia were scheduled for a completion colonoscopy. Bowel imaging was completed in appropriate patients using barium enema, CT colonography or colonoscopy.

All patients referred to the rapid access colorectal clinic between 2001 and 2006 were included in the study. Patients younger than 40 years old have been excluded from analysis as it has been shown that their cancer diagnostic yield is limited.<sup>12</sup> Other exclusion criteria were history of inflammatory bowel disease, incomplete data, refusal of sigmoidoscopy and incomplete sigmoidoscopy reports. All new cancers diagnosed within five years from the initial sigmoidoscopy were recorded.

## Statistical analysis

The statistical analysis was performed using SPSS 20 (SPSS Inc. Chicago, IL, USA). Descriptive statistics such as rates and percentages were used for categorical data while mean  $\pm$  Standard Deviations (SD) were used for continuous data. The categorical variables were tested using  $\chi^2$  test, Fisher's exact test or Wilcoxon rank-sum test. Continuous variables were tested using a Student's t-test. Standard logistic regression analysis was used to calculate the relative risk as Odds Ratios (OR) with 95% Confidence Intervals (CI). A p-value of less than or equal to 0.05 was considered significant.

## RESULTS

After exclusion, a total of 445 patients were included in the study and deemed suitable for analysis. None of the excluded patients was diagnosed with cancer throughout the study period.

The average age of referred patients was 58.7 $\pm$ 13.05 years (52 years mean). Under half of the referred patients (49.4%, n=220) were males and 50.6% (n=225) were females. Most patients (87.2%, n= 388) had their flexible sigmoidoscopy in their index visit. The average waiting time from referral to clinical review was 19.5 ( $\pm$  SD 16.7) days. The average distance of assessed colon from the anal verge was 52.4 $\pm$ 16.8 cm (55.95 cm in males and 48.95 cm in females). Some pa-

-tients (41.1%) then required a completion barium enema (n=183) and 4.5 % of patients had other tests to investigate their bowel (n=20) (Table 1).

Patients characteristics		N = 445
<b>Age</b>	<b>Mean</b>	58.7(± SD 13.1)
	<b>Median</b>	52
	Male	220(49.4%)
	Female	225(50.6%)
	Sigmoidoscopy at first visit	388(87.2%)
	Clinic waiting time(days)	19.5(± SD 16.7)
	Sigmoidoscopy distance in cm	54.4(± SD 16.8)
	Completion barium enema	183(41.1%)
	Other investigations	20(4.5%)
<b>Indication for referral</b>		
	Bleeding PR	233(52.4%)
	Change in bowel habits	239(53.7%)
	Weight loss	33(7.4%)
	Family history	58(13 %)
	Abdominal pain	66(14.8%)
	Tenesmus	70(15.7%)
	Mucus	25(5.6%)
	Incontinence	24(5.4%)
	Other complaints	8(1.8%)
<b>Diagnosis</b>		
	Diverticular disease	66(14.8%)
	Haemorrhoids	65(14.6%)
	Colitis	29(6.5%)
	Irritable bowel syndrome	12(2.7%)
	Inflammatory bowel disease	9(2%)
	Anal fissure	10(2.2%)
	Celiac disease	4(0.9%)
	Polyps	56(12.6%)
	Cancers	31(7%)
	NAD	141(31.7%)
	Others	22(4.9%)

Table 1: Patients characteristics, presenting symptoms and diagnosis

The commonest presenting symptom of the referred patients was change in bowel habit accounting for 53.7% (n=239) followed by 52.4% of patients presenting with bleeding per rectum (n=233). The commonest diagnosis was diverticular disease (14.8 %, n=66) followed by haemorrhoids (14.6 %, n=65). Almost one third of patients (31.7%) did not show any pathology in their investigations (n=141). The polyp detection rate was 12.6% (n=56), and the cancer detection rate was 7 % (n=31). (Table 1).

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tum (n=233). The commonest diagnosis was diverticular disease (14.8 %, n=66) followed by haemorrhoids (14.6 %, n= 65). Almost one third of patients (31.7%) did not show any pathology in their investigations (n=141). The polyp detection rate was 12.6% (n=56), and the cancer detection rate was 7 % (n= 31) (Table 1).

