# National audit of the use of surgery and radiological embolization after failed endoscopic haemostasis for non-variceal upper gastrointestinal bleeding

V. Jairath<sup>1,2</sup>, B. C. Kahan<sup>3,4</sup>, R. F. A. Logan<sup>5</sup>, S. A. Hearnshaw<sup>6</sup>, C. J. Dore<sup>3,4</sup>, S. P. L. Travis<sup>2</sup>, M. F. Murphy<sup>1</sup> and K. R. Palmer<sup>7</sup>

<sup>1</sup>NHS Blood and Transplant and <sup>2</sup>Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, <sup>3</sup>Medical Research Council Clinical Trials Unit, London, <sup>4</sup>NHS Blood and Transplant Clinical Studies Unit, Cambridge, <sup>5</sup>Division of Epidemiology and Public Health, and Nottingham Digestive Disease Centre, University of Nottingham, Nottingham, <sup>6</sup>Royal Victoria Infirmary, Newcastle, and <sup>7</sup>Western General Hospital, Edinburgh, UK Correspondence to: Dr V. Jairath, NHS Blood and Transplant and Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford OX3 9DU, UK (e-mail: vipul.jairath@nhsbt.nhs.uk)

Background: Following non-variceal upper gastrointestinal bleeding (NVUGIB), 10–15 per cent of patients experience further bleeding. Although surgery has been the traditional salvage therapy, there is renewed interest in transcatheter arterial embolization (TAE). This study examined the use, clinical characteristics and outcomes of patients receiving salvage surgery or TAE after failed endoscopic haemostasis for NVUGIB.

**Methods:** A UK national audit of upper gastrointestinal bleeding was undertaken in May and June 2007. A logistic regression model was used to identify clinical predictors of endoscopic failure.

Results: Data were analysed from 4478 patients involving 212 UK centres. Some 533 (11.9 per cent) experienced further bleeding, of whom 163 (30.6 per cent) proceeded to salvage therapy with surgery (97), TAE (60) or both (6). Among surgical patients (mean age 71 years), 66.0 per cent (68 of 103) had a Rockall score of at least 3 and emergency surgery was carried out between midnight and 08.00 hours in 21 per cent, with a consultant surgeon present in 89 per cent of operations. Some 9 per cent of patients had further bleeding after TAE, resulting in later surgery. The mortality rate was 29 per cent after surgery, 10 per cent after TAE and 23.2 per cent among those with further bleeding after the index endoscopy that was managed by endoscopy alone. The strongest predictors of endoscopic failure were coagulopathy (odds ratio 3.27, 95 per cent confidence interval 2.37 to 4.53) and a haemoglobin level of 10 g/dl or less (odds ratio 2.22, 1.71 to 2.87, for haemoglobin 8–10 g/dl).

**Conclusion:** Salvage surgery and embolization are required in fewer than 4 per cent of patients with NVUGIB. The high postoperative mortality rate, reflecting age, co-morbidity and severity of bleeding, warrants a prospective study to establish the effectiveness and safety of TAE as an alternative to surgery in the management of bleeding after failure of endoscopic therapy.

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# Introduction

Non-variceal upper gastrointestinal tract bleeding (NVUGIB) is a common medical emergency<sup>1-3</sup>. Despite advances in endoscopic and pharmacological therapies, 10–15 per cent of patients still experience further

bleeding<sup>4–6</sup>, either as persistent bleeding at the end of the index endoscopy or as recurrent bleeding despite achieving endoscopic haemostasis<sup>7–9</sup>. Mortality rates are four to five times greater in patients who experience further bleeding than in those who do not. Apart from resuscitative care, therapeutic options include repeat endoscopy with

application of additional haemostatic modalities, surgery and transcatheter arterial embolization (TAE).

First described in 1972<sup>10</sup>, with success in case series<sup>11</sup>, the role of TAE as an alternative or adjunct to surgery remains poorly characterized. There are few reports beyond single-centre studies<sup>12–15</sup>. The present study characterized the use, features and outcomes of patients undergoing salvage surgery or TAE following failed endoscopic haemostasis for NVUGIB from a comprehensive nationwide UK study. The study also sought to identify simple clinical parameters predicting failure of endoscopic therapy, to facilitate early identification and risk stratification of patients likely to require a salvage procedure.

### **Methods**

Data were analysed from the 2007 UK national audit of acute upper gastrointestinal bleeding and the use of blood<sup>16</sup>. Detailed methods of case ascertainment have been described<sup>4,16,17</sup>. All National Health Service (NHS) hospitals accepting acute admissions in the UK were invited to participate. Data were collected prospectively on all adults (16 years or over) presenting with acute upper gastrointestinal bleeding between 1 May and 30 June 2007. At no time did the study group have access to patient records or any data that identified patients. This analysis included baseline clinical

