

Acute gastrointestinal haemorrhage in anticoagulated patients: diagnoses and response to endoscopic treatment

C P Choudari, C Rajgopal, K R Palmer

Abstract

The underlying diagnosis and clinical course of 52 patients who presented with severe acute gastrointestinal haemorrhage while taking the anticoagulant warfarin is reviewed. A bleeding site was identified in 83% of cases, only slightly fewer than the 92% found in a control group of 710 patients not taking warfarin who presented in the same four year period. The degree or duration of anticoagulation was unrelated to the frequency of establishing a diagnosis. The commonest diagnosis was peptic ulcer (25 cases) and endoscopic treatment by injection or heater probe was attempted in 23 of these. The outcome in this subgroup was compared with that in 50 closely matched control subjects who had similar risk factors for rebleeding from peptic ulcer. Permanent haemostasis was achieved in (91%) of the anticoagulated and in 92% of the control patients. There were no complications related to endoscopy. Patients who present with acute gastrointestinal haemorrhage while taking warfarin usually bleed from mucosal disease. They should be endoscoped after resuscitation and those with major bleeding from a peptic ulcer should be offered endoscopic treatment. (*Gut* 1994; 35: 464-466)

Anticoagulated patients who present with acute gastrointestinal haemorrhage pose great therapeutic challenges. Most are being anticoagulated for life-threatening conditions and the clinician is faced with the difficult choice of reversing anticoagulation and risking thrombo-embolic consequences or continuing anticoagulation and risking exsanguination. Bleeding has been recognised as the major treatment-limiting complication of anticoagulant treatment, and the risk of bleeding complications has been the subject of a number of studies.¹⁻⁵ The risk of bleeding is influenced by the intensity of anticoagulation therapy,^{1,2,6,7} the patient's underlying disorder,^{1,5} comorbid conditions,^{1,2,5} and the concomitant use of aspirin.^{8,9} Despite various advances in monitoring these patients,^{10,11} bleeding related to anticoagulation treatment is frequent, and major bleeding occurs in up to 20%.^{1,4,5}

Previous series have shown that most anticoagulated patients who present with gastrointestinal bleeding do so from mucosal disease^{12,13} but none have addressed the response to treatment. Over a four year period we have prospectively collected information on the diagnosis and treatment of a large number of patients who presented with severe gastrointestinal bleeding to a single Scottish health region. This

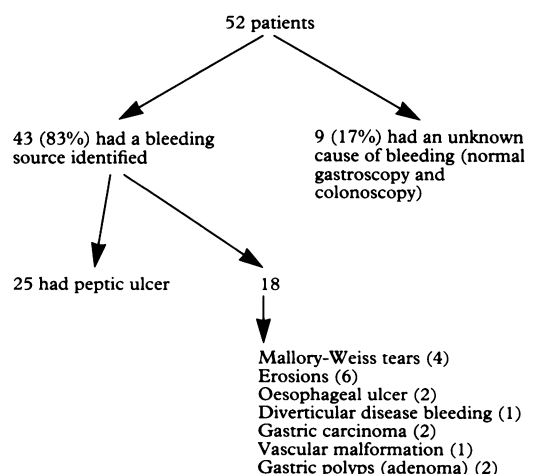
study is concerned with the diagnosis and outcome of the cohort of patients who presented with severe bleeding while taking the anticoagulant warfarin. The particular purposes of the study were to (i) determine the diagnostic yield of endoscopy and (ii) define the response to endoscopic treatment in patients with a bleeding peptic ulcer.

Patients and methods

Between January 1989 and December 1992, urgent endoscopy was performed in 710 patients because of severe acute gastrointestinal haemorrhage. These patients presented to the four major admitting units in the Lothian region of Scotland (Royal Infirmary, Western General, and Eastern General in Edinburgh and St John's Hospital, Livingston). Fifty two of the patients had developed bleeding while taking the anticoagulant warfarin. The international normalised ratio (INR)¹⁴ in these patients ranged from 1.5-6.0, but was corrected to 1.5-2.5 with fresh frozen plasma before endoscopy.

