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Anaemia investigation in practice: inappropriate, cost inefficient with a risk of missing gastrointestinal cancer. Can we improve?

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ABSTRACT – Iron-deficiency anaemia (IDA) is often inappropriately investigated. This study aimed to improve referrals, estimate cost implications and determine effectiveness of referral criteria for diagnosing cancer. Patients referred for investigation of anaemia were studied. IDA was defined as haemoglobin <12.5 g/dl (M) and <11.5 g/dl (F), with ferritin <15 ng/l (if normal erythrocyte sedimentation rate) or mean corpuscular volume <76 fl. After referral form redesign/trust education, data were recollected. Sixty-six of 118 referred patients had non-IDA with annual cost of inappropriate referrals £176,840. The haematology database identified 37 patients (30 F) with uninvestigated IDA (lost revenue £120,254). After changes, 43/103 referred patients had non-IDA ($p<0.05$), with an annual saving of £72,600. Fourteen of 112 patients with IDA had cancer versus 4/109 non-IDA ($p<0.025$), overall prevalence 8.1%. Many referrals for anaemia investigation are inappropriate and a 35% reduction was achieved. The sensitivity and negative predictive value of the referral criteria for diagnosing gastrointestinal cancer were 77.8% and 96.3% respectively.

KEY WORDS: anaemia, cost effectiveness, investigation, iron-deficiency, validation

Introduction

Iron-deficiency anaemia (IDA) accounts for approximately 4–13% of referrals to gastroenterology, with a prevalence of 2–5% in men and post-menopausal women.[1,2] In this population, gastrointestinal (GI) blood loss is the most common cause (www.bsg.org.uk), with colorectal cancer being the most common final diagnosis (5–10% of cases).[3,4] British Society of Gastroenterology (BSG) guidelines recommend that a minimum of 90% of patients with asymptomatic IDA (other than menstruating women) should be screened for coeliac disease (by serology) and should undergo an upper GI endoscopy. Lower GI investigations should be performed if coeliac disease or upper GI cancer is not found. The investigation of IDA therefore places a considerable burden on diagnostic services. In the current climate it is increasingly important for the NHS to maintain an efficient elective diagnostic service.[5] This study was conducted to highlight the rate of inappropriate referrals for endoscopic investigation of anaemia and to determine whether the referral pattern could be improved, using pre-determined cut-off criteria, while minimising the potential for missed GI cancer.[4]

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Methods

All adult patients with a referring indication of 'anaemia', with or without accompanying symptoms, were identified retrospectively from the endoscopy database (GeneCis®, Real Software, Inc) for a three-month period (February to April 2006). Details of final diagnosis and other investigations, including endoscopic, radiological, histological and haematological tests, were obtained from relevant hospital databases or case notes. Requests for endoscopy were generated by hospital doctors, at all levels of seniority, from either ward admissions or outpatient visits. Requests were placed on the standard hospital form for endoscopy with 'free-form' entry of clinical details at the discretion of the referring doctor. All referrals were included whether inpatient, outpatient or referrals from general practitioners.

Patients were termed IDA or non-IDA according to whether they met the following BSG criteria: haemoglobin (Hb) <12.5 g/dl for males and <11.5 g/dl for females, in addition to either mean corpuscular volume (MCV) <76 fl or ferritin <15 ng/l. The presence of both microcytosis and hypoferritinaemia was not insisted upon. Patients with a raised erythrocyte sedimentation rate (ESR) were termed IDA if ferritin <50 ng/l. Only those patients with IDA were classed as appropriate referrals for endoscopic investigation of anaemia.

In this period, adult patients (over 50 years to exclude menstruating women) with undoubted iron deficiency (low Hb and both low MCV and low ferritin) were identified separately from the haematology results database. Case notes were analysed to determine whether these patients were appropriately investigated (having at least coeliac screen and upper GI endoscopy, followed by lower GI investigation if no upper GI pathology found – in line with BSG guidelines). After the initial, retrospective data collection, the hospital endoscopy request form was redesigned to include an instruction for the mandatory entry of MCV and ferritin if referring for investigation of 'anaemia'. The new form was publicised by trust-wide email to medical and clerical staff, presentation at grand round and junior doctor teaching (single session). Referrals for the next three months (May to June 2007) were analysed as before and results compared.