Table 1 Definitions

Non-variceal upper gastrointestinal tract bleeding	Haematemesis, passage of melaena and/or firm clinical or laboratory evidence of acute blood loss from the upper GI tract with a confirmed non-variceal source at endoscopy. Patients presenting with iron deficiency anaemia without evidence of AUGIB were not included
Haematemesis	Vomiting of blood or blood clots. Patients presenting with 'coffee ground' vomiting were included only if this was witnessed by medical or nursing staff
Melaena	Passage of dark tarry stools witnessed by medical or nursing staff or discovered on rectal examination
Further bleeding	Continued bleeding at index endoscopy or further haematemesis, passage of fresh melaena, continuing or recurrent hypotension and tachycardia ± fall in haemoglobin level despite achieving haemostasis at first endoscopy
Mortality	Death within the hospital admission and up to 30 days after index AUGIB
Shock	Tachycardia (pulse ≥ 100 beats/min) and/or hypotension (systolic BP < 100 mmHg)
Coagulopathy	$INR > 1 \cdot 5$ and/or prothombin time $> 3$ s prolonged

GI, gastrointestinal; AUGIB, acute upper gastrointestinal bleeding; BP, blood pressure; INR, international normalized ratio.

characteristics, medications, co-morbidities, transfusion data, timing and nature of surgical procedures, radiological data and outcomes of patients requiring salvage surgery or TAE for NVUGIB. Definitions are provided in Table 1.

# Statistical analysis

A mixed-effects logistic regression model was used to identify clinical predictors of endoscopic failure. Hospitals were modelled as random effects in order to account for correlation between patients presenting to the same hospital, and to adjust for betweenhospital differences. The model was adjusted for a prespecified set of potentially confounding variables and potential predictors of death, selected from a list of variables based on clinical relevance among baseline clinical characteristics, endoscopic findings, pharmacological therapies and admission status. These variables were: age, sex, presentation with shock, at least two co-morbid illnesses (ischaemic heart disease, heart failure, respiratory disease, cancer, stroke, dementia, cirrhosis and renal failure), presentation with frank haematemesis, presentation with melaena, haemoglobin concentration at presentation, urea concentration on admission, a prolonged coagulation screen (defined as

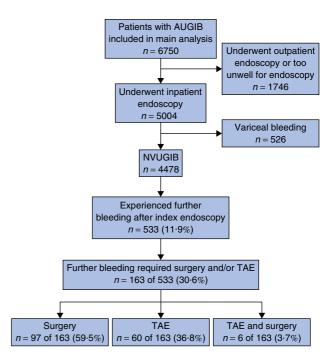


Fig. 1 Study flow chart. AUGIB, acute upper gastrointestinal bleeding; NVUGIB, non-variceal upper gastrointestinal bleeding; TAE, transcatheter arterial embolization

Table 2 Baseline characteristics

	Surgery (n = 97)	TAE (n = 60)	TAE and surgery (n = 6)	Endoscopy alone (n = 4315)	Further bleeding treated by endoscopy alone (n = 370)	Proportion with data missing (n = 4478)
Baseline characteristics						
Age (years)*	71.2(14.0)	66.5(17.0)	70-2(11-2)	66-6(18-6)	70.8(15.8)	0 (0)
Sex ratio (M : F)	52:45	37:23	5:1	2591:1722	280:88	2 (0)
New admission	76 (79)	42 (71)	3 (50)	3536 (83.0)	300 (81.1)	57 (1.3)
Disease presentation						
Shock	63 (65)	37 (62)	4 (67)	1500 (35.4)	218 (58.9)	80 (1.8)
Haematemesis	41 (42)	13 (22)	4 (67)	1426 (33.1)	123 (33-2)	3 (0.1)
Melaena	66 (68)	42 (71)	4 (67)	2405 (55.8)	292 (78.9)	3 (0.1)
Clinical Rockall score*	3.3(1.7)	3.1(1.8)	4.7(1.5)	2.5(1.8)	3.3(1.8)	0(0)
Clinical Rockall score ≥ 3 (high risk)	63 (65)	34 (57)	5 (83)	2170 (50.3)	281 (75.9)	0 (0)
Total Rockall score*	6.0(2.1)	4.7(2.5)	7.2(1.9)	3.8(2.3)	5.3(2.3)	15(0.3)
Drug history						
Aspirin	35 (39)	19 (34)	3 (60)	1379 (33.6)	141 (38-1)	228 (5.1)
NSAID	14 (16)	12 (21)	1 (20)	554 (13-6)	48 (13.0)	256 (5.7)
Clopidogrel	6 (7)	3 (6)	0 (0)	264 (6.5)	34 (9.2)	276 (6.2)
PPI	21 (24)	20 (36)	2 (40)	1143 (28.1)	126 (34-1)	264 (5.9)
Warfarin	6 (7)	7 (13)	0 (0)	355 (8.8)	41 (11.1)	278 (6.2)
Laboratory parameters						
Haemoglobin (g/dl)*	8.1(2.7)	8.8(3.1)	6.3(2.1)	10.7(3.2)	9.1(2.6)	298 (6.7)
Urea (10 mmol/l)†	12.6 (7.1-18.2)	10.1 (7.2-18.1)	7.1 (7-14.4)	9-3 (5-4-14-9)	13.1 (8.6-18.7)	483 (10-8)
Coagulopathy‡	34 (35)	11 (18)	2 (33)	535 (12.4)	97 (26-2)	0 (0)
Creatinine (µmol/l)†	90 (67-121)	91 (72-130)	74 (55-95)	90 (74-116)	99 (78–131	395 (8.8)
Co-morbidities						
Ischaemic heart disease	21 (22)	10 (17)	0 (0)	902 (20.9)	108 (29-2)	0 (0)
Dementia	3 (3)	1 (2)	0 (0)	202 (4.7)	24 (6.5)	0 (0)
Cirrhosis	5 (5)	4 (7)	2 (33)	168 (3.9)	25 (6.8)	45 (1.0)
Renal disease	6 (6)	4 (7)	1 (17)	370 (8.7)	51 (13.8)	53 (1.2)
Stroke	5 (5)	3 (5)	0 (0)	324 (7.5)	37 (10.0)	0 (0)
Cancer	7 (7)	7 (12)	1 (17)	357 (8-3)	64 (17.3)	0 (0)
Respiratory disease	13 (13)	9 (15)	1 (17)	484 (11.2)	60 (16-2)	0 (0)
Cardiac failure	7 (7)	4 (7)	1 (17)	257 (6.0)	45 (12-2)	0 (0)
≥ 2 co-morbidities	16 (16)	8 (13)	1 (17)	735 (17.0)	107 (28-9)	0 (0)

