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Can the colour of per-rectal bleeding estimate the risk of lower gastrointestinal bleeding caused by malignant lesion?

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Abstract

Purpose: To estimate the risk of lower gastro-intestinal bleeding (LGIB) caused by malignant lesion in patients presenting with per-rectal bleeding (PRB), by using visual aid as an objective measurement of PRB colour.

Methods: This was a prospective observational study on patients presented with PRB to Family Medicine Specialty Clinic, who undergo flexible sigmoidoscopy (FS) or colonoscopy (CLN) from December 2012 to September 2013. Patients aged 40 years old or above, haemodynamically stable, with normal haemoglobin level were included. Patients with history of previous colonic surgery, refused to have FS or CLN, with ophthalmologic diseases such as colour blindness were excluded. Parameters including subjective description of PRB colour, number of chosen red colour by patients, source and distance of bleeding from anal verge were recorded for analysis. Receiver operating characteristic (ROC) curve was used to identify the optimal cutoff level of colour for diagnosing colonic lesion. Diagnostic accuracy was assessed by area under the ROC curve (AUC). Accountability of this model was assessed by logistic regression.

Results: The dark PRB colour was associated with diagnosis of tumour ($p<0.001$) and advanced neoplastic polyp ($p<0.001$). The light PRB colour was associated with the diagnosis of piles ($p<0.001$). The performance of our model to predict tumour or advanced neoplastic polyps by colour (AUC: 0.798) had a better discriminative power than that to predict colonic lesion alone (AUC: 0.610) by ROC curve analysis.

Conclusion: Objective measurement of PRB colour accurately estimated the risk of LGIB caused by malignant lesion in patients presenting with PRB.

Keywords: lower gastro-intestinal bleeding; per rectal bleeding; colour cards; colonoscopy; sigmoidoscopy.

What does this paper add to the literature?

Objective measurement of per-rectal bleeding colour is a valid and non-invasive tool for estimating the risk of lower gastro-intestinal bleeding caused by malignant lesion.

Manuscript Text

Introduction

Per-rectal bleeding (PRB) is a common presentation in primary care. (1) Although most cases of PRB are due to local conditions like haemorrhoids and many other non-malignant conditions, this symptom is a major sign of colorectal cancer and is frequently the first presenting symptom. (2-5)

The physician's interrogation of the patient for a description of PRB is the standard initial approach to diagnosing lower gastro-intestinal bleeding (LGIB). (6, 7) And yet, this subjective clinical approach had not been tested or validated in primary care. There are variability and inconsistency in subjective colour reporting by patients. It is worthy to verify patients' subjective description by an objective visual aid.

From the literature review, the appearance of the passed blood could be dependent on two factors. The first is the length of time in the intestine. (7) It shows that the darkness of the red colour of PRB is related to the distance from the anal verge. The second is the proportion of oxygenated blood: deoxygenated blood. It is because arterial blood contains oxygenated blood which is lighter in colour while venous blood contains deoxygenated blood which is darker in colour. (8,9) Therefore, the objective PRB colour can help to correlate the cause and site of LGIB.

As PRB is a common clinical problem, there is a large and increasing demand of both flexible sigmoidoscopy (FS) and colonoscopy (CLN). Due to limitation in health resources, the waiting list of FS and CLN in public health sector is quite long. It is important to decide which patients with PRB need either FS or CLN most so that we can pick up those high risk cases of colorectal cancer for early investigation. (10-14)

This study aimed at estimating the risk of LGIB caused by malignant lesion in patients presenting with PRB by an objective measurement of the colour of PRB so that we can identify which patient with PRB needs flexible sigmoidoscopy or colonoscopy earlier. Another aim was to use visual aid to assist in history taking for the description of colour of PRB, so that we can have a more objective assessment of the colour of PRB.

Method

This was a prospective observational study on patients presented with PRB to the Family Medicine Specialty Clinic (FMSC) in Hong Kong and those who underwent flexible sigmoidoscopy or colonoscopy subsequently during the period from December 2012 to September 2013.

Patients who were aged 40 or older, haemodynamically stable, with normal haemoglobin level were included. Patients were excluded if they had history of previous colonic resections or surgical alterations, refused to have FS or CLN, had blindness or ophthalmologic diseases such as colour blindness which affect the differentiation of colour.