The clinical course of the anticoagulated patients who were found to have sustained a major peptic ulcer haemorrhage was compared with that of 50 patients who presented with gastrointestinal haemorrhage but were not taking warfarin. These control patients were matched in terms of age, sex, the presence of shock on admission, and endoscopic findings. At least two control subjects were selected for each anticoagulated patient from a large data base of patients who presented to us over the same four year period. The control and anticoagulated

Causes of bleeding in 52 anticoagulated patients with severe gastrointestinal haemorrhage



GI Unit, Western General Hospital, Edinburgh
C P Choudari
C Rajgopal
K R Palmer

Correspondence to:
Dr K R Palmer, GI Annexe,
Crewe Road, Edinburgh
EH4 2XU.

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subjects were managed by the same teams in an identical manner.

Patients (anticoagulated and control) found at endoscopy to have either active haemorrhage from a peptic ulcer bed or a protuberant vessel that was not bleeding received endoscopic treatment. This comprised injection with 2–10 ml of 1:100 000 adrenaline plus 0.5–2 ml of 5% ethanolamine oleate or applications of the heater probe (Keymed Ltd, UK). The details of the technique of endoscopy therapy are described elsewhere.^{15 16} One of two experienced endoscopists (CPC or CR) was entirely responsible for treatment. Rebleeding (defined as fresh haematemesis or melaena associated with the sudden development of shock), operation rates, transfusion requirements, duration of hospital admission, and 30 day mortality were recorded.

Warfarin was restarted five days after bleeding had stopped in patients in whom it was considered essential.

Differences in outcome were analysed using the χ^2 test and Student's *t* test as appropriate.

The study was approved by the Ethics of Medicine and Oncology Committee of the Lothian Health Board. When possible written consent was obtained from each patient, otherwise permission was obtained from a relative or, in rare circumstances, retrospectively.

Results

PATIENT CHARACTERISTICS

The median age of the 52 anticoagulated patients was 70 years (range 51–84); 32 were men. The indications for anticoagulation were valvular heart disease (27 patients), venous thromboembolic disease (13), peripheral arterial grafts (3), coronary artery disease (4), cerebrovascular disease (2), recurrent atrial fibrillation (2), and left ventricular aneurysmectomy (1). Only six patients had had recent dyspeptic symptoms, although seven had a previous history of peptic ulcer disease.

A bleeding source was identified in 43 (83%) patients (Figure). Twenty three patients were anticoagulated within the therapeutic range at presentation (INR 2.5–3.5 for prosthetic heart valves, 2.0–3.0 for other indications). A bleeding source was identified in 19 (83%) of these. Twenty nine patients were anticoagulated beyond the therapeutic range and a source of

TABLE II Results of treatment in patients with peptic ulcer

	Warfarin (n=23)	No warfarin (n=50)
Technical success	22	47
Injection:heater probe	18:4	36:11
Continued bleeding/rebleeding	4	9
Emergency surgery	2	4
Mean (SEM) of blood transfused (U)	6.0 (0.79)	4.48 (0.50)
Median (range) duration of admission (d)	10 (4–57)	7 (3–84)
30 Day mortality	0	2

bleeding was found in 24. No relationship was found between the INR and likelihood of finding an underlying cause of bleeding.

The duration of warfarin treatment before the first bleeding episode ranged from 1 week to 18 years (median 44 months). Ten patients were also taking non-steroidal anti-inflammatory drugs (NSAIDs) and nine were taking aspirin. In 16 of these 19 patients a bleeding source was identified (gastric ulcer in four, duodenal ulcer in six, Mallory-Weiss tear in one, adenoma in one, gastric carcinoma in one, and gastric erosions in three). Eleven of these patients were anticoagulated beyond the therapeutic range.

ENDOSCOPIC FINDINGS

The commonest diagnosis was peptic ulcer (25 patients), and 23 of these were associated with major endoscopic stigmata of recent haemorrhage. The patients who presented with Mallory-Weiss tears, gastric erosions, and oesophageal ulcers ran a benign course without the need for endoscopic or surgical intervention. The patient who presented with major haemorrhage from diverticular disease was elderly, had multisystem disease, and died without a surgical operation. The patient with vascular malformations of the stomach responded well to Nd Yag laser therapy and the two gastric polyps were removed electively by endoscopic snare diathermy.

Despite upper gastrointestinal endoscopy and colonoscopy, no diagnosis was achieved in nine patients (17%). In four of these patients the INR was within the therapeutic range, and in five it was beyond the therapeutic range. The prognosis of this group was excellent and none rebled in hospital. This contrasts with a negative endoscopy rate of 8% in 710 patients who presented with gastrointestinal bleeding of similar intensity over this period but had not been taking anticoagulants.