Values in parentheses are percentages unless indicated otherwise; values are \*mean(s.d.) and †median (interquartile range). ‡Defined as international normalized ratio above 1.5 or prothrombin time more than 3 s prolonged. TAE, transcatheter arterial embolization; NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor.

an international normalized ratio (INR) of more than 1.5 and/or a prothrombin time over 3 s prolonged), use of non-steroidal anti-inflammatory drugs, clopidogrel, aspirin, warfarin or proton pump inhibitors, severity of endoscopic stigmata (blood in the upper gastrointestinal tract, visible vessel, spurting vessel, adherent clot, dark spot) and admission status (new admission versus inpatient).

At least one clinical baseline variable was missing in 20.3 per cent of patients. Multiple imputation was used to account for missing data, a technique that accounts for the uncertainty caused by missing data and gives more reliable results than complete case analysis in most situations<sup>18</sup>. Mortality, receipt of red blood cell transfusion, length of hospital stay and all clinical baseline variables were included in the imputation model and 25 imputations were performed. Imputation was done with chained equations

using the Stata® package ice<sup>19</sup> (StataCorp LP, College Station, Texas, USA). Continuous variables were analysed using fractional polynomials<sup>20</sup>. All analyses were conducted in Stata® SE version 11.

### **Results**

Of the 257 hospitals invited to participate, 223 agreed and 212 submitted data (http://www.bsg.org.uk/clinical/ general/uk-upper-gi-bleeding-audit.html). A flow chart detailing case ascertainment is shown in Fig. 1. Some 4478 (89.5 per cent) of all 5004 patients who underwent inpatient endoscopy had an endoscopically confirmed nonvariceal source of bleeding. In total, 533 (11.9 per cent) of 4478 patients experienced further bleeding, of whom 163

Table 3 Endoscopic, transfusion and clinical outcome data

	Surgery (n = 97)	TAE (n = 60)	TAE and surgery (n = 6)	Endoscopy alone (n = 4315)	Further bleeding treated by endoscopy alone (n = 370)	Proportion with data missing (n = 4478)
Endoscopic data						
No. of endoscopies						0 (0)
1	67 (69)	32 (53)	4 (67)	3946 (91.5)	218 (58.9)	
2	24 (25)	17 (28)	1 (17)	328 (7.6)	169 (45.7)	
3	4 (4)	8 (13)	1 (17)	32 (0.7)	26 (7.0)	
≥ 4	2 (2)	3 (5)	0 (0)	9 (0.2)	7 (1.9)	
Therapeutic endoscopy	53 (56)	15 (25)	1 (17)	764 (17.9)	150 (40.5)	59 (1.3)
No. of therapeutic procedures						20 (0.4)
1	36 (38)	5 (8)	0 (0)	461 (10.9)	98 (26.5)	
2	11 (12)	8 (13)	1 (17)	266 (6.3)	44 (11.9)	
≥ 3	4 (4)	2 (3)	0 (0)	19 (0.5)	3 (0.8)	
High-risk stigmata	83 (86)	26 (43)	5 (83)	999 (23-2)	222 (60.0)	0 (0)
Time to index endoscopy (h)						296 (6.6)
< 12	40 (45)	21 (36)	2 (50)	771 (19-1)	111 (30.0)	
12-24	21 (24)	17 (29)	2 (50)	1150 (28.5)	107 (28.9)	
> 24	27 (31)	20 (34)	0 (0)	2111 (52.4)	162 (43.8)	
Blood components transfused						
Received RBCs within 12 h	83 (86)	41 (68)	6 (100)	1524 (35-3)	258 (69.7)	0 (0)
Received RBCs	91 (94)	47 (78)	6 (100)	2043 (47-3)	357 (96.5)	0 (0)
Amount (units)*	9 (5-14)	8 (3-12)	22 (13-25)	3 (2-4)	5 (3-8)	236 (5.3)
Received FFP	45 (46)	12 (20)	4 (67)	206 (4.8)	58 (15.7)	0 (0)
Amount (units)*	4 (4-8)	4.5 (3.5-10)	4 (3-8.5)	3 (2-4)	4 (2-7)	0 (0)
Received platelets	22 (23)	7 (12)	2 (33)	68 (1·6)	28 (7.6)	0 (0)
Amount (units)*	2 (1-3)	2 (1-2)	1.5 (1-2)	2 (1-3)	2 (1-5)	0 (0)
Outcomes						
In-hospital death	28 (29)	6 (10)	3 (50)	254 (5.9)	86 (23.2)	0 (0)
Hospital stay (days)*†	19 (12–19)	17-5 (7-29)	29 (7–29)	6 (3–15)	14 (8–28)	298 (6.7)