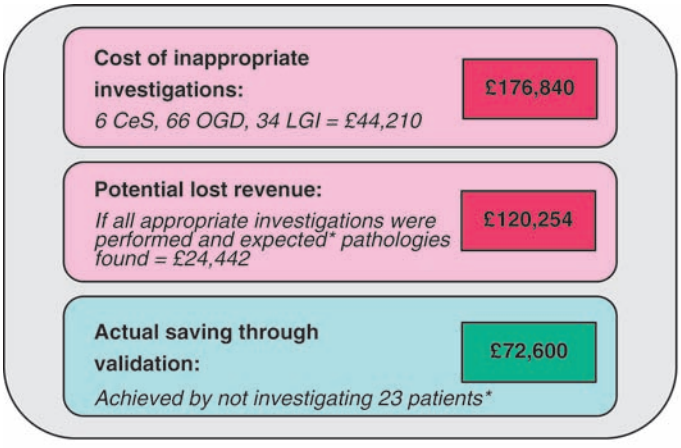
A cost analysis was also conducted using local trust Payment by Results (PbR) tariff data (Fig 1) – subject to an inflationary multiple of 2.5% for the year 2007/8 and a 'market forces multiple' of 1.23 to arrive at final costs – which were then extrapolated to a one-year period. The IDA and non-IDA groups were compared for the prevalence of GI malignancy. Statistical comparisons were performed using the Chi-squared test, with significance assumed at a p-value (two-tailed) of <0.05.

Results

A total of 221 patients (149 female; mean age 68.5 (16.9 years)) were analysed. In the retrospective analysis, 118 patients (52 female) were referred for endoscopic investigation of anaemia. Sixty-six of these were non-IDA and therefore considered inappropriate. All in this group had an upper GI endoscopy (oesophagogastro-duodanoscopy OGD). In addition, six coeliac serology screens (CeS), six barium enemas (BaE), six computed tomography with rectal contrast (CTrc), 14 colonoscopic (CS) and eight flexible sigmoidoscopic (FS) examinations were performed. In the cohort of patients, all had had a full blood count prior to procedure although it was not stipulated as an inclusion criteria.

An additional 37 patients were identified from the haematology database as having undoubted IDA (all three criteria fulfilled). After analysis of case records to ensure they were appropriate to be investigated for IDA, 13 were found to have had an OGD, none had coeliac serology and 10 had a lower GI investigation (five CS, three FS, two BaE and one CTrc). Twenty-five (68%) had no GI investigation. In the prospective data collection period, 103 patients (67 female) were referred. Of these 43 had non-IDA ($p<0.05$ for comparison of proportions).

Overall, 112 patients with IDA and 109 with non-IDA were identified in this study. There were 14 cancers found in the IDA group (12.5% of patients in this group) compared to four (3.7%) in the non-IDA group ($p=0.025$), an overall prevalence of 8.1%. In the IDA group, two oesophageal, seven gastric, one jejunal, two caecal and two rectal cancers were diagnosed. All the diagnoses made in the IDA group are detailed in Tables 1 and 2. In the non-IDA group, one oesophageal, one gastric, one caecal and one colonic cancer were found (Table 1). Of these, two patients did not have serum ferritin measured prior to investigation, and one patient presented with 'alarm' symptoms for gastrointestinal malignancy (namely weight loss and anorexia).[4,6] All four non-IDA cancers are included in the subsequent analysis. The BSG criteria therefore returned a sensitivity and negative predictive value (NPV) for GI malignancy of 77.8% and 96.3% respectively.



Calculations based on local trust Payment by Results tariff as explained in text. Costs in bold are annual figures extrapolated from actual quarterly costs.
* Expected frequencies of pathology and need for further investigation as predicted by British Society of Gastroenterology guidelines.

CeS = coeliac screen; LGI = lower gastrointestinal investigation (ie colonoscopy, flexible sigmoidoscopy or contrast enema); OGD = oesophagogastroduodenoscopy.

Fig 1. Summary of estimated annual costs.

Discussion

These results demonstrate that many patients with anaemia are referred unnecessarily for investigation, but that it is possible to alter referral patterns by simple measures. Referral criteria for endoscopy will be included into junior doctor teaching for each 'intake' in an attempt to maintain or improve these results. In the prospective arm of this study, a deliberate decision was taken not to 'vet' or refuse inappropriate referrals. This was to determine whether a minimum-input strategy could impact significantly on referral patterns as requests for investigations for iron deficiency could arise from a variety of sources. Vetting of referrals by a gastroenterologist in practice was also deemed to be ineffective as there is often insufficient clinical information to exclude patients. To arrange for appropriate iron indices prior to investigation, for example by pre-assessment clinics, could delay both upper and lower GI cancer diagnostic pathways.

Aside from the clinical risk of inappropriate investigations, the cost implications highlighted by this study are significant (summarised in Fig 1). The cost for investigating inappropriate referrals was £44,210 – extrapolated to an annual cost of £176,840 in 2006/7 (this figure would be subject to a multiple of 2.5% for 2007/8). This figure does not include the costs of: biopsy equipment; preparation analysis and reporting of histological specimens; outpatient appointments (new £193 and follow-up £95), so the true cost is likely to be much higher than the calculated figure. This rate of inappropriate referrals is by no means unique and represents a significant burden on endoscopic service provision (66 OGD, 14 CS and eight FS in three months).[6]

In addition, the 37 patients with IDA from the haematology databases might have generated additional

Table 1. Summary of all patients with a final diagnosis of gastrointestinal malignancy.

