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Chest trauma and aetiology of achalasia

Achalasia is a motility disorder caused by neural dysfunction which may involve both the myenteric plexus of the oesophagus, the vagal nerves, and the dorsal motor nucleus.^{1,2} The aetiology of the disorder is still obscure, viral infection and autoimmunity having been suggested. Recently, Park and Vaezi¹ proposed that different environmental factors in patients with genetic predisposition could lead to the same clinical picture and manometric findings.

As part of an ongoing prospective study in patients with achalasia,¹ we have investigated if chest trauma could be involved in the development of achalasia. Twenty consecutive achalasia patients (eight men), aged 18–79 years (median age 53) at the time of diagnosis, and 20 consecutive patients matched for sex and age (eight men; 17–83 years (median 49)), evaluated at our outpatient clinic, were included. Control patients presented with symptoms other than dysphagia and, at the end of evaluations, diagnosis of irritable bowel syndrome (n = 8), gastro-oesophageal reflux disease (n = 6), peptic ulcer disease (n = 4), chronic constipation (n = 1), and anal incontinence (n = 1) were made. Achalasia patients underwent clinical evaluation, upper endoscopy, x ray barium study, and oesophageal manometry to confirm diagnosis. All patients included in the study underwent a standard questionnaire regarding occurrence of chest trauma. Arbitrarily, only traumas serious enough to require hospitalisation or to determine loss of work of ≥ 7 days were considered. Type of trauma and type of accident causing trauma were also recorded. Traumas were divided according to their occurrence before or after the onset of dysphagia.

Chest trauma was reported by 5/20 (25%) achalasia patients and no control patients ($p < 0.05$ by Fisher's exact test). All traumas occurred before the onset of dysphagia (median 2 years (range 1–13) before), being caused by a road accident in three patients and work accident in two. All traumas were non-penetrating. Hospitalisation was required in three patients. Achalasia patients with and without chest trauma had a similar age at onset of dysphagia (mean 45 (SEM 9) and 43 (5) years, respectively), clinical score (8.8 (0.5) and 7.6 (0.5)) according to Eckardt and colleagues,⁴ oesophageal diameter at x ray barium swallow (4.9 (0.3) and 4.4 (0.5) cm), amplitude of oesophageal pressure waves (41 (18) and 31 (7) mm Hg), and lower oesophageal sphincter pressure (26 (5) and 27 (4) mm Hg) at diagnosis. Independently of previous occurrence of chest trauma, all patients achieved stable clinical remission (that is, clinical score of ≤ 3 for ≥ 1 year after dilatation)³ and a low lower oesophageal sphincter pressure (< 10 mm Hg)⁴ after one (n = 11) or two (n = 9) pneumatic dilatations. Recent retrospective data support our findings⁵: a history of operative or non-operative chest trauma prior to the development of dysphagia was present in 16/64 (25%) achalasia patients compared with 7/73 (9.5%; $p < 0.05$) control patients presenting with dysphagia and normal oesophageal manometry.

In conclusion, chest trauma may be one of the aetiological factors of achalasia. This could occur through ischaemia or compression of neural structures leading to their irreversible damage in susceptible individuals.

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doi: 10.1136/gut.2006.094359

Conflict of interest: None declared.

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British Society of Gastroenterology guidelines for ulcerative colitis surveillance: creating consensus or confusion?

Absence of grade A evidence combined with discrepancies between retrospective studies in reported survival benefit has led to controversy surrounding the colonoscopic surveillance of ulcerative colitis (UC) patients. Such controversy was demonstrated in 2000 by an audit which revealed widespread variations in surveillance practice.¹ Following the introduction of British Society of Gastroenterology (BSG) guidelines in 2002,² concern was expressed regarding the medicolegal implications posed by national recommendations based on inconclusive evidence and lacking multicentre consensus.³ Three years after the publication of the guidelines, a questionnaire survey has indicated that widespread disparities in opinion and practice still exist.

