Predicting what can go wrong at endoscopic ultrasound: a large series experience

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Objective Although prior studies have evaluated complications following endoscopic ultrasound (EUS), data on the incidence of unplanned events at EUS, defined as any deviation from the preprocedure plan, are lacking. The aim of this study was to define the incidence, nature, clinical predictors and implications of unplanned events at EUS.

Design Case control study.

Setting Tertiary referral centre.

Patients 4624 consecutive patients undergoing EUS during a 6 year period were enrolled. For each patient with an unplanned event, two patients with a successful EUS in the same calendar year were randomly selected as controls.

Main outcome measurements Unplanned events occurring prior to, during or after EUS procedures were prospectively recorded in a database.

Results 192/4624 patients had an unplanned event (4.1%). In all, 2.1% had a failed procedure for anatomical reasons, 1.3% because of restlessness despite standard sedation and 0.5% for technical reasons. Adverse events occurred in 0.2%. There was no mortality but 4/6 patients with adverse events had to be admitted to hospital (2/4 operated). Eighty-two per cent of patients with an unplanned event had incomplete examinations, 14% had no procedure performed and 4% had complete procedures. In a multivariate analysis, only Afro-Caribbean patient origin, inpatient procedure and cancer staging procedure were independently related to unplanned events ($p < 0.05$ for all).

Conclusions Unplanned events at EUS are mainly due to anatomical reasons and restlessness, despite sedation. They commonly result in incomplete examination and are related to Afro-Caribbean origin, inpatient procedure and cancer staging.

Introduction

Endoscopic ultrasound (EUS) is one of the most accurate imaging technologies for the diagnosis and staging of gastrointestinal malignancies as well as for the diagnostic work-up of patients with pancreaticobiliary disorders.^{1–3} Also, EUS is

frequently undertaken to obtain tissue for histological diagnosis⁴ and it is being increasingly used to perform interventional procedures such as EUS guided drainage of pancreatic pseudocysts.⁵

EUS shares the risks and complications of other endoscopic procedures, including (but not limited to) cardiovascular events and complications of conscious sedation. Certain features of echoendoscopes which have a long rigid tip and EUS guided interventions may be related to the complication risk at EUS.⁶ Prior studies have evaluated complications following EUS, and severe and even lethal complications have rarely been reported.^{6–8} EUS is generally considered to be a safe procedure.^{6–13}

Unplanned events, defined as any deviation from the preprocedure plan, are known to have potentially important clinical and financial implications in gastrointestinal endoscopy.¹⁴ Unplanned events, a broader term that includes—but is not limited to—adverse events or complications, may be related to equipment malfunction, sedation issues or procedure failure because of unexpected findings (eg, failure to perform EUS–fine needle aspiration (FNA) due to intervening blood vessels); they may be related to adverse events as a result of the direct effect of the endoscope on sites or organs transversed or treated during the procedure (eg, perforation, bleeding, pancreatitis) or indirect effects in organs not directly involved in the endoscopic procedure (eg, heart or lungs).¹⁴ Data on the incidence and nature of unplanned events (other than complications) at EUS and their potential clinical implications are largely lacking.

The aim of the current study was to define the incidence and nature of early unplanned events at EUS. A secondary aim was to study the clinical predictors and implications of unplanned events.

Methods

Patients

All unplanned events occurring prior to, during or after EUS procedures (after written informed consent and before discharge from the endoscopy unit) performed at Guy's and St Thomas' hospital in London, UK, between January 2001 and December 2007 were identified. All patients undergoing EUS in this period had been prospectively registered in an endoscopy database along with the indication of the procedure, endosonographer, type and amount of sedation, EUS findings and any unplanned event. For each patient with an unplanned event, two patients with a successful EUS in the same calendar year were randomly selected from the database as controls (case control study). The study protocol was approved by the institutional review board of the hospital.