The mean age of the 56 patients diagnosed with colonic polyps was 60.8 years ± 12.3 (61 years median). The mean age in male patients in this group was 56.3 years while females were slightly older (62.1 years). The average detection distance for polyps was 23.1 cm (± SD 18.9). Half of the polyps were in the sigmoid colon (50%, n= 28) followed by the rectum (37.5%, n=21). The commonest detected polyp was an adenomatous polyp (30.4%, n= 17) followed by hyperplastic polyps (28.6%, n=16). The characteristics of detected polyps are shown in Table 2.

Polyp characteristics		N = 56, 12.6%
<b>Patients age</b>	<b>Mean</b>	60.8 ± SD 12.3
	<b>Median</b>	61
<b>Average polyp distance</b>		23.1 cm ± SD
<b>Anatomical location</b>		
	Rectum	21(37.5%)
	Rectosigmoid junction	6(10.7%)
	Sigmoid colon	28(50%)
	Descending colon	1(1.8%)
<b>Polyp histology</b>		
	Adenoma	17(30.4%)
	Villous	11(19.6%)
	Hyperplastic	16(28.6%)
	Dysplastic	1(1.8%)
	Inflammatory	4(7.1%)
	Mucosa	7(12.5%)

Table 2: Characteristic of colorectal polyps

The commonest complaint was change in bowel habits (60.7%, n=34) followed by 51.8% reporting bleeding per rectum (n=29). Passing mucus per rectum (12.5%, n=7, *p*= 0.05) and episodes of faecal incontinence (12.5%, n=7, *p*=0.035) were the only significant symptoms seen in the univariate analysis. However, faecal incontinence was the only significant symptom identified by multivariate analysis (*p*=0.043, OR 3.143, CI 1.04-9.53) (see Table 3)

Thirty-one cancers (7%) were diagnosed in the referred population. Three patients were diagnosed with non-colonic cancers which were pancreatic, anal and small bowel lymphoma on subsequent investigations. The total number of the detected colonic cancers was 28 patients (6.3%) with mean age of 66.4±13.3 years (65.9 years old in males and 67.4 years old in females) and median of 65 years. The average tumour distance was 21.95±16.6 cm from the anal verge. The majority of cancer patients presented with advanced disease. The rec-

Colonic polyps	Polyps N = 56, 12.6%	No polyps N = 389	Univariate analysis <i>p</i> value	Multivariate analysis <i>p</i> value, OR & CI
Age	60.8 ± SD 12.3	58.72 ± SD 12.6	0.340	-
Gender				
Male	35 (62.5%)	185 (47.6%)	0.069	
Female	21 (37.5%)	204 (52.4%)	-	-
Presenting symptom				
Bleeding PR	29 (51.8%)	204 (52.4%)	0.89	-
Change in bowel habits	34 (60.7%)	205 (52.7%)	0.176	-
Weight loss	1 (1.8%)	32 (8.2%)	0.051	-
Family history	10 (17.9%)	48 (12.3%)	0.377	-
Abdominal pain	10 (17.9%)	56 (14.4%)	0.999	-
Tenesmus	8 (14.3%)	62 (15.9%)	0.814	-
Mucus	7 (12.5%)	18 (6.2%)	0.05	0.058,OR 2.89 (CI 0.96 -8.68)
Incontinence	7 (12.5%)	17 (4.4 %)	0.035	0.043,OR 3.143 (CI 1.04-9.53)

Table 3: Univariate and multivariate analysis of polyps symptoms

tum was the commonest site for cancer (53.6%, n=15) followed by rectosigmoid junction (28.6%, n=8) (see Table 4). Within this group, the commonest symptoms were bleeding per rectum which was seen in 57.1% (n=16) and change in bowel habits in 57.1% (n=16). Weight loss, tenesmus and passing mucus per rectum were the three significant symptoms seen in univariate and multivariate analysis of this group (see Table 5).

