ORIGINAL ARTICLE

Does endoscopy diagnose early gastrointestinal cancer in patients with uncomplicated dyspepsia?

N Sundar, V Muraleedharan, J Pandit, J T Green, R Crimmins, G L Swift

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See end of article for
authors' affiliations

Correspondence to:
Dr N Sundar, Llandough
Hospital, Department of
Gastroenterology, Penlan
Road, Penarth, Cardiff
CF64 2XX, UK; neelasvu@
yahoo.com

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Background: Recent guidelines from NICE have proposed that open access gastroscopy is largely limited to patients with "alarm" symptoms.

Aims and methods: This study reviewed the outcome of all our patients with verified oesophageal or gastric carcinoma who presented with uncomplicated dyspepsia to see if endoscopic investigation is warranted in this group. All patients with histologically verified upper gastrointestinal (GI) cancers who presented over a period from 1998 to 2002 were identified. Their presenting symptoms, treatment, and outcome were analysed.

Results: 228 upper GI cancers (119 oesophageal, 109 gastric; mean age 72 years (29–99 years); 130 male, 82 female) were identified in 11 145 endoscopies performed. Only 14 patients (6.2%) presented without alarm symptoms; three patients were under 55 years of age and all had gastric carcinoma—one of these had chronic diarrhoea only. Eleven had dyspepsia or reflux symptoms only, and two were under surveillance for Barrett's oesophagus. Only five patients had a curative surgical resection and are still alive two–six years from diagnosis. A sixth patient had a curative operation but died of a cerebrovascular accident one year later. The remaining eight patients unfortunately had either metastatic disease or comorbidity, which precluded surgery. All of these died within two years of diagnosis, mean survival 10 months.

Conclusion: Only five patients with dyspepsia and no alarm symptoms had resectable upper GI malignancies over a four year period. Limiting open access gastroscopy to those with alarm features only would "miss" a small number of patients who have curable upper GI malignancy.

In England and Wales, oesophageal and gastric cancer constitute 7% of all cancers diagnosed and 9% of deaths from cancer per year.¹ Up to 96% of patients with upper gastrointestinal (GI) cancer present with alarm symptoms and signs such as dysphagia, unexplained weight loss, persistent vomiting, GI bleeding, iron deficiency anaemia, and epigastric mass when they seek medical attention.² The rest present with uncomplicated dyspepsia, which is defined as dyspepsia without alarm symptoms/signs. This justifies the overall consensus that the presence of alarm symptoms needs immediate endoscopic investigation.^{3–4} However, it is still debatable whether dyspepsia alone should lead to prompt endoscopic investigation or be treated on the basis of symptoms alone.^{5–6} One reason patients with dyspepsia are referred for endoscopy is concern about cancer. However, upper GI cancer is rare in this group of patients and is reported in less than 2% of patients in endoscopic studies.⁷ In the United Kingdom, the number of dyspepsia patients without alarm symptoms constitute an important part of the endoscopic workload as rapid access endoscopy has become more widely available.⁸

Over the years specialist societies such as the American Society for Gastrointestinal Endoscopy (ASGE) and the British Society of Gastroenterology (BSG) together with review groups like the ROME working party and RAND corporation have all recommended that patients with new onset dyspepsia who are above 45 years of age be referred for endoscopic investigation.^{9–12} The age of 45 years was used as a cut off because the probability of finding structural disease including cancer rises with increasing age¹³; it has recently been suggested that this age can safely be increased from 45 to 55 years.³ Studies looking at cost effective analysis of various management strategies of uncomplicated dyspepsia have consistently shown that empirical medical treatment

reduces the need for endoscopy and provides significant cost savings.^{14–16}

In 2004, NICE recommended that the guidelines for open access gastroscopy are changed so that routine endoscopic investigation for dyspepsia is not necessary for patients who present without alarm symptoms at any age.¹⁴ The exception being patients over 55 whose symptoms persist despite *Helicobacter pylori* testing and acid suppression treatment and if patients have one or more of the following: previous gastric ulcer or surgery; continuing need for NSAID treatment or raised risk of gastric cancer, or anxiety about cancer. The rest should receive empirical drug therapy. This change has caused concern that we may miss early cancers, however studies have suggested that this strategy on the whole is safe.^{17–18}

AIMS

The objective of our study was to review the outcome of all patients with verified oesophageal or gastric carcinomas over a four year period who presented with uncomplicated dyspepsia to see if endoscopic investigation aids in diagnosing cancer at an early stage.