Values in parentheses are percentages unless indicated otherwise; \*values are median (interquartile range). †Data values censored at 29 days. TAE, transcatheter arterial embolization; RBC, red blood cell; FFP, fresh frozen plasma.

(30.6 per cent) went on to require salvage surgery (97), TAE (60) or both (6) to control the haemorrhage.

### Patient characteristics

Baseline clinical characteristics are summarized in Table 2. Patients in the surgery group were older (71.2 versus 66.5 years), more likely to present with shock (65 versus 62 per cent) or haematemesis (42 versus 22 per cent), to have a clinical Rockall score of at least 3 (65 versus 57 per cent), a lower haemoglobin concentration (8.1 versus 8.8 g/dl), coagulopathy (35 versus 18 per cent) and at least two co-morbidities (16 versus 13 per cent) than those having TAE.

# Endoscopic procedures and transfusion of blood components

Details of endoscopic procedures and transfusion of blood components are outlined in Table 3. Compared with those who had TAE alone, a greater proportion of patients in the surgery group underwent only one endoscopy before the salvage procedure (69 versus 53 per cent), were reported to have high-risk stigmata of haemorrhage (86 versus 43 per cent) at the index endoscopy and received a therapeutic procedure at the index endoscopy (56 versus 25 per cent). A similar proportion of patients in the surgery and TAE groups underwent endoscopy within 24 h of presentation (69 versus 66 per cent respectively). Some patients who underwent surgery and/or TAE were reported to have more than one endoscopic diagnosis, although the major lesion in those undergoing surgery/TAE was reported as peptic ulcer disease (72.4 per cent), malignancy (6.4 per cent), vascular ectasia (3.2 per cent), haemobilia (14.1 per cent) and other (5.2 per cent).

A greater proportion of patients in the surgery group than in the TAE group received red blood cells (94 versus 78 per cent), fresh frozen plasma (46 versus 20 per cent) and platelets (23 versus 12 per cent) while in hospital, although the median numbers of units of each blood component transfused per patient was similar in both groups.

Table 4 Details of surgical procedures

	No. of patients $(n = 103)$ †	No. with data missing
Timing of surgery		
Weekend or weekday		5 (4.9)
Mon-Fri	74 (76)	0 (1.0)
Sat-Sun	24 (24)	
Timing		13 (12-6)
Mon-Fri 08.00-17.00 hours	34 (38)	
Mon-Fri 17.01-23.59 hours or	37 (41)	
Sat-Sun 08.01-23.59 hours		
Mon-Sun 00.00-07.59 hours	19 (21)	
Time from presentation to index	13.7 (5.1–24.9)	11 (10.7)
endoscopy (h)*	4 (0 4)	F (4.0)
Time from index endoscopy to surgery (h)*	1 (0-4)	5 (4.9)
Time from presentation to surgery	2 (1-6)	8 (7.8)
(days)*	2 (1-0)	0 (7.0)
Indication for surgery		
Uncontrolled bleeding	85 (82.5)	0 (0)
Peritonitis/perforation	7 (6.8)	0 (0)
Malignancy	5 (4.9)	0 (0)
Other	9 (8.7)	0 (0)
Surgical procedure		
Under-run of ulcer	67 (69)	6 (5.8)
Excision of ulcer	3 (3)	6 (5.8)
Excision of ulcer with	2 (2)	6 (5.8)
vagotomy/pyloroplasty	- (-)	- /
Partial gastrectomy	9 (9)	6 (5.8)
Other Grade of lead surgeon	16 (16)	6 (5.8)
Consultant	76 (78)	6 (5.8)
Registrar (supervised)	10 (10)	6 (5.8)
Registrar (unsupervised)	7 (7)	6 (5.8)
Associate specialist/staff grade	4 (4)	6 (5.8)
Grade of most senior anaesthetist	( )	- ()
Consultant	63 (76)	20 (19-4)
Specialist registrar	14 (17)	20 (19-4)
Senior house officer	6 (7)	20 (19-4)
Other	0 (0)	20 (19-4)
Postoperative complications		
Pneumonia	22 (21.4)	0 (0)
Renal failure	11 (10.7)	0 (0)
Sepsis	9 (8.7)	0 (0)
Significant cardiac event	10 (9.7)	0 (0)
Pulmonary embolism/deep vein thrombosis	2 (1.9)	0 (0)
Stroke	1 (1.0)	0 (0)
Wound dehiscence/infection	4 (3.9)	0 (0)
Liver failure	3 (2.9)	0 (0)
	()	(-)

Values in parentheses are percentages unless indicated otherwise; \*values are median (interquartile range). †Included 97 patients who had surgery only; the remaining six underwent surgery and transcatheter arterial embolization.