<b>Cancer characteristics</b>	<b>N = 28, 6.3%</b>
<b>Patients age (Mean)</b>	66.4±13.3
<b>Median</b>	65
<b>Average cancer distance</b>	21.95 ± SD 16.64
<b>Anatomical location</b>	
<b>Rectum</b>	15 (53.6%)
<b>Rectosigmoid junction</b>	8 (28.6%)
<b>Sigmoid colon</b>	3 (10.7%)
<b>Hepatic flexure</b>	1 (3.6%)
<b>Cecum</b>	1 (3.6%)
<b>Cancer type</b>	
<b>Duke A</b>	5 (17.86%)
<b>Duke B</b>	8 (28.57%)
<b>Duke C</b>	15 (53.57%)

Table 4: Characteristic of colorectal cancers

Colonic cancers	Cancer N = 28, 6.8%	No Cancer N = 417	Univariate analysis <i>p</i> values	Multivariate analysis <i>p</i> values, OR & CI
Age	66.4 ± SD 13.29	57.76 ± SD 12.77	0.004	-
Gender				
Male	19 (67.9%)	201 (48.2%)	0.062	
Female	9 (32.1%)	214 (51.8%)	-	-
Presenting symptom				
Bleeding PR	16 (57.14%)	217 (52.03%)	0.971	-
Change in bowel habits	16 (57.14%)	223 (53.5%)	0.390	-
Weight loss	7 (25%)	26 (6.2%)	0.005	0.01,OR 4.5, CI 1.4-14.1
Family history	5 (17.86%)	53 (12.7%)	0.458	-
Abdominal pain	3 (10.7%)	63 (15.1%)	0.745	-
Tenesmus	9 (31.1%)	61 (14.6%)	0.006	0.014, OR 3.3, CI 1.27-8.64
Mucus	5 (17.86%)	20 (4.8%)	0.008	0.031, OR 3.96,CI 1.13-13.9
Incontinence	1 (3.6%)	23 (5.5%)	0.093	-

Table 5: Univariate and multivariate analysis of colorectal cancers symptoms

One patient was diagnosed with right sided Duke’s A colonic cancer five years after his initial visit. His initial diagnosis was adenomatous polyp in the sigmoid colon and the cancer was detected during his follow up visit.

The estimated cost difference between flexible sigmoidoscopy and a day case colonoscopy is around 220 Euros. If all patients in this study (n=388) had undergone a colonoscopy, an additional cost of 80,309 Euros would have been incurred without any difference in the detection of major disease compared to the combination of flexible sigmoidoscopy and selective barium enema. Even with the addition of all patients who required completion colonoscopy for polyps or cancer or other means of bowel evaluation, our savings were around 27,500 Euros.

**DISCUSSION**

Flexible sigmoidoscopes reach 70% of bowel cancers and their combination with barium enema increases their sensitivity to 94% and specificity to 99% for the detection of bowel neoplasia<sup>14</sup> Moreover, the ability of a physician to perform this test in most health care settings makes it more accessible. This combined with the relative ease of performing sigmoidoscopies could enable primary care physicians and para-medical staff to perform the procedure after relatively short training.<sup>15</sup>

The early detection and removal of adenomas has a positive impact on the subsequent development of cancers.<sup>12</sup> The national polyp study demonstrated a 76-90% reduction in the development of colorectal cancer after successful endoscopic removal of polyps even after a prolonged surveillance period.<sup>16</sup> Although screening an already symptomatic population with more advanced disease will not result in any survival benefit;<sup>8</sup> the elective

treatment of colorectal cancer can significantly improve patients prognosis compared to outcomes after emergency surgery for an obstructing or perforated tumor.<sup>17</sup>

In our study, colonic polyps were detected on 12.6% of patients with the median age at the time of detection being 61 years. As seen in many studies, there is a preponderance of the disease in the male population.<sup>18</sup> We identified that passing mucus per rectum and episodic faecal incontinence are unique presenting symptoms for distal colonic polyp which has not been described in previous reports. However, the relatively small number of polyps detected and the overall small patient pool may have resulted in a Type I error or false positives in other words Therefore large studies looking specifically at symptoms related to distal polyps will be required to further validate these findings.