EUS procedure

Procedures were carried out in a standard fashion by one of two experienced endosonographers (a consultant gastroenterologist (JM) or a nurse endoscopist trained in EUS) under conscious sedation using intravenous fentanyl and midazolam. Conscious sedation was administered by the endosonographer. During the EUS procedure, supplemental oxygen was administered routinely to all patients and pulse, saturation as well as arterial blood pressure were monitored. Endosonography was performed using the radial echoendoscopes Olympus GF-UM20 or GF-UM200 and/or the linear echoendoscopes Olympus GF-UCT240 (Olympus/KeyMed, Southend-on-Sea, UK). Stenotic malignant oesophageal tumours that could not be transversed with a standard radial echoendoscope were staged with a non-optical wire guided slim probe (Olympus MH-908; Olympus/KeyMed); oesophageal dilatation was not performed. After the procedure, all patients were observed in a recovery unit by experienced endoscopy staff. Patients had periodic evaluations by the nursing staff, and pulse, saturation and arterial blood pressure were monitored. Laboratory blood tests were not obtained routinely. Patient recovery time generally ranged between 1 and 3 h. Patients were subsequently discharged from the endoscopy unit (outpatients) or returned to a medical or surgical ward (inpatients).

Data collection

Data extracted from the endoscopy database and patient files included demographics (age, gender, race) and clinical factors such as indication, instrument type (linear/radial), EUS-FNA, endoscopist, in/outpatient procedure, sedative type and dose, comorbid illness and patient medications. For patients with unplanned events, the nature of the event was also registered and the procedure was classified as complete, incomplete or 'not started'. Also, data on the clinical implications of unplanned events were extracted from the patient files of patients followed-up in our institution.

Statistical analysis

Data are expressed as mean (SD) or n (%), as appropriate. The Student's *t* test or the Mann-Whitney test was used for significance calculations of differences between groups, as appropriate. The χ^2 or Fisher's exact test was used for comparisons between qualitative variables, as appropriate. The Pearson's coefficient was calculated for correlation analysis. In an attempt to explore independent predictors for unplanned events, all parameters that were univariately correlated at <0.1 with unplanned events were entered into a forward conditional logistic regression analysis. All tests were two tailed and conducted at a 5% significance level.

Results

Overall, 192 out of 4624 patients (4.1%) undergoing an EUS procedure in the 6 year study period had an unplanned event. No patient had more than one unplanned event. No particular trend (increase or decrease) could be seen in the frequency of unplanned events during the study period (figure 1). Unplanned events were most commonly due to anatomical factors or patient restlessness/discomfort (leading to incomplete or failed procedures) whereas technical factors and adverse events were less common (table 1). The proportions of patients with oesophagogastric, staging, linear echoendoscope or EUS-FNA/intervention procedures within groups of different demographic or clinical variables are shown in table 2.

Clinical implications of unplanned events

A total of 157 of 192 (82%) patients with unplanned events at EUS had incomplete examinations, 28/192 (14%) had no procedure performed and 7/192 (4%) had complete procedures performed. As the majority of patients undergoing EUS in our institution are referred from other hospitals, further clinical implications of unplanned events could be assessed only in 52/192 (26%) cases: those with other types of unplanned

Figure 1 Frequency of unplanned events on endoscopic ultrasound in each year of the study period.

Table 1 Nature and frequency of unplanned events occurring at endoscopic ultrasound during the 6 year study period

Adverse events	11 (0.2%)
Allergic reaction to sedation	3
Desaturation	2
Supraventricular tachycardia	2
Duodenal perforation	1
Gallbladder perforation	1
Bleeding from gastroduodenal artery post EUS–FNA	1
Bleeding in pancreatic cystic lesion post EUS–FNA	1
Anatomical factors leading to incomplete or failed procedure	98 (2.1%)
Strictures not transversed*	83
Previous gastric surgery	12
Oesophageal pouch	2
Large diverticulum in the second part of the duodenum	1
Technical factors leading to incomplete or failed procedure	23 (0.5%)
Oesophageal stent in situ	6
Excessive looping of echoendoscope in the stomach	4
Excessive food remnant in the stomach	2
EUS–FNA not performed due to clopidogrel/warfarin	3
EUS–FNA not performed due to intervening blood vessel	2
EUS–FNA not performed due to mobile lesion	1
EUS–FNA not performed due to patient coughing	1
Pancreatic pseudocyst not drained due to distance from stomach wall	1
Equipment failure	1
Unspecified reasons for failing to obtain good views	2
Patient restlessness/discomfort leading to incomplete or failed procedure	59 (1.3%)
Consent withdrawal prior to procedure start	1 (0.02%)
Total	192 (4.1%)

Total number of procedures, n=4624.

*Mostly malignant oesophageal strictures encountered during oesophageal cancer staging.