METHODS

Llandough Hospital serves West Cardiff and the Vale of Glamorgan—a population of about 250 000. Since 1997, our endoscopy unit has offered open access gastroscopy to patients presenting with new onset of dyspepsia if they are 45 years or older and to patients with alarm symptoms regardless of age. If cancer was found at endoscopy, the patients were staged by abdominal/chest computed tomography (CT) and abdomen and endoscopic ultrasound (for

Abbreviations: GI, gastrointestinal; CT, computed tomography

Table 1 Age distribution of upper GI cancers

	Total number of patients	<45 years	46–55 years	>56 years
Total number of patients with upper GI cancer	228	2 (0.9%)	23 (10%)	203 (89%)
Patients with alarm symptoms	214 (93.8%)	2 (0.9%)	20 (8.7%)	192 (84%)
Patients with uncomplicated dyspepsia	11 (4.8%)	0	2 (0.9%)	9 (3.9%)
Patients endoscoped for other reasons	3 (1.31%)	0	1 (0.43%)	2

oesophageal cancers); they were all discussed at our multi-disciplinary meetings. All patients with histologically verified oesophageal and gastric cancer who presented over a four year period from 1998 to 2002 were identified from our hospital pathology database, which process all of our endoscopic biopsies. The endoscopy reports were obtained and presenting symptoms, treatment, and outcome at least two years after diagnosis were analysed from patients' medical records.

RESULTS

During the study period of four years, a total of 11 145 gastroscopies were performed. Altogether 228 patients had upper gastrointestinal (119 oesophageal and 109 gastric) cancer diagnosed. Table 1 gives the age distribution of the cancers.

The average age of patients with verified upper GI cancer was 72 years (range 29–99 years). Twenty five patients were under the age of 55 years and two of these were less than 45 years. There was a male preponderance (130 male: 82 female).

Most patients presented with alarm symptoms (93.8%) including both patients under 45 years, 20 of 23 who were aged 46–55 years. The remaining 14 patients (6.14%) had no alarm symptoms (fig 1). Table 2 lists the clinical characteristics of these patients.

Of these, 11 patients presented with uncomplicated dyspepsia, two had surveillance procedures for Barrett's oesophagus, and one patient had an endoscopy to obtain small bowel biopsy specimens. Only five patients (patient numbers 3, 4, 5, 6, and 7, table 2) who presented without alarm symptoms underwent curative surgical resection and are alive to date, three to six years later.

Three patients who presented without alarm symptoms were under 55 years of age—patients 1 and 2 (table 2), presented with abdominal pain and dyspepsia had oesophageal

and gastric malignancy respectively—unfortunately both had metastatic disease. Patient 3 presented with diarrhoea only and had an endoscopy to obtain small bowel biopsy specimens to rule out coeliac disease—these were normal. However, he was found to have a malignant gastric ulcer as an incidental finding and he underwent gastrectomy; he is still alive five years later. Patients 8, 9 had no distal metastases on CT. Patient 8 had surgery but died of a cerebrovascular accident one year later and patient 9 had severe chronic obstructive airway disease, which precluded surgery. Patients 10–13 all had liver metastases on imaging at diagnosis, had palliative care, and died between one and six months from diagnosis.

One patient (number 14) had initial chemo-radiotherapy as there was no evidence of distant metastases on initial CT scan, but had local nodal disease on endoscopic ultrasound. Unfortunately he developed liver metastases on the post-treatment CT scan and so subsequently received palliative care only.

DISCUSSION

During a four year period, 214 (93.8%) patients diagnosed with upper GI cancer presented with alarm symptoms that were absent in the other 14 (6.1%) patients. Twenty five (10.9%) were 55 years or younger. Two (0.9%) patients were aged less than 45 years and both presented with alarm symptoms. This is comparable to other studies that have reported that upper GI cancer is rare in patients under 45 years and that they usually present with alarm symptoms.^{19 20} Only 2 of 25 (8%) patients with cancer under the age of 55 presented with uncomplicated dyspepsia. This discounts patient number 3 (table 2) who had diarrhoea only. This is similar to American and European studies where the figures range between 2.9% and 7.7%.^{2 17 18} Similarly in patients who are older than 55 years, 9 of 203 (4.4%) presented with uncomplicated dyspepsia, which is again similar to a previous study.²

An important aspect of any empirical treatment for dyspepsia is to minimise the risk of missing a GI malignancy particularly if it is at a treatable stage. Of the 14 patients with upper GI cancer without alarm symptoms, seven had no distant metastases on imaging. One of these seven had significant comorbidity precluding surgery and another had a complete surgical resection but died one year postoperatively of a cerebrovascular accident. Only 5 of the 14 are alive to date—one of these did not have any dyspeptic symptoms (patient 3, table 2) and was being investigated for possible coeliac disease.