				Blood results at referral				
	Age	Gender	Symptoms	Hb	MCV	Ferritin	Coeliac screen	Final diagnosis
IDA								
1	68	F	–	7.7	61	2	NO	Ca-rectal
2	32	M	–	6.2	74	3	NO	Ca-jejunal
3	91	M	–	9.5	71	4	NO	Ca-gastric
4	86	M	–	4.7	52	6	NO	Ca-oesophageal*
5	80	M	Melaena	9.7	82	8	NO	Ca-gastric
6	45	F	Dyspepsia	9.8	70	9	YES -ve	Ca-gastric
7	79	F	Weight loss, diarrhoea	7.9	80	10	NO	Ca-gastric
8	86	M	Dyspepsia	7.6	83	13	NO	Ca-gastric
9	72	M	Weight loss	8.5	62	14	NO	Ca-gastric*
10	61	F	–	9.6	71	20	NO	Ca-rectal
11	84	M	–	9.3	65	–	NO	Ca-caecal*
12	80	F	–	8.1	74	32	NO	Ca-gastric
13	72	M	–	7.6	77	33	NO	Ca-caecal
14	94	F	–	7.9	76	61	NO	Ca-oesophageal
Non-IDA								
1	78	M	Anorexia, weight loss	8.9	80.1	17	NO	Ca-gastric*
2	97	M	–	8.9	87.4	76	YES -ve	Ca-oesophageal*
3	84	M	–	12	93.7	–	NO	Ca-colonic
4	65	F	–	8.7	77.2	–	NO	Ca-colonic

Age (years), gender (M = male, F = female). Hb (haemoglobin g/dl); IDA = iron-deficiency anaemia; MCV (mean corpuscular volume fl); ferritin (ng/l).

* Only upper or lower GI investigation performed (related to final diagnosis).

revenue if investigated appropriately. Assuming a 10% incidence for both coeliac disease and upper GI cancer,[1] this group should have undergone 24 more OGDs, 37 CSs and at least 29 LGIs. Using CS as the lower GI investigation of choice, this would amount to potential lost revenue (under PbR) of £24,442 – extrapolated to an annual figure of £120,254 in 2006/7 (when subjected to market forces multiple).

Around a 35% reduction in the rate of inappropriate referrals was achieved by simple measures, concentrating on secondary care referrals alone (since anaemia referrals from primary care may also be sent via a two-week wait system, it was not felt appropriate to include these). The cost saving from not investigating 23 additional patients, assuming all would have had upper GI endoscopy and CeS, with 20 CS, was calculated at £18,150 – extrapolated to an annual figure of £72,600.

The sensitivity and NPV of the criteria for GI malignancy are high, but might be improved by increasing the cut-off level of ferritin, although with significant increase in the number of GI investigations performed. In line with these results, other studies have highlighted the relatively high rate of serious pathology in patients with what would be considered a normal ferritin level by the current criteria.[8,9] In addition, laboratory reference ranges for Hb were used to determine anaemia, which might explain the relatively high sensitivity and specificity of this approach compared to other studies (although these were for lower GI malignancy alone).[10,11]

Using these data, increasing the cut-off to ferritin <50 ng/l for all patients, regardless of ESR, would increase sensitivity and NPV to 94.4% and 99.1% respectively – while insistence on both ferritin and MCV being low (at original cut-off levels) would result in a fall to 55.6% and 93.3% respectively. No patients with hypoferritinaemia and normal Hb were referred in either of the three-month periods analysed. However, this phenomenon is three times more common than IDA,[12] and associated with a frequency of GI malignancy in 0.9% of men and post-menopausal women, but 0% in pre-menopausal women. The BSG guidelines recommend routine investigation of hypoferritinaemia in men and post-menopausal women only.[3]

In summary, the results confirm the heavy burden of investigating IDA on secondary care and demonstrate that the appropriate use of cut-off criteria to guide (but not limit) investigations, with simple measures to improve adherence to them, can be both time and cost effective.

Table 2. Summary of all patients without a final diagnosis of gastrointestinal malignancy.

Diagnoses	Number of patients
Iron-deficiency anaemia	
Angiodysplasia	3
Peptic ulcer	4
Crohn's disease/ulcerative colitis	3
Diverticular disease	4
Haemorrhoids	1
Gastritis/oesophagitis	3
Upper gastrointestinal varices	0
No abnormality found	80
Non iron-deficiency anaemia	
Angiodysplasia	3
Peptic ulcer	13
Crohn's Disease/ulcerative colitis	1
Diverticular disease	6
Haemorrhoids	1
Gastritis/oesophagitis	14
Upper gastrointestinal varices	1
No abnormality found	66

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