EUS–FNA, endoscopic ultrasound guided–fine needle aspiration.

events followed-up at our institution (41/192) or those with early adverse events (11/192). A change in the care plan following an unplanned event on EUS occurred in 29/52 (56%) patients whereas the rest of the patients (23/52, 44%) were followed-up with extra outpatient clinic appointments. Fifteen of 29 patients had a follow-up abdominal scan, mostly MR cholangiopancreatography or CT, 3/29 had endoscopic retrograde cholangiopancreatography (ERCP) (one experiencing post-ERCP sepsis with prolonged hospital admission), 4/29 had percutaneous biopsies and 1/29 had a repeat successful EUS–FNA. In all, 4/29 patients had adverse events requiring unplanned hospital admissions. One patient who had a duodenal perforation and another one with a gallbladder perforation were admitted to hospital and underwent surgery. They both had an uneventful recovery and were discharged 6 days later. One of the patients with adverse events had fast atrial fibrillation during the procedure and was admitted to a medical ward for medical treatment. He was discharged 3 days later. One patient experienced luminal gastrointestinal bleeding following puncture of the gastroduodenal artery at EUS–FNA and was treated in the same endoscopic session with metal clips. Bleeding was controlled adequately with endoscopic therapy and he did not require blood transfusions. He was admitted to a medical ward for observation and was discharged the following day. All other patients experiencing an adverse event were discharged from the endoscopy unit after medical therapy. There was no mortality and all patients with adverse events made a complete recovery.

Factors associated with unplanned events at EUS

In univariate analysis, unplanned events were related to non-Caucasian origin but not to age, gender or comorbidity (table 3). In particular, patients of Afro-

Table 2 Proportions of patients with oesophagogastric, staging procedure, linear echoendoscope or EUS guided FNA/ intervention procedures within groups of different demographic and clinical variables in the cohort of patients with unplanned events

	Age >60 vs ≤60 year†	Male vs female gender	Caucasian vs non-Caucasian	Nurse vs physician endosonographer	Comorbidity (yes vs no)‡	Inpatient vs outpatient	Regular opiates or benzodiazepines (yes vs no)
Oesophagogastric EUS§	62% vs 33%*	53% vs 47%	51% vs 11%*	72% vs 41%*	38% vs 73%*	23% vs 55%*	22% vs 54%
Linear echoendoscope	23% vs 21%	26% vs 17%	21% vs 30%	0% vs 30%*	25% vs 14%	32% vs 20%	44% vs 18%
Upper GI cancer staging	61% vs 27%*	50% vs 43%	45% vs 7%	74% vs 36%*	35% vs 70%	23% vs 52%*	22% vs 51%
EUS guided FNA or intervention	6% vs 11%	6% vs 11%	9% vs 11%	0% vs 11%*	6% vs 5%	16% vs 6%	11% vs 8%

n=192.

*p<0.05.

†The mean age in the cohort of patients with unplanned events at EUS was 60 years.

‡Patients who had other types of disease apart from the disorder for which EUS was performed.

§Procedures done for indications related to the oesophagus, stomach or duodenum as opposed to liver/biliary and pancreatic indications.

EUS, endoscopic ultrasound; FNA, fine needle aspiration; GI, gastrointestinal.

Table 3 Demographic and clinical data in cases with unplanned events at EUS (n=192) and controls with uneventful EUS procedures

	Patients with unplanned events	Patients without unplanned events	p Value
Age (year)	60 (17)	59 (18)	0.702
Male	83/192 (43%)	173/384 (45%)	0.727
Non-Caucasian	27/94 (29%)	43/295 (15%)	0.003
Midazolam (mg)	8.6 (3.9)	8.5 (3.0)	0.648
Fentanyl (µg)	100 (32)	97 (30)	0.303
Oesophagogastric EUS*	96/192 (50%)	152/384 (40%)	0.021
Upper GI cancer staging	90/192 (47%)	113/384 (29%)	<0.001
Linear echoendoscope	42/192 (22%)	100/384 (26%)	0.274
EUS guided FNA or intervention	15/192 (8%)	63/384 (16%)	0.004
Inpatient procedure	25/192 (13%)	20/384 (5%)	0.02
Nurse endosonographer	51/192 (27%)	76/384 (20%)	0.196
Comorbidity†	85/122 (70%)	244/377 (65%)	0.316
Regular opiates or benzodiazepines	9/114 (8%)	35/357 (10%)	0.542

n=384. Data are presented as mean (SD) or n (%), as appropriate. The lack of available information about race, comorbidity and regular opiate/benzodiazepine use in some patients explains differences in the denominator.