Procedure

Before FS or CLN, complete blood pictures were done to make sure that they were not anaemic due to massive blood loss. It was because massive bleeding may affect the transit time of the blood in the intestine and then affect the colour of the blood in the stool. Blood pressure and pulse were checked to ensure that the patients were haemodynamically stable. All subjects were asked to describe in words the colour of PRB. Patients were free to use their own terms without any direction from the physician. After that, the patients were shown by the physician a colour card (Figure 1) composing of four numbered colours from the left of brightest red to the right of darkest red and were invited to point to a specific colour that was best approximate to the colour of the PRB. The choices were recorded as a colour number ranging from 1 to 4. Either FS or CLN would be performed by endoscopist to find out the site and source of LGIB.

The parameters including the subjective description of PRB colour, the number of the chosen red colour from the card by the patient, the source of bleeding and the distance from the anal verge to the causative lesion found in FS or CLN, were all recorded for outcome analysis. Research ethics of this study was approved by the Kowloon West Cluster Research Ethics Committee, Hong Kong.

Data Analysis

Descriptive statistics were presented with median and interquartile range for continuous variables, and frequency and proportion for categorical variables Differences in patients' characteristics between the PRB colour were tested using Chi-square test or Mann-Whitney U-test, where appropriate.

Accuracy in terms of the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the use of PRB colour in diagnosing colonic lesions (polyp or tumour), or diagnosing ominous colonic lesion (tumour or advanced neoplastic polyps), as well as tumour alone, were compared to diagnosis confirmed by FS or CLN as the diagnostic standard. The receiver operating characteristic (ROC) curve would be obtained by plotting sensitivity against (1-specificity) for each cutoff value for identification of the optimal cutoff level of PRB colour for diagnosing colonic lesion or tumour among this population compared to diagnosis confirmed by FS or CLN. Diagnostic accuracy was assessed by the area under the ROC curve (AUC). The accountability of this model was assessed by logistic regression analysis, accounting for all other clinical and socio-demographic characteristics. Finally, predicted probabilities of diagnosing colonic lesion outcomes were estimated with respect to the PRB colour.

All data analyses were conducting SPSS Version 21.0. P-value of <0.05 was considered as statistical significance.

Sample Size

The sample size required was estimated by two parameters: prevalence of PRB and odds ratio. The prevalence of PRB was estimated as 14.7% in Turkish population. Since there was no literature showing the prevalence of PRB in Hong Kong, and Turkish as an Asian population, we used it to calculate our study sample size. Given an estimate of prevalence rate in Turkey from previous study, sample size of 283 subjects was large enough to detect an odds ratio of 1.6 with 80% power at the 0.05 significance level with a two-sided test. By assuming 87.3% of colonoscopy attendance rate we needed 325 subjects in total. (15-17)

Results

A total of 325 eligible patients were consented to join the study. Amongst them, 293 patients were completed with either FS or CLN. 32 patients were lost to follow up due to the default of endoscopy appointment. In this study, the majority of patients presented with PRB were male. The gender, smoking status, complaints of change of the bowel habit, change of the stool and procedure were more frequently associated with change of colour in PRB. (Table 1) The other demographic and clinical characteristics of our patients did not vary significantly between different colour

groups. The dark colour change of the PRB was statistically significant associated with diagnosis of tumour ($p<0.001$) and advanced neoplastic polyp ($p<0.001$) in our study. (Table 2) On the other hand, the light colour change of PRB was statistically significant associated with the diagnosis of piles ($p<0.001$). The other benign lesions like colonitis, proctitis, anal fissure did not vary significantly between different colour groups. The colour change of the PRB was also significantly associated with the distance of the lesion from the anal verge. The light red colour was significantly associated with the site of rectum and the dark red colour was associated significantly with the transverse colon, but not the other sites of the colon. (Table 2)

When the demographic, clinical and diagnostic factors were further adjusted in the logistic regression model, the diagnosis of polyps or tumour were more significantly associated with the darker colour change of PRB (Colour $\geq$2), and diagnosis of malignant lesions like tumour or advanced neoplastic polyps were more significantly with a trend towards the darkest colour change of PRB (Colour 3 & 4). In other words, the light PRB colour (Colour 1) had higher likelihood of neither polyp nor tumour. The performance of our model to predict tumour or advanced neoplastic polyps by the change of colour of PRB had a better discriminative power than that to predict colonic lesion alone by ROC curve analysis (Table 3 & 4, figure 2-4).