TABLE I Risk factors in each group

	Warfarin (n=23)	No warfarin (n=50)
Sex M:F	15:8	34:16
Mean (SEM) age (y)	71 (1.67)	73.5 (1.09)
Mean (SEM) admission haemoglobin (g/dl)	7.9 (0.35)	8.9 (0.27)*
Shocked (%)	11 (48)	25 (50)
NSAID users (%)	4 (17)	14 (28)
Aspirin ingestion (%)	6 (26)	18 (32)
Previous peptic ulcer disease (%)	3 (13)	12 (24)
Duodenal ulcer (%)	13 (56.5)	27 (54)
Bleeding	9	14
Non-bleeding vessel	4	13
Gastric ulcer (%)	10 (43.5)	23 (46)
Bleeding	8	13
Non-bleeding vessel	2	10

**p*<0.05.

OUTCOME IN PATIENTS TREATED FOR MAJOR PEPTIC ULCER HAEMORRHAGE

The characteristics of anticoagulated patients who presented with major stigmata of recent haemorrhage and their controls is shown in Table I. The two groups were well matched for known risk factors except for the mean haemoglobin concentration on admission to hospital, which was significantly lower in the anticoagulated group.

Endoscopic treatment was possible in 22 patients taking warfarin and in 47 controls. The failures were a consequence of inaccessibility of the ulcer to injection or the heater probe. The

outcome of treatment is presented in Table II. Uncontrolled haemorrhage or rebleeding were relatively infrequent in both groups and a similar proportion required emergency surgery. Transfusion requirements and hospital stay tended to be slightly greater in the anticoagulated patients, but this did not achieve statistical significance.

There were no significant complications after endoscopic treatment in any patient. Two patients from the control group died from post-operative complications of emergency surgery.

RE-ANTICOAGULATION

Warfarin was restarted in 28 patients (54%) five days after the bleeding had stopped. Patients with peptic ulcer received long term maintenance treatment with H₂ receptor antagonists. Patients were followed for a median period of 9.5 months (range 4–46 months) and two rebled from gastric erosions after three and seven months respectively. Five patients died during the follow up period – the two gastric cancer patients, one patient who developed disseminated ovarian carcinoma, and two patients with cerebral haemorrhage (both were taking warfarin at the time).

Discussion

This study confirms that most anticoagulated patients who present with severe acute gastrointestinal bleeding have underlying mucosal disease. Endoscopy is therefore mandatory in these patients.

Patients presented with gastrointestinal bleeding an extremely variable time after beginning warfarin, and the duration of anticoagulation did not influence the chances of discovering a bleeding source. Indeed, 13 patients presented within three weeks of starting warfarin and a cause for bleeding was found in most (85%). In contrast, 12 had received anticoagulants for more than 10 years and eight of these were also found to have an upper gastrointestinal bleeding source.

The degree of anticoagulation did not seem to be related to the frequency of identifying a bleeding site. It has been suggested that bleeding that occurs when the INR is below 3.0 is frequently associated with an obvious underlying cause.^{2,17} We found that patients who were over-anticoagulated had also usually bled from a mucosal lesion and we would stress that this group of patients should be as assiduously investigated as patients anticoagulated within the therapeutic range or indeed patients not receiving warfarin.

The commonest cause of bleeding in anticoagulated patients was peptic ulcer, and this study shows that patients who have major endoscopic stigmata of bleeding can safely undergo

endoscopic treatment by injection or heater probe treatment. The outcome in these patients is good, even when anticoagulation is incompletely reversed. Treated patients in this series had an INR of 1.5–2.5 and yet the frequency of rebleeding and operation rates were low and similar to those in patients not receiving anticoagulation.¹⁶ Anticoagulated patients tended to receive more blood transfusions and to be in hospital for longer than those who have not been anticoagulated, but this is probably because of comorbid diseases rather than more severe bleeding. There were no deaths in the bleeding ulcer patients in the warfarin group, while two (4%) of those not on warfarin died. After endoscopic treatment, continued anticoagulation seems safe, although we believe it wise to ensure ulcer healing by endoscopic means and to recommend long term maintenance drug treatment in this group.

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