This was a retrospective study carried out in a secondary care setting. We recognise the limitations in that we did not have access to the primary care records that may have recorded pre-existing symptoms, duration of symptoms, *Helicobacter pylori* status, and proton pump inhibitor use before referral. National guidelines (before BSG 2002 and NICE 2004) recommended test and treat strategies in patients under 45 years of age and referral if over 45 years. As our 14

Figure 1 Presenting symptoms of patients with verified upper GI

Table 2 Clinical features of patients with upper gastrointestinal cancer who presented without alarm symptoms

Patient number	Age (y)	Sex	Symptom	Site	Histology	Stage	Treatment	Outcome from diagnosis
1	54	M	Abdominal pain	Oesoph	Squamous cell	T3N1- metastases	Palliative chemoradiotherapy	Died 24 months
2	54	F	Dyspepsia	Gastric	Adenocarcinoma	Peritoneal metastases at laparotomy	Gastrectomy and palliative	Died 14 months
3	52	M	Diarrhoea	Gastric	Adenocarcinoma	T2N0	Gastrectomy	Alive 5 years
4	64	M	Reflux	Gastric	Adenocarcinoma	No metastases	Gastrectomy	Alive 3 years
5	66	M	Dyspepsia	Gastric	Adenocarcinoma	T3N1	Gastrectomy	Alive 6 years
6	60	M	Barretts surveillance	Oesoph	Adenocarcinoma	No metastases	Oesophagectomy	Alive 6 years
7	71	M	Dyspepsia	Gastric	Adenocarcinoma	T2N1	Gastrectomy	Alive 4 years
8	69	F	Dyspepsia	Gastric	Adenocarcinoma	T3N1	Gastrectomy	Died 12 months
9	63	M	Dyspepsia	Oesoph	Squamous cell	T3N1	Palliative chemoradiotherapy	Died 9 months
10	75	M	Dyspepsia	Gastric	Adenocarcinoma	Liver metastases	Palliative	Died 6 months
11	88	M	Abdominal pain	Gastric	Adenocarcinoma	Liver metastases	Palliative	Died 1 month
12	72	M	Dyspepsia	Gastric	Adenocarcinoma	Liver metastases	Palliative	Died 6 months
13	81	F	Dyspepsia	Gastric	Adenocarcinoma	Liver metastases	Palliative	Died 3 months
14	64	M	Barretts surveillance	Oesoph	Adenocarcinoma	Liver metastases	Initial chemo-radiotherapy and palliative	Died 12 months

M, male; F, female; Oesoph, oesophagus; T, tumour; N, nodal metastases.

patients were aged over 45 years at the time of referral we do not know whether the previous guidelines had been adhered to in primary care.

Our findings that most patients with upper GI cancer present with alarm symptoms, support the new NICE guidelines that recommend prompt endoscopy for patients presenting with alarm symptoms regardless of age. Also we found that only a very small proportion of patients with uncomplicated dyspepsia had upper GI cancer diagnosed at a curative stage over this four year period. A recent validation study showed that uncomplicated dyspepsia in patients over 55 years was a negative predictive factor for upper GI cancer.²¹ However, limiting open access endoscopy to those with alarm symptoms would have potentially "missed" 14 patients, seven of whom had no evidence of metastases on imaging.

CONCLUSION

We believe that our findings contribute to the current debate that patients with dyspepsia should undergo open access gastroscopy. *Helicobacter pylori* eradication therapy and acid suppressant treatment before endoscopy in patients with uncomplicated dyspepsia should reduce endoscopy workload and help to concentrate resources on those with alarm symptoms. However, our study suggests that a small number of patients with potentially curable disease would not be endoscoped if only those with alarm symptoms are considered for open access gastroscopy.

Authors' affiliations

N Sundar, V Muraleedharan, J Pandit, J T Green, R Crimmins, G L Swift, Llandough Hospital, Department of Gastroenterology, Cardiff, UK

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