# Surgical and transcatheter arterial embolization procedures

One hundred and three (2.3 per cent) of the 4478 patients underwent surgery (Table 4). The median (interquartile

**Table 5** Details of transcatheter arterial embolization

	No. of patients $(n = 66)$	No. with data missing
Underwent diagnostic angiography		
Underwent diagnostic angiography first	34 (76)	21 (32)
Bleeding source identified	21 (66)	34 (52)
Therapeutic angiography and embolization	20 (43)	20 (30)
Bleeding controlled successfully	13 (68)	47 (71)
Other radiological procedure		
Other radiological procedure	7 (16)	22 (33)
Bleeding controlled successfully	3 (60)	61 (92)

Values in parentheses are percentages.

range, i.g.r.) time from presentation to index endoscopy in the group receiving surgery was 13.7 (5.1-24.9) h. The median interval from index endoscopy to surgery was 1 (0-4) days and that from presentation to surgery was 2 (1-6 days). Some 38 per cent of operations (34 of 90) took place between 08.00 and 17.00 hours on Monday to Friday, and 21 per cent (19 of 90; data missing for 13 patients) were carried out between midnight and 08.00 hours, Monday to Sunday.

The most common indication for surgery was uncontrolled bleeding (82.5 per cent, 85 of 103) and the most commonly performed surgical procedure was under-run of an ulcer (69 per cent, 67 of 97; data missing for 6 patients). A consultant surgeon was present at 89 per cent of all operations (86 of 97; data missing for 6 patients) and was listed as the lead surgeon in 78 per cent (76 of 97; data missing for 6 patients). A consultant anaesthetist was present at 76 per cent of all operations (63 of 83; data missing for 20 patients).

Sixty (1.3 per cent) of 4478 patients underwent TAE only and a further six patients had TAE followed by surgery (Table 5). These six patients experienced further bleeding despite TAE, necessitating surgery. There were no reported instances of gastrointestinal tract ischaemia or necrosis as a direct complication of TAE.

# Mortality and length of hospital stay

The in-hospital mortality rate was 29 per cent (28 of 97) among the patients who underwent surgery, 10 per cent (6 of 60) among those who had TAE, and 50 per cent (3 of 6) in the six patients who required both TAE and surgery (Table 3). The mortality rate in the group of patients who experienced further bleeding after the index endoscopy and were subsequently managed by endoscopy alone was 23.2 per cent (86 of 370); this group had a greater burden of co-morbid illness in comparison with patients who

Table 6 Clinical and endoscopic characteristics predictive of further bleeding

	Further bleeding in patients without characteristic*	Further bleeding in patients with characteristic*	Odds ratio†§	Р
Age ≥ 65 years	158 (9.1)	375 (13-9)	1.09 (0.86, 1.38)	0.491
Male	185 (10.3)	347 (12.9)	1.36 (1.09, 1.70)	0.006
In-hospital bleeding	383 (11.1)	144 (19-0)	1.54 (1.20, 1.98)	0.001
NSAID use	434 (11.9)	70 (12.0)	0.94 (0.69, 1.28)	0.683
PPI use	351 (11.6)	153 (12.9)	1.38 (1.09, 1.75)	0.008
Aspirin use	325 (11.5)	186 (13.0)	0.81 (0.64, 1.03)	0.082
Warfarin use	455 (11·6)	48 (13.0)	0.31 (0.19, 0.48)	< 0.001
Clopidogrel use	463 (11.8)	39 (14-3)	1.07 (0.72, 1.61)	0.732
Coagulopathy‡	397 (10.2)	136 (23.4)	3.27 (2.37, 4.53)	< 0.001
Urea ≥ 10 mmol/l	153 (7.3)	306 (17.1)	1.51 (1.23, 1.85)	< 0.001
Haemoglobin (g/dl)				< 0.001
< 8		208 (20.8)	1.65 (1.40, 1.95)	
8–10		127 (15.3)	2.22 (1.71, 2.87)	
> 10		155 (7⋅0)	1.00	
≥ 2 co-morbidities	408 (11.0)	125 (16-4)	1.06 (0.81, 1.39)	0.663
Shock	228 (8-2)	300 (18·7)	1.57 (1.27, 1.95)	< 0.001
Haematemesis	366 (12.2)	165 (11.1)	1.05 (0.82, 1.33)	0.721
Melaena	157 (8.0)	374 (14-9)	1.54 (1.21, 1.96)	< 0.001
Stigmata at index endoscopy				
Blood in upper GI tract	299 (8.0)	234 (29.8)	2.93 (2.32, 3.69)	< 0.001
Visible vessel	454 (11.1)	79 (27-2)	1.39 (1.00, 1.93)	0.054
Spurting vessel	494 (11.0)	39 (41.2)	2.42 (1.47, 4.00)	0.001
Adherent clot	430 (9.9)	103 (32·1)	2.29 (1.70, 3.09)	< 0.001
Dark spot in ulcer base	517 (12·1)	16 (19-0)	1.36 (0.72, 2.54)	0.343