Although there is a myriad of symptoms a colorectal cancer patients can present with, few of these are unique. It is very important to understand that these symptoms are more likely to occur in clusters rather than in isolation. Most of isolated symptoms lack sensitivity and specificity and in clusters they increase the likelihood of cancer.<sup>19</sup> Most patients referred to secondary centres with colorectal cancers have more than one symptom (85%).<sup>13</sup> Furthermore, these symptoms are subjected to selection bias which affects their predictive value in both the primary and secondary care settings.<sup>20</sup>

Rectal bleeding is one of the most widely known and feared symptom. It is important to evaluate both the nature and duration of bleeding before considering flexible sigmoidoscopy or any other investigation. The estimated predictive value of bleeding per rectum for colorectal cancer in the general population is around 1 in 1000.<sup>21</sup> Furthermore, 6% of the population above the

age of 40 years had recent rectal bleeding.<sup>22</sup> In most cases, bleeding per rectum is a symptom of benign pathology rather than from a cancerous origin. This was reflected in our study as 233 patients (52.4%) were referred with bleeding per rectum and only 16 (6.9%) were diagnosed with cancer.

When looking at change in bowel habits, constipation is considered as a low risk symptom for colorectal cancer.<sup>23</sup> Many studies reported that increased bowel frequency and loose motion is associated with 60-91% in distal and 40-61% in proximal cancers.<sup>24</sup> However, it was reported that the predictive value of diarrhoea is 0.63% in patients below 70 years and 1.7% in those over 70.<sup>25</sup> Similar to rectal bleeding, out of 239 patients (53.7%) referred with change in bowel habits, only 16 (6.7%) were diagnosed with cancer.

Unintentional weight loss is one of the most alarming symptoms of colorectal cancers despite being shared with benign conditions. The incidence of weight loss in general population is about 2.3-3.3%.<sup>26</sup> In our study, weight loss was a significant predictor for colorectal cancers. Out of 33 patients referred with unintentional weight loss, 7 (21.2%) had colorectal cancer ( $p < 0.05$ ). A higher incidence rate was seen in a study by Majumdar et. al in which 39% of a cohort of 194 cancer patients presented with weight loss. The study also showed that weight loss was less common in distal cancers without reaching statistical significance.<sup>8</sup> This high figure drops to 1.2% in non-selected primary care patient cohort.<sup>19,25</sup> Likewise, colonoscopy findings in patients with abdominal pain compared to asymptomatic patients showed no difference in the detection of major colorectal diseases.<sup>27</sup>

The combinations of two or more symptoms can increase the predictive ability to detect colorectal cancer.<sup>19</sup> The association of rectal bleeding and change of bowel habit is described in many studies.<sup>25</sup> Likewise, the combination of weight loss and rectal bleeding or change in bowel habits increases the positive predictive value.<sup>19</sup> Despite the low predictive value of abdominal pain, its combination with rectal bleeding can raise its predictive value significantly.<sup>25</sup> In our study, 79% of patients had more than one symptom in their presentation.

The colorectal cancer detection rate of 6.3% in this study is comparable to the detection range of 4-16% described in previous reports.<sup>5,12,28</sup> Moreover, the 57% incidence of rectal bleeding and change in bowel habits in bowel cancer was very similar to 58 and 51% in a symptomatic colorectal study.<sup>13</sup> In our study, 92.8% of all cancers were within the reach of the sigmoidoscope and 7.2% were on the right side which is in keeping with previous reports.<sup>29</sup> Unexplained weight loss, peri-anal pain and passing mucus per rectum were the most significant independent predictors of colorectal carcinoma in our symptomatic population.

Currently, our rapid access clinic has further transformed and it is almost entirely managed by our advanced nurse practitioner who is supervised by consultant colorectal surgeons. This has further reduced the operator cost from an average of 50 Eu

ros per hour to 20 Euros per hour. Furthermore, twice the number of sigmoidoscopies can be performed compared to colonoscopies in each endoscopy session. This further reduced the cost, the endoscopic waiting time and the burden on the day-case services. Within 2011, our service was able to deliver 818 flexible sigmoidoscopies through the rapid access clinic.

One potential weakness of this study is the variability of symptoms among different referring GPs. It is quite possible that they might be more thorough in their referrals if there was a suspicion of malignancy. As such, the predictive value of the symptoms could be overestimated. We were also hampered by our inability to accurately collect information from the referral forms about dietary habits and medications that may have had relevance to the patient presentation.

In conclusion, in the presence of the alarming symptoms identified in this study or combination of two or more, patient's referral should be flagged as urgent. Most importantly, flexible sigmoidoscopy is relatively easy, safe, sensitive and cost effective investigation for patients with lower colonic symptoms especially in such a difficult economic climate.

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