*Procedures done for indications related to the oesophagus, stomach or duodenum as opposed to liver/biliary and pancreatic indications.

†Patients who had other types of disease apart from the disorder for which EUS was performed.

EUS, endoscopic ultrasound; FNA, fine-needle aspiration; GI, gastrointestinal.

Caribbean origin experienced unplanned events more frequently compared with non-Afro-Caribbean patients (25% vs 9%; $p<0.001$). Unplanned events were not related to the amount of sedation, endosonographer or type of echoendoscope used, but to oesophagogastric indications, in particular upper gastrointestinal cancer staging (as opposed to pancreaticobiliary indications), as well as inpatient and non-FNA procedures (table 3).

In multivariate analysis, unplanned events were found to be independently related to procedure for upper gastrointestinal cancer staging (OR 1.74, 95% CI 1.02 to 3.98), inpatient procedure (OR 4.08, 95% CI 1.92 to 8.65) and Afro-Caribbean patient origin (OR 3.65, 95% CI 1.88 to 7.10).

Compared with outpatients, inpatients had comorbid disease (66% vs 90%; $p<0.05$) and used regular opiates and/or benzodiazepines (5% vs 27%; $p<0.05$) more frequently but did not show any significant differences in the amount of sedation used during EUS or in the types of unplanned events (data not shown).

Patients of Afro-Caribbean origin were younger (46 (16) vs 58 (16); $p<0.05$), experienced restlessness/discomfort more frequently (70% vs 30%; $p<0.05$) and underwent EUS for staging of gastrointestinal malignancies less frequently (9% vs 42%; $p<0.05$) compared with the rest of the cohort. However, patient origin did not affect any of the other factors listed in table 2 (data not shown).

Data on ethnic origin were available for 94/192 (49%) patients with unplanned events on EUS and

for 295/384 (77%) controls. The ethnic composition of the cohort of patients with unplanned events was as follows: British 66/94 (70%), five Caribbean (5%), three Nigerian (3%), two Somalian (2%), one (1%) each of Ghanaian, Ugandan, Chinese, Pakistani and Portuguese, two other unspecified African (2%) and 11 unspecified other (12%). Although level of knowledge of the English language was not registered, we attempted to study its potential effect indirectly by comparing the occurrence of unplanned events in patients from English speaking compared with those from non-English speaking backgrounds. A total of 66/94 patients with an unplanned event on EUS were from an English speaking background (70%), 12/94 (13%) were from a non-English speaking background whereas the language background of 16/94 (17%) patients could not be determined. In controls, 244/295 (83%) patients were from an English speaking background and 32/295 (11%) from a non-English speaking background whereas the language background of 19/295 (6%) patients could not be determined. No significant difference could be found in the proportions of patients from non-English speaking backgrounds between patients with and those without unplanned events ($p>0.05$).

Discussion

A discussion about potential complications is part of normal consent. Equally, being able to discuss the likelihood of failure and its consequences are central to an informed process. In the current study, we found

that unplanned events occurred in 4.1% of all EUS procedures and that they are mainly due to anatomical reasons and restlessness, despite adequate sedation. They commonly resulted in incomplete examinations and were related to cancer staging procedures, inpatient procedures and Afro-Caribbean patient origin. Unplanned events led to changes in the care plan (mainly in the form of further imaging) in more than half of all cases and generated extra outpatient appointments in the rest. To our knowledge, this is the first study to systematically evaluate unplanned events—including, but not limited to, adverse events—in a large volume EUS centre.

In our series of more than 4000 examinations, morbidity (adverse events) following EUS was 0.2% and no mortality was observed, which is in keeping with previous studies showing that EUS is a safe technique.^{6–13} Published data on the incidence of EUS related adverse events vary from 0.03% to 2.9%^{7 8 1–13} and on EUS related mortality from 0% to 0.06%,^{6–8 11–13} with different case mix (diagnostic vs interventional procedures), study design (prospective vs retrospective) and adverse event definitions probably accounting for most of the variation. In the current study, only acute or immediate (until discharge from the endoscopy unit) complications were recorded and patients were not systematically followed-up with a postprocedure re-evaluation. However, our results are similar to the EUS related morbidity rate of 0.3% reported by Mortense *et al*⁷ who performed a prospective study on 3324 consecutive patients undergoing EUS.

Anatomical factors were the most frequent cause of unplanned events. These consisted mainly of malignant strictures in cases of oesophageal cancer staging and cases with previous gastrectomy. About one-fifth to one-third of patients with oesophageal cancer have stenoses at presentation that are significant enough to prevent the passage of a standard echoendoscope.^{15–17} Sequential dilation (often requiring two or three endoscopy sessions) and passage of a standard echoendoscope have been advocated. Early reports suggested high perforation rates with dilation of malignant strictures^{18 19} but subsequent experience indicated perforation rates to be much lower, yet a risk remains.^{20–22} Furthermore, even with this approach, complete staging after dilatation might only be achieved in 62% of cases.²³ Dilation for non-passable oesophageal tumours is not the usual practice in our institution. Instead, we routinely use a non-optical wire guided slim probe. In our experience, this approach permits complete staging in 95% of cases without the need for dilatation.¹⁷ However, during the study period about 80 cases of tight malignant strictures that could not be transversed with the non-optical slim probe accumulated. A detailed analysis of the final staging and outcome of this patient group was beyond the scope of this paper but the staging of the vast majority of these patients relied on CT and positron emission tomography scans.

Although Billroth II gastrectomy per se is not an absolute contraindication for pancreaticobiliary EUS, this is impossible to perform in 9% of cases, and in the remaining, the superior pancreatic head, the pancreatic neck and porta hepatis may not be easy to visualise, especially if a radial echoendoscope is used.²⁴ Experience from ERCP has shown that in 8–29% of cases it might be impossible for the endoscope to be passed to the papilla of Vater²⁵ and perforation may occur in up to 5% of cases.²⁶ Endoscopic access of the papilla might be significantly more difficult to achieve in patients with Roux-en-Y gastrojejunostomy.²⁵ In the current series, 12 patients with previous gastrectomy (mainly Billroth II) could not have a complete pancreaticobiliary EUS with a radial echoendoscope. In view of our experience and the complication risks, we now routinely advocate the use of alternative imaging modalities (such as MR cholangiopancreatography or pancreatic protocol CT scans) in these patients.

EUS procedures on inpatients were four times more likely to result in unplanned events. Inpatients are usually more sick and they are more frequently on regular benzodiazepines or opiates which could influence the incidence of adverse or unplanned events. A previous study has shown that cardiopulmonary events after gastrointestinal endoscopy (including EUS) occur more frequently in inpatients.¹³ However, in our series the frequency of different types of unplanned events did not differ between inpatients and outpatients (data not shown). Thus no firm conclusions can be drawn from the current study as to the particular factors related to unplanned events on EUS performed in inpatients.

Afro-Caribbean origin was found to be an independent predictor of unplanned events, particularly due to discomfort/restlessness during EUS, despite the fact that neither the type nor the amount of sedation used differed from the rest of the patients (ie, paradoxical effect). Ethnic or racial differences in drug pharmacokinetics and pharmacodynamics have been reported^{27 28} and could, at least in part, explain our findings. However, according to a recent report, the incidence of cardiopulmonary events after gastrointestinal endoscopy does not differ among patients with different racial backgrounds¹³ and recent reports suggest that previously published data on racial differences in drug pharmacokinetics and pharmacodynamics should be interpreted with caution.²⁹ In our institution, patients without adequate knowledge of English are given information about their healthcare and give their informed consent to all endoscopic procedures with the help of an interpreter. Although we did not register the level of knowledge of English of patients included in the current study, it is possible that several Afro-Caribbean patients may (to a greater extent compared with Caucasians) have had a non-English language background and thus a worse command of English. Despite the use of an

interpreting service (which is sometimes offered only over the telephone), it is conceivable that Afro-Caribbean patients in our study may have been less informed on the details of their procedure (eg, waiting times, the roles of different members of staff in the endoscopy unit, etc). This may have led to increased anxiety levels prior to EUS which, in turn, could result in poor cooperation and satisfaction during gastrointestinal endoscopy.³⁰ We attempted to study the potential effect of level of knowledge of English indirectly by comparing the proportion of patients from non-English speaking countries among cases and controls but could not identify any significant difference. This could be due to loss of power as the country of origin of some patients could not be defined, and also country of origin is a less accurate surrogate for the command of English an individual patient has. Further studies are warranted to fully delineate the potential differences in the incidence of unplanned events among patients of various racial/ethnic backgrounds.

The vast majority (96%) of patients with unplanned events during EUS had