Values in parentheses are \*percentages and †95 per cent confidence intervals. Overall, 533 (11.9 per cent) of 4478 patients had further bleeding. ‡Defined as international normalized ratio above 1.5 or prothrombin time more than 3s prolonged. NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor; GI, gastrointestinal. §Mixed-effects logistic regression.

underwent surgery, in particular malignancy, ischaemic heart disease and a greater proportion with at least two major co-morbidities. Length of hospital stay was similar between the surgery and TAE groups (*Table 3*).

# Clinical and endoscopic predictors of failure to achieve endoscopic haemostasis

Clinical and laboratory parameters at presentation with NVUGIB (before endoscopy) most strongly associated with endoscopic failure were coagulopathy (odds ratio (OR) 3.27, 95 per cent confidence interval (c.i.) 2.37 to 4.53; P < 0.001), haemodynamic shock (OR 1.57, 1.27 to 1.95; P < 0.001), melaena (OR 1.54, 1.21 to 1.96; P < 0.001), blood urea concentration at least 10 mmol/l (OR 1.51, 1.23 to 1.85; P < 0.001), and a presenting haemoglobin concentration of 10 g/dl or less (OR 2-22 (95 per cent c.i. 1.71 to 2.87) for 8-10 g/dl and OR 1.65 (1.40 to 1.95) for less than 8 g/dl, compared with a haemoglobin level of more than 10 g/dl; P < 0.001) (Table 6). Endoscopic stigmata most strongly associated with failure to achieve haemostasis were fresh blood in the upper gastrointestinal tract (OR 2.93, 2.32 to 3.69; P < 0.001), an adherent clot (OR 2.29, 1.70 to 3.09; P < 0.001) and a spurting vessel (OR 2.42, 1.47 to 4.00; P = 0.001).

# **Discussion**

Nationwide coverage of case ascertainment reflected reallife practice across 212 UK hospitals and showed that surgery and TAE were rarely needed as salvage procedures. Fewer than 4 per cent of all presentations with NVUGIB required either surgery or TAE to control bleeding, the remainder being managed by endoscopy. The rates of surgery in this study were similar to those from other large registries, including the Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy<sup>5</sup>, the Italian Progetta Nazionale Emorragia Digestiva database<sup>21</sup> and that from Hong Kong<sup>12</sup>. Given that rates of surgery reported 20 years ago were as high as 15–20 per cent<sup>22–24</sup>, this is most likely to be a reflection of improvements in endoscopic treatments and the use of high-dose proton pump inhibition.

Surgery has been the traditional salvage therapy in patients with uncontrolled bleeding or further bleeding that cannot be managed endoscopically. In the present study 69 per cent of patients had only one endoscopy before surgery, suggesting that bleeding may have been torrential at the index endoscopy or that an early decision was made not to repeat endoscopy in the event of further

bleeding. The low rates of endoscopic therapy at the index endoscopy are surprising. This may have been due to massive bleeding prohibiting the use of endoscopic therapy.

Despite the fact that a consultant surgeon was present at 89 per cent of all operations, the exceptionally high postoperative mortality rate of 29 per cent is undoubtedly a reflection of patient age, co-morbidity and severity of bleeding.

In recent years, TAE has become increasingly available as an alternative to surgery and has been proposed as potentially less hazardous, especially in high-risk patients<sup>25-27</sup>. The present study lends further support to this, given that only 9 per cent had further bleeding after TAE that necessitated surgery and 86 per cent of patients requiring TAE as a salvage procedure survived. In this study it was paradoxical that those who underwent surgery were older, had more co-morbidities and appeared to present with more serious bleeding than those who had TAE. This may reflect the limited availability of interventional radiology in many UK hospitals at the time of the audit. In 2009 fewer than 10 per cent of all acute hospital trusts in the UK were able to provide 24 h access to interventional radiology<sup>28</sup>.

A significant concern with use of TAE is the risk of gastrointestinal tract ischaemia and necrosis. Although there were no such reports in this study, TAE is considered to be safe above the ligament of Treitz, owing to the rich collateral blood supply to the stomach and duodenum<sup>11</sup>. Although there have been reports of acute ischaemia after embolization, most cases present later as duodenal stenosis<sup>29</sup> after embolization of the gastroduodenal artery. Risk factors associated with this are use of embolic agents such as cyanoacrylate glue and a history of previous surgery in this area<sup>30</sup>.