Predicted probability of colonic lesion was gradually increased with the darker colour of PRB (Figure 1). Colour 4 indicated the predicted probability of 86.6% for any colonic lesion, 60.9% for ominous colonic lesion, and 34.5% for tumour.

Discussion

PRB is a common presenting symptom of colorectal cancer, though most cases of PRB encountered in primary care are due to local benign causes, such as piles. However, a useful tool is still lacking for the family physician to predict the benign causes from the malignant causes and to prioritize the patients for further invasive investigations like enemas or endoscopies.

In clinical practice, it is common to perform FS or CLN in patients with bowel symptoms because of the concern about colorectal cancer. (10,18) Change of bowel habit and PRB are significantly associated with left-sided cancers. (10,12) In Choi et al, it reported that FS was a valuable initial investigation for patients older than 40 years presenting with bright red PRB without other bowel symptoms instead of colonoscopy. (10)

Since PRB is a very common clinical problem in Hong Kong, the demand of both FS and CLN is ever increasing. The waiting lists of both FS and CLN in the public hospitals become longer and longer due to the limited health resources. It is important to differentiate those patients with PRB at high risks of colorectal cancer for early investigations. (10-14)

PRB represents a diverse range of bleeding sources and severities, ranging from haemorrhoidal bleeding to blood loss from colorectal tumours.(19) The described colouration of PRB by patients is frequently transposed to medical terminology by physicians. (7) Various terms are used to describe blood emanating from the lower gastrointestinal tract, including hematochezia, rectal bleeding and bright red blood per-rectum. These terms, even when defined, are somewhat non-specific and do not indicate the acuity or severity of bleeding and do not always localize the bleeding sources. (19) When PRB is not witnessed by the physicians, they usually rely on the patients' description of the blood colour (7) e.g. 'bright red', 'light red', 'dark-red', 'brown', etc. Again, these subjective descriptions of colour had not been tested in any systemic fashion in our locality and in primary care. (6,7)

In a study done by Zuckerman GR et al (6), evaluated prospectively if an objective test of stool colour would correlate with or improve upon subjective descriptions in predicting bleeding locations. The objective test employed was a simple pocket sized card containing five numbered colours that typify the spectrum of stool colours. This study revealed marked variability and surprisingly inconsistency in subjective colour reporting for both patients and physicians and the superiority of several card colours for separating upper from lower bleeding sources. (7)

Choi et al reported that flexible sigmoidoscopy was a valuable initial investigation for patients older than 40 years presenting with bright red PRB without other bowel symptoms. (10) However, the description of 'bright red' PRB was not standardized either. Patients' description may not be accurate but the darkness of the red colour of PRB may actually give us a clue on the site and source of bleeding in the distal lower intestinal tract. The darkness of the colour of PRB may be helpful in the general evaluation of the level of bleeding, i.e. the distance of bleeding site from the anus. (6) Moreover, it may be related to the pathology of the bleeding. For example, haemorrhoidal bleeding may have a lighter red colour as haemorrhoids are arterio-venous shunts. (20) The arterial component made the red colour lighter as it contains oxygenated blood. (8) The mucus from malignant tumour may make the

PRB darker in colour. Therefore, light red PRB may point to benign and distal lesion while dark red PRB may point to malignant and proximal lesion.

Therefore, we would like to verify the validity of patient's history on the PRB colour with an objective confirmation and try to find out the relationship between colour of PRB and the site and source of LGIB. In our study, a colour card (Figure 1) containing four numbered colours (from bright red to dark red with RGB colour coding) was used. These colours had been determined in a pilot study to approximate the spectrum of PRB colour most commonly reported by patients with PRB.

Most of the previous studies focus on the acute LGIB in hospitalized patients. The area is grossly under-explored in primary care, and yet it is very important in our daily practice. We need to identify the prediction of outcome of our patients with PRB upon their presentation with objective assessment so that we can decide which patients with PRB need FS or CLN most.

In this study, we used the visual aid to assist in history taking for the description of colour of PRB, so that we could have a more objective assessment of the colour of the PRB. It was found to have a marked variability and inconsistency of the colour chosen from the card by patients in responding to their subjective description of the colour of the PRB. Despite most patients complained of "fresh PRB" chose colour 1 & 2, some patients still chose colour 3 & 4 from the card. On the other hand, a few patients complained of dark coloured PRB, they chose colour 1 from the cards finally. (Table 6) These all reflect the facts that inconsistency between subjective and objective assessment in history taking and a more accurate objective method is needed for a better and more consistent communication between the patient and the physician. Accurate and good history taking is certainly the first step in making the right diagnosis.