Questionnaires were distributed to all consultants and specialist registrars in gastroenterology within the Wales deanery. A 45.1% (23/51) response rate was achieved. Although a significant majority (73.9% (95% confidence interval (CI) 56.0–91.8%)) agreed that colonoscopic surveillance of UC patients was a worthwhile exercise, opinions of what constituted “best practice” varied considerably. Only a marginal majority of respondents (52.2% (95% CI 31.8–72.6%)) agreed with BSG recommendations that the initial screening colonoscopy for pancolitis patients should take place 8–10 years after symptom onset, and a substantial proportion (26.1% (95% CI 8.2–44.0%)) felt (contrary to BSG guidelines) that surveillance in left sided colitis was unnecessary, with five respondents

commenting that they knowingly contravened these recommendations in practice. Responses to seven short clinical scenarios elicited opinions regarding the most appropriate intervals between colonoscopic surveillances (table 1).

Despite a consensus with BSG recommendations in cases of lone proctitis, pancolitis, and pancolitis with concomitant primary sclerosing cholangitis (PSC), considerable divergence from the guidelines was eluded to in the response to the remaining cases. As well as repeating concerns over surveillance of left sided disease, respondents repeatedly commented on the difficulties of using age as an inclusion criteria and of the uncertainty surrounding the optimum management of a patient with proctitis and PSC (an admittedly rare scenario). One hundred per cent of respondents reported familiarity with BSG guidelines. Within this context, the disparities of opinion demonstrated indicate that practitioners commonly either misinterpret or knowingly contravene current guidelines.

The controversial nature of the current evidence is further highlighted by differences in the surveillance protocols recommended by major societies. Whereas a consensus exists as to the carrying out of colonoscopy 8–10 years after symptom onset in all UC patients, differences regarding the frequency of surveillance thereafter remain. While the BSG,² American Gastroenterological Association (AGA) (who only recommend that surveillance per se should “be considered”),⁴ and American Society for Gastrointestinal Endoscopy (ASGE)⁵ advise initiation of regular surveillance of left sided colitis 15 years after symptom onset, as opposed to eight (AGA and ASGE) or 8–10 years (BSG) for pancolitis, the American College of Gastroenterology (ACG)⁶ do not consider the evidence “sufficiently strong” to justify discrimination between patient groups, and recommend regular surveillance for all colitis patients after 8–10 years. There is also disagreement surrounding the optimum interval between subsequent surveillances, with the BSG advocating reductions in interval with disease progression (initially three yearly), the ASGE and AGA recommending 1–2 yearly intervals, and the AGA recommending annual or biannual surveillance.^{2,4–6}

If the lack of consensus in opinion and practice demonstrated in the current work is representative of broader opinion, it would indicate that introduction of BSG guidelines have only partially reduced the aforementioned variations in practice.¹ Considering the inconclusivity of the evidence and apparent disparities in professional opinion, and in light of the potential medicolegal implications of deviating from the protocol of a national body, it would seem prudent to review current guidelines with a view to producing more flexible recommendations which would representatively encompass the discrepancies within the evidence and range of professional opinion.

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doi: 10.1136/gut.2006.092643

Conflict of interest: None declared.

Table 1 Summary of responses to the question "What is the most appropriate interval between colonoscopic surveillances in the following cases"

Clinical scenario	Most appropriate interval between colonoscopic surveillances					
	Surveillance not currently necessary	Annually	2 yearly	3 yearly	5 yearly	Other (please state)
37 y male. Left sided colitis of 18 y duration with concomitant PSC		73.9 (56.0–91.8)	17.4 (1.9–32.9)	8.7 (–2.8–20.2)		
44 y male. Proctitis rectum of 15 y duration with concomitant PSC	34.8 (15.3–54.2)	47.8 (27.4–68.2)	8.7 (–2.8–20.2)		4.3 (–4–12.6)	4.3 (–4–12.6)
73 y female. Extensive colitis of 45 y duration	4.3 (–4–12.6)	47.8 (27.4–68.2)	30.4 (11.6–49.2)	13.0 (–0.7–26.7)		4.3 (–4–12.6)
30 y male. Mild proctitis rectum of 9 y duration	95.7 (87.4–104.0)				4.3 (–4–12.6)	
45 y female. Crohn's colitis for 15 y	8.7 (–2.8–20.2)		34.8 (15.3–54.2)	52.2 (31.8–72.6)	4.3 (–4–12.6)	
50 y male. Left sided colitis of 22 y duration	39.1 (9.2–59.0)		17.4 (1.9–32.9)	39.1 (9.2–59.0)		4.3 (–4–12.6)
40 y female. Pancolitis of 11 y duration		4.3 (–4–12.6)	26.1 (8.15–44.0)	69.6 (50.8–88.4)		

Values are per cent respondents (95% confidence interval).
 Answers corresponding to BSG guidelines are in bold type.
 PSC, primary sclerosing cholangitis.