The practice of prophylactic embolization of high-risk peptic ulcers in which endoscopic haemostasis has been achieved in order to prevent further bleeding cannot be recommended routinely based on current evidence, nor can it be ascertained from this audit whether this approach was used in any of the patients who underwent TAE.

Close liaison between emergency medicine physicians, gastroenterologists, surgeons and interventional radiologists is important to facilitate early processes and algorithms of care in patients who present with severe bleeding. The present study identified clinical predictors that can be used at presentation to identify those more likely to fail endoscopic therapy, including presentation with coagulopathy (INR over 1.5), shock, urea concentration of 10 mmol/l and a haemoglobin level of 10 g/dl or less. These simple parameters could be used in addition to established risk scores to facilitate early recognition of patients most likely to fail endoscopic therapy, in whom the need for a further intervention is highest. It is not possible in this retrospective analysis to make a direct comparison of the outcomes of patients undergoing surgery or TAE, nor to understand the decision-making process in centres where both TAE and surgery are available as salvage therapy when endoscopy fails. The characteristics of patients in the two groups were different and differing processes of care within institutions may have influenced the decision to offer patients surgery rather than embolization. Similarly, this study cannot explain why some patients who had further bleeding were managed without recourse to surgery other than the likelihood that this decision was made on the basis of the extent of co-morbidity (as outlined in Table 2). Other limitations include lack of data relating to the timing of TAE, technical details of the procedure (such as embolization agent and technique) and missing

Salvage surgery or TAE is required in fewer than 4 per cent of patients in the modern management of NVUGIB in the UK. The apparent success of TAE in this retrospective analysis, coupled with its increasing availability, merits a prospective study to establish whether TAE could be used routinely as an alternative to surgery in the management of patients in whom endoscopic therapy fails to control NVUGIB. A randomized clinical trial in Hong Kong comparing surgery versus embolization for high-risk ulcers failing endoscopic haemostasis is currently listed as recruiting<sup>31</sup> and this may define the place of TAE as an alternative to surgery in the current management algorithm of NVUGIB.

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# References

1 Lassen A, Hallas J, Schaffalitzky de Muckadell OB. Complicated and uncomplicated peptic ulcers in a Danish county 1993-2002: a population-based cohort study. Am 7 Gastroenterol 2006; 101: 945-953.

- 2 Targownik LE, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993-2003. Clin Gastroenterol Hepatol 2006; 4: 1459-1466.
- 3 van Leerdam ME, Vreeburg EM, Rauws EA, Geraedts AA, Tijssen JG, Reitsma JB et al. Acute upper GI bleeding: did anything change? Time trend analysis of incidence and outcome of acute upper GI bleeding between 1993/1994 and 2000. Am 7 Gastroenterol 2003; 98: 1494-1499.
- 4 Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Use of endoscopy for management of acute upper gastrointestinal bleeding in the UK: results of a nationwide audit. Gut 2010; 59: 1022-1029.
- 5 Barkun A, Sabbah S, Enns R, Armstrong D, Gregor J, Fedorak RN et al.; RUGBE Investigators. The Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy (RUGBE): endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting. Am J Gastroenterol 2004; 99: 1238-1246.
- 6 Vreeburg EM, Snel P, de Bruijne JW, Bartelsman JF, Rauws EA, Tytgat GN. Acute upper gastrointestinal bleeding in the Amsterdam area: incidence, diagnosis, and clinical outcome. Am J Gastroenterol 1997; 92: 236-243.
- 7 Barkun AN, Bardou M, Kuipers EJ, Sung J, Hunt RH, Martel M et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2010; 152: 101 - 113.
- 8 Rockall TA, Logan RF, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering Committee and members of the National Audit of Acute Upper Gastrointestinal Haemorrhage. BM7 1995; 311: 222-226.
- 9 Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnoses and outcomes in the 2007 UK audit. Gut 2011; 60: 1327-1335.
- 10 Rosch J, Dotter CT, Brown MJ. Selective arterial embolization. A new method for control of acute gastrointestinal bleeding. Radiology 1972; 102: 303-306.
- 11 Loffroy R, Guiu B. Role of transcatheter arterial embolization for massive bleeding from gastroduodenal ulcers. World 7 Gastroenterol 2009; 15: 5889-5897.
- 12 Wong TC, Wong KT, Chiu PW, Teoh AY, Yu SC, Au KW et al. A comparison of angiographic embolization with surgery after failed endoscopic hemostasis to bleeding peptic ulcers. Gastrointest Endosc 2011; 73: 900-908.
- 13 Poultsides GA, Kim CJ, Orlando R III, Peros G, Hallisey MJ, Vignati PV. Angiographic embolization for gastroduodenal hemorrhage: safety, efficacy, and predictors of outcome. Arch Surg 2008; 143: 457-461.
- 14 Ripoll C, Bañares R, Beceiro I, Menchén P, Catalina MV, Echenagusia A et al. Comparison of transcatheter arterial embolization and surgery for treatment of bleeding peptic ulcer after endoscopic treatment failure. 7 Vasc Interv Radiol 2004; **15**: 447–450.