Furthermore, the objective measurement of the colour of the PRB can help estimating the risk of LGIB caused by malignant lesion in patients presenting with PRB, after adjusting for demographic, clinical and diagnostic factors. In this study, it is shown that the darker coloured PRB had higher likelihood of predicting colonic polyp or tumour. On the other hand, the lighter coloured PRB like colour 1 had higher likelihood of predicting neither polyp nor tumour. This result is very helpful in our clinical practice, not only for the family physicians, but also for the surgeons. We can use this assessment model to identify which patient with PRB needs endoscopy earlier,

so that we can make better use of our limited health resources in the public health sector. In addition, the colour change of the PRB is also significantly associated with the distance of the colonic lesion from the anal verge. Therefore, the visual aid colour scheme can be a useful tool for triaging those high risk patients with PRB for either flexible sigmoidoscopy or colonoscopy, in order to make economic use of the endoscopic investigations.

Hence, a suggested treatment algorithm is formulated (figure 5). Patients presented with PRB are instructed to choose a colour from the colour card that is best approximate to the colour of the PRB. If colour 3 or 4 is chosen, early CLN should be arranged as soon as possible. On the other hand, if colour 1 or 2 is chosen, routine CLN can be arranged. However, for patients with previous CLN and have been diagnosed to have benign conditions, e.g. haemorrhoids, they could be observed with regular follow up. During each follow up, they are instructed to choose a colour from the colour card again, according to the colour of the PRB. The choice of colour should be monitored closely during each visit. Early CLN should be arranged promptly if the patients choose colour 3 or 4.

Conclusion

The objective measurement of the colour of PRB can help estimating the risk of LGIB caused by malignant lesion in patients presenting with PRB, so that we can prioritize those high risk patients with PRB to have flexible sigmoidoscopy or colonoscopy earlier, especially in those units with long waiting list of endoscopy. Furthermore, the use of a standard objective visual aid can assist in history taking for the subjective description of the colour of PRB, facilitating decision making for the choice of endoscopic investigations.

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Competing interest

None declared.

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Table

Table 1. Demographic and Clinical Characteristics of Subjects

		Colour of PRB				
	Total (N=293)	1 (N=178)	2 (N=73)	3 (N=26)	4 (N=16)	P-value*
Demographic						
Age (median, IQR)	58 (51-66)	56 (51-65)	58 (50-64)	61 (52-69)	60.5 (55-69.5)	0.275
Male	153 (52.2%)	81 (45.5%)	40 (54.8%)	18 (69.2%)	14 (87.5%)	0.002
Smoking Status						0.022
Smoker	39 (13.3%)	18 (10.1%)	12 (16.4%)	6 (23.1%)	3 (18.8%)	
Non-smoker	203 (69.3%)	137 (77.0%)	45 (61.6%)	12 (46.2%)	9 (56.3%)	
Ex-smoker	51 (17.4%)	23 (12.9%)	16 (21.9%)	8 (30.8%)	4 (25.0%)	
Clinical						
BMI (median, IQR)	23.6 (22.0-26.1)	23.6 (22.0-26.1)	24.0 (22.3-26.7)	22.0 (26.0-24.3)	23.2 (22.5-26.1)	0.752
History of colorectal neoplasia	8 (2.7%)	4 (2.2%)	2 (2.7%)	0 (0.0%)	2 (12.5%)	0.084
Family History of CRC	40 (13.7%)	25 (14.0%)	9 (12.3%)	5 (19.2%)	1 (6.3%)	0.668
Change of bowel habit						0.001
No change	253 (86.3%)	155 (87.1%)	67 (91.8%)	22 (84.6%)	9 (56.3%)	
Less frequent	22 (7.5%)	15 (8.4%)	4 (5.5%)	1 (3.8%)	2 (12.5%)	
More frequent	18 (6.1%)	8 (4.5%)	2 (2.7%)	3 (11.5%)	5 (31.3%)	
Change of stool						<0.001
No change	250 (85.3%)	157 (88.2%)	64 (87.7%)	21 (80.8%)	8 (50.0%)	
Harder stool	16 (5.5%)	11 (6.2%)	5 (6.8%)	0 (0.0%)	0 (0.0%)	

Looser stool	27 (9.2%)	10 (5.6%)	4 (5.5%)	5 (19.2%)	8 (50.0%)	
Significant weight loss	8 (2.7%)	5 (2.8%)	3 (4.1%)	0 (0.0%)	0 (0.0%)	0.636
Hb level (median, IQR)	14.0 (13.0-15.0)	14.0 (13.0-15.0)	14.0 (13.0-15.0)	13.0 (15.0-13.5)	14.0 (12.5-15.0)	0.296
Procedure						<0.001
Colonoscopy	206 (70.3%)	129 (72.5%)	60 (82.2%)	12 (46.2%)	5 (31.3%)	
Flexible sigmodoscopy	87 (29.7%)	49 (27.5%)	13 (17.8%)	14 (53.8%)	11 (68.8%)	

Note:

PRB=Per Rectal Bleeding; IQR=Interquartile Range; BMI=Body Mass Index; CRC=Colorectal Cancer

* Significant difference by Chi-square test or Mann-Whitney U-test, where appropriate

Table 2. Diagnosis of Subjects

	Total (N=293)	Colour of PRB				
		1 (N=178)	2 (N=73)	3 (N=26)	4 (N=16)	P-value*
Diagnosis						
Tumour	17 (5.8%)	4 (2.2%)	2 (2.7%)	7 (26.9%)	4 (25.0%)	<0.001
Advanced neoplastic polyp	11 (3.8%)	2 (1.1%)	2 (2.7%)	3 (11.5%)	4 (25.0%)	<0.001
Polyp size <1cm	78 (26.6%)	46 (25.8%)	20 (27.4%)	5 (19.2%)	7 (43.8%)	0.361
Colonitis / Proctitis	5 (1.7%)	3 (1.7%)	2 (2.7%)	0 (0.0%)	0 (0.0%)	NA
Pile	188 (64.2%)	125 (70.2%)	48 (65.8%)	12 (46.2%)	3 (18.8%)	<0.001
Others	2 (0.7%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	NA
Distance						
<=10cm	197 (67.2%)	127 (71.3%)	50 (68.5%)	15 (57.7%)	5 (31.3%)	0.008
>10-20cm	28 (9.6%)	13 (7.3%)	6 (8.2%)	4 (15.4%)	5 (31.3%)	0.012
>20-60cm	23 (7.8%)	8 (4.5%)	6 (8.2%)	1 (3.8%)	8 (50.0%)	<0.001
>=60cm	4 (1.4%)	3 (1.7%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	NA
Site						
Rectum	214 (73.0%)	136 (76.4%)	52 (71.2%)	19 (73.1%)	7 (43.8%)	0.044
Rectosigmoid	3 (1.0%)	2 (1.1%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	NA

junction						
Sigmoid colon	48 (16.4%)	25 (14.0%)	12 (16.4%)	6 (23.1%)	5 (31.3%)	0.246
Descending colon	16 (5.5%)	7 (3.9%)	4 (5.5%)	2 (7.7%)	3 (18.8%)	0.089
Splenic flexure	1 (0.3%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Transverse colon	8 (2.7%)	4 (2.2%)	1 (1.4%)	0 (0.0%)	3 (18.8%)	<0.001
Hepatic flexure	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	NA
Ascending colon	15 (5.1%)	11 (6.2%)	4 (5.5%)	0 (0.0%)	0 (0.0%)	0.441
Caecum	9 (3.1%)	5 (2.8%)	2 (2.7%)	0 (0.0%)	2 (12.5%)	0.129

Note:

PRB=Per Rectal Bleeding

* Significant difference by Chi-square test

Table 3. Performance Characteristics of PRB colour at various cutoff level for diagnosis

PRB colour cutoff level	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive likelihood ratio	Negative likelihood ratio	AUC (95%CI)
Diagnosis of Tumour or Polyps (n+=102 vs n-=191)							0.610 (0.540-0.681)
≥2	50.00%	66.49%	44.35%	71.35%	1.492	0.752	
≥3	26.47%	92.15%	64.29%	70.12%	3.371	0.798	
≥4	12.75%	98.43%	81.25%	67.87%	8.114	0.886	
Diagnosis of Tumour or Advanced Neoplastic Polyps (n+=28 vs n-=265)							0.798 (0.695-0.901)
≥2	78.57%	64.91%	19.13%	96.63%	2.239	0.330	
≥3	64.29%	90.94%	42.86%	96.02%	7.098	0.393	
≥4	28.57%	96.98%	50.00%	92.78%	9.464	0.737	
Diagnosis of Tumour (n+=17 vs n-=276)							0.773 (0.639-0.908)
≥2	76.47%	63.04%	11.30%	97.75%	2.069	0.373	
≥3	64.71%	88.77%	26.19%	97.61%	5.761	0.398	
≥4	23.53%	95.65%	25.00%	95.31%	5.412	0.799	

Note

PRB=Per Rectal Bleeding; PPV=Positive predictive value; NPV=Negative predictive value; AUC=Area under ROC curve

Table 4. Association between the diagnosis of colonic lesions and colour of PRB

	Logistic Regression			
	Crude OR	P-value	Adjusted OR*	P-value
Diagnosis of Tumour or Polyps				
≥2	1.984 (1.215-3.242)	0.006	18.661 (1.994-174.634)	0.010
≥3	4.224 (2.126-8.393)	<0.001	4.749 (0.510-44.252)	0.171
≥4	9.154 (2.544-32.937)	0.001	0.956 (0.042-21.890)	0.978
Diagnosis of Tumour or Advanced Neoplastic Polyps				
≥2	6.781 (2.656-17.313)	<0.001	6.600 (1.934-22.523)	0.003
≥3	18.075 (7.501-43.556)	<0.001	20.941 (4.726-92.799)	<0.001
≥4	12.850 (4.362-37.856)	<0.001	3.408 (0.782-14.848)	0.102
Diagnosis of Tumour				
≥2	5.544 (1.761-17.457)	0.003	5.362 (1.050-27.387)	0.044
≥3	14.489 (5.007-41.929)	<0.001	17.651 (2.355-132.319)	0.005
≥4	6.769 (1.918-23.892)	0.003	1.173 (0.150-9.154)	0.879

Note:

OR=Odds Ratio

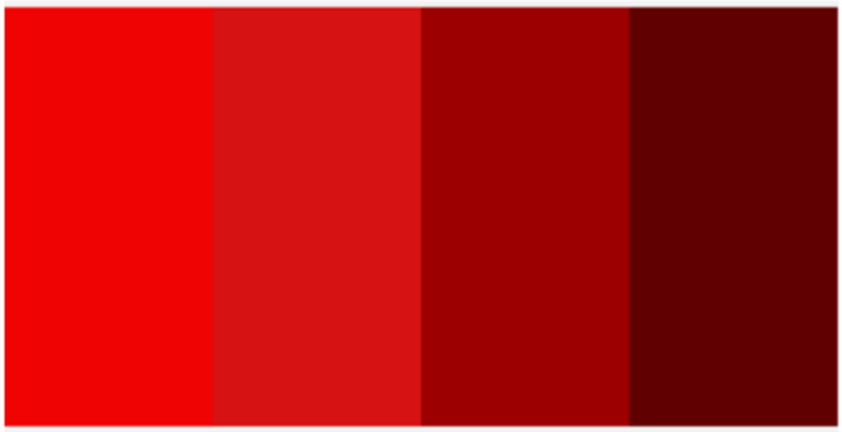
* Adjusted for demographic, clinical and diagnosis variables in logistic regression

Table 5. Consistency of the colour of PRB reported verbally and by colour plate

Verbal \ Colour plate number	1 (N=166)	2 (N=68)	3 (N=22)	4 (N=15)
Light Red (N=9)	6	3	0	0
Fresh Red (N=241)	157	65	13	6
Dark Red (N=18)	3	0	9	6
Old Red (N=3)	0	0	0	3

Figure 1.

Per-rectal bleeding colour card and predicted probabilities of colonic lesion with respect to colour



	1	2	3	4
Tumour or Polyps	0.294	0.304	0.524	0.866
Tumour or Advanced Neoplastic Polyps	0.035	0.074	0.257	0.609
Tumour	0.025	0.036	0.169	0.345

Note: RBG coding of colour 1 / 2 / 3 / 4 = 24033 / 2141818 / 15600 / 9700.

Figure 2.

Receiver operating characteristics curve of PRB colour at various cutoff level for detecting diagnosis of tumour or polyps

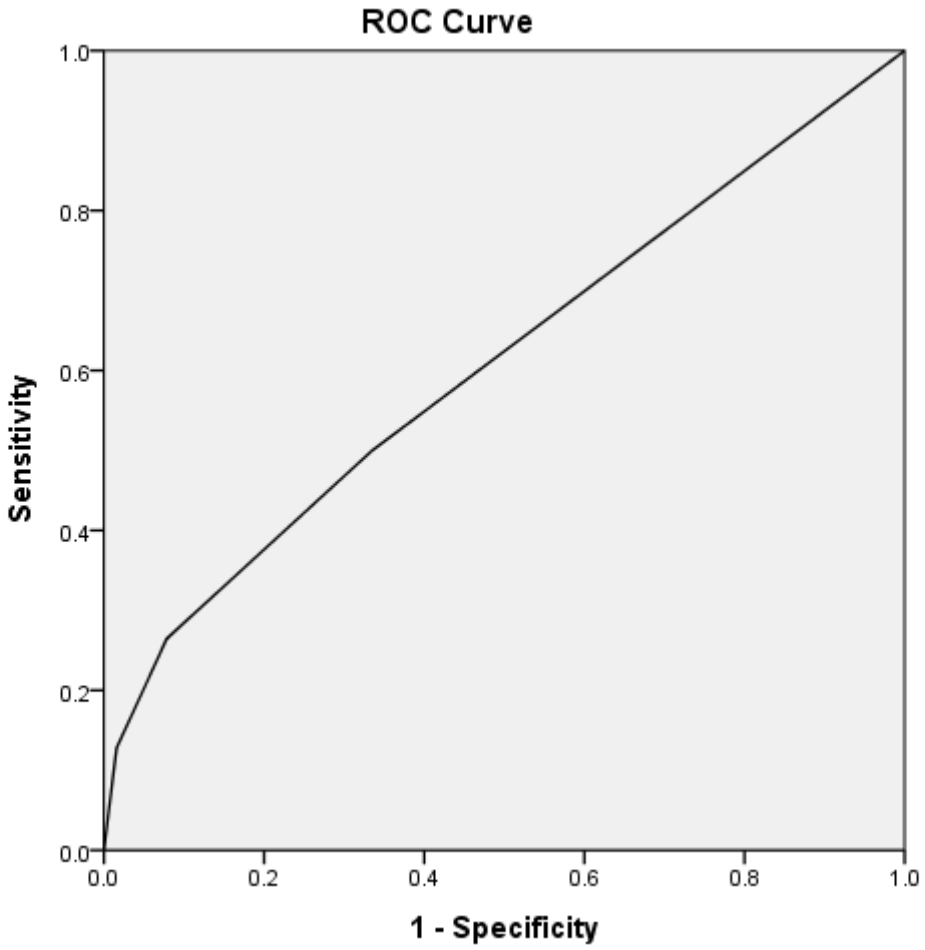


Figure 3.

Receiver operating characteristics curve of PRB colour at various cutoff level for detecting diagnosis of tumour or advanced neoplastic polyps

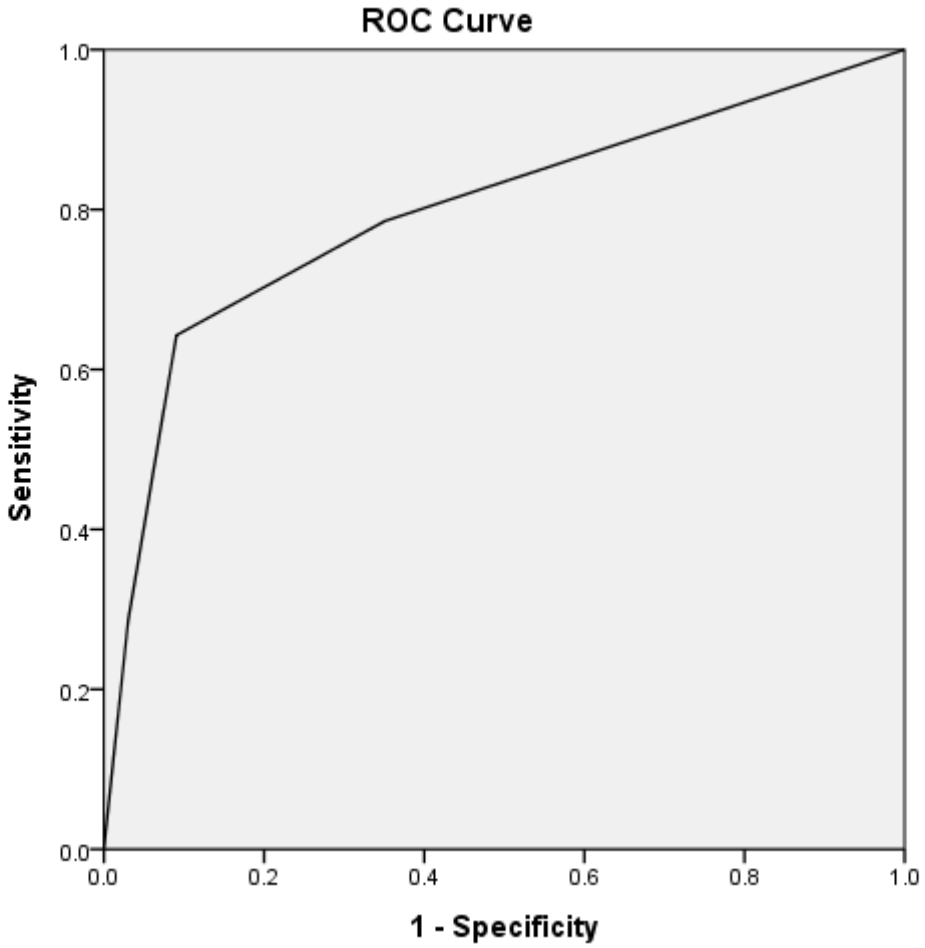


Figure 4.

Receiver operating characteristics curve of PRB colour at various cutoff level for detecting diagnosis of tumour

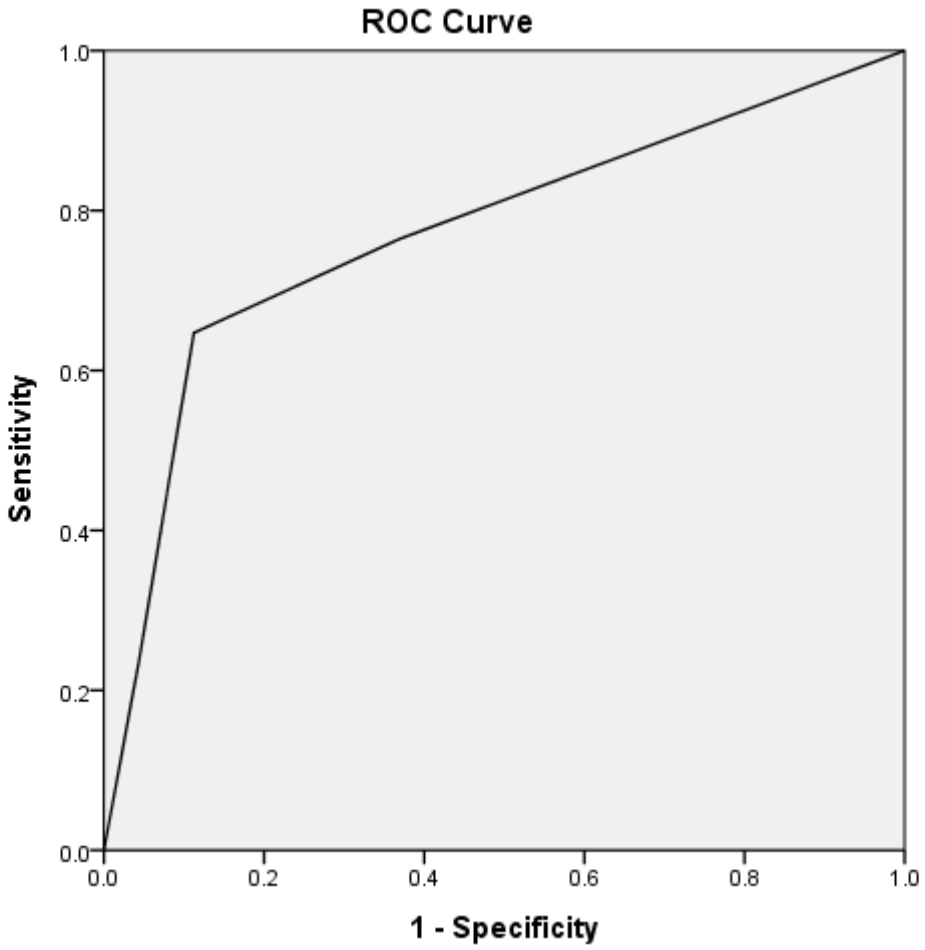


Figure 5.
Treatment Algorithm