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Glucocorticoid receptor polymorphisms in inflammatory bowel disease

We read with interest the article by Mawdsley and Rampton on the relationship between psychological stress, increased disease activity in inflammatory bowel diseases (IBD), and the role of alterations in the hypothalamic-pituitary-adrenal (HPA) axis function (*Gut* 2005;**54**:1481–91). In IBD patients, chronic colonic inflammation induces downregulation of HPA axis responses, and animal studies have shown that altered function of the HPA axis renders rodents susceptible to stress induced increases in gastrointestinal inflammation. Central receptors located in the medial prefrontal cortex and hippocampus play a crucial role in glucocorticoid (GC) mediated counterregulation of stress induced HPA axis activation.¹

Polymorphisms of the GC receptor (GR) gene may contribute to the large interindividual variations in sensitivity to GCs and HPA axis activity that are frequently observed in healthy individuals. Several polymorphisms of the GR gene have been described, and three of these are relatively frequent; however, knowl-

edge of the influence of these polymorphisms on HPA axis response is very limited.

A genetic study was carried out in our laboratory to evaluate the incidence of these polymorphisms in 57 young patients with IBD (34 with Crohn's disease (CD) and 23 with ulcerative colitis (UC); mean age 13.8 years (range 1–45); 41.4% males, 58.6% females). The study was approved by the local ethics committee and written informed consent was obtained from all patients or their relatives or guardians. Studied polymorphisms have included *BclI*, in intron 2, and the N363S polymorphism in exon 2, that have been associated with an increased sensitivity to GCs in vivo,^{2,3} and the ER22/23EK polymorphism, in exon 2, associated with a partial form of GC resistance.⁴ Genomic DNA was extracted from peripheral leucocytes, amplified with specific primers, and subsequently digested with *MnI* (ER22/23EK), *Tsp509I* (N363S), or *BclI* restriction enzymes.^{3,6}

The results of the analysis are presented in table 1. We found a significantly higher frequency of the *BclI* mutated genotype in patients with CD compared with healthy controls ($p=0.03$, Fisher test; odds ratio 3.84 (95% confidence interval 1.23–11.91)). In contrast, no difference was observed between UC patients and controls.

The *BclI* polymorphism has been associated with high systolic pressure, insulin sensitivity, body mass index, and abdominal fat distribution^{2,7}; carriers of the mutated allele have increased GC sensitivity and higher cortisol suppression after low dose dexamethasone.⁸ A higher frequency of the mutated genotype was observed in this study in patients with CD; this mutation could lead to increased sensitivity in peripheral and central GRs, determining a raised susceptibility to feedback inhibition of GCs on the HPA axis. It is of interest that previous studies have demonstrated,⁹ in a subgroup of patients with CD, alterations of the HPA axis resulting in relative hypocortisolism.

In contrast, no difference was observed for the N363S polymorphism, associated with increased sensitivity to GCs,^{3,10} or for the ER22/23EK polymorphism, associated with a partial form of GC resistance (table 1).⁴

This is the first study to examine the possibility that IBD may be associated with

GR polymorphisms; our results support the hypothesis that common polymorphisms in the GR gene may have modulating effects on the relation between psychological factors and HPA axis regulation in patients with CD. However, these data need to be confirmed in a larger group of patients.

Acknowledgements

This research was supported by grants from the Italian Ministry of University and Scientific Research (PRIN projects 2004065777 and 2003053403) and the Italian Ministry of Health. Dr Sara De Iudicibus, Dr Gabriele Stocco, and Dr Ilenia Drigo are recipients of research fellowships from IRCCS Burlo Garofolo, Trieste.

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Conflict of interest: None declared.

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