- 15 Eriksson LG, Ljungdahl M, Sundbom M, Nyman R. Transcatheter arterial embolization versus surgery in the treatment of upper gastrointestinal bleeding after therapeutic endoscopy failure. 7 Vasc Interv Radiol 2008; 19: 1413-1418.
- 16 British Society of Gastroenterology. UK Comparative Audit of Upper Gastrointestinal Bleeding and the Use of Blood. http://www.bsg.org.uk/pdf\_word\_docs/blood\_audit\_ report\_07.pdf. [accessed 1 March 2012].
- 17 Jairath V, Kahan BC, Logan RF, Hearnshaw SA, Travis SP, Murphy MF et al. Mortality from acute upper gastrointestinal bleeding in the United Kingdom: does it display a 'weekend effect'? Am J Gastroenterol 2011; 106: 1621-1628.
- 18 Rubin D. Inference and missing data. Biometrika 1976; 63: 581-592.
- 19 Royston P. Multiple imputation of missing values: further update of ice, with an emphasis on interval censor monitoring. Stata Journal 2007; 7: 445-464.
- 20 Royston P, Sauerbrei W. Multivariable Model-Building. A Pragmatic Approach to Regression Analysis Based on Fractional Polynomials for Modelling Continuous Variables. Wiley-Blackwell: Chichester, 2008.
- 21 Marmo R, Koch M, Cipolletta L, Capurso L, Pera A, Bianco MA et al. Predictive factors of mortality from nonvariceal upper gastrointestinal hemorrhage: a multicenter study. Am J Gastroenterol 2008; 103: 1639-1647.
- 22 Dronfield MW, Langman MJ, Atkinson M, Balfour TW, Bell GD, Vellacott KD et al. Outcome of endoscopy and barium radiography for acute upper gastrointestinal bleeding: controlled trial in 1037 patients. Br Med 7 (Clin Res Ed) 1982; **284**: 545-548.
- 23 Masson J, Bramley PN, Herd K, McKnight GM, Park K, Brunt PW et al. Upper gastrointestinal bleeding in an open-access dedicated unit. 7 R Coll Physicians Lond 1996; 30: 436-442.
- 24 Jones PF, Johnston SJ, McEwan AB, Kyle J, Needham CD. Further haemorrhage after admission to hospital for gastrointestinal haemorrhage. Br Med 7 1973; 3: 660-664.
- 25 Loffroy R, Guiu B, Cercueil JP, Lepage C, Latournerie M, Hillon P et al. Refractory bleeding from gastroduodenal ulcers: arterial embolization in high-operative-risk patients. 7 Clin Gastroenterol 2008; **42**: 361-367.
- 26 Aina R, Oliva VL, Therasse E, Perreault P, Bui BT, Dufresne MP et al. Arterial embolotherapy for upper gastrointestinal hemorrhage: outcome assessment. J Vasc Interv Radiol 2001; 12: 195-200.
- 27 Loffroy R, Rao P, Ota S, De Lin M, Kwak BK, Geschwind JF. Embolization of acute nonvariceal upper gastrointestinal hemorrhage resistant to endoscopic treatment: results and predictors of recurrent bleeding. Cardiovasc Intervent Radiol 2010; 33: 1088-1100.
- 28 Royal College of Radiologists. Standards for Providing a 24-hour Diagnostic Radiology Service. The Royal College of Radiologists: London, 2009. http://www.rcr.ac.uk/docs/ radiology/pdf/BFCR(09)3\_diagnostic24hr.pdf [accessed 1 March 2012].

- 29 Lang EK. Transcatheter embolization in management of hemorrhage from duodenal ulcer: long-term results and complications. *Radiology* 1992; **182**: 703–707.
- 30 Shapiro N, Brandt L, Sprayregan S, Mitsudo S, Glotzer P. Duodenal infarction after therapeutic Gelfoam embolization
- of a bleeding duodenal ulcer. *Gastroenterology* 1981; **80**: 176–180.
- 31 Clinical Trials.gov. Trans-catheter Arterial Embolization and Surgery in Patients with Peptic Ulcer Bleeding Uncontrolled by Endoscopic Therapy. Study identifier NCT00766961. http://www.clinicaltrials.gov [accessed 1 March 2012].

# **Supporting information**

Additional supporting information may be found in the online version of this article:

 Table S1 Participating hospitals (Word document)

# **Snapshot Quiz**

Answer

# **Snapshot Quiz 12/20**

This man has transanal evisceration of the small bowel. At laparotomy, the small bowel was observed to have herniated through a longitudinal tear in the anterior rectum. Avital small bowel was repositioned into the abdomen and resected with primary anastomosis. The rectosigmoid was resected with construction of an end colostomy. Transanal evisceration of the small bowel is a rare entity that carries a high mortality and may be caused by thinning of the anterior rectum due to chronic prolapse<sup>1</sup>.

# References

1 Morris AM, Setty SP, Standage BA, Hansen PD. Acute transanal evisceration of the small bowel: report of a case and review of the literature. *Dis Colon Rectum* 2003; **46**: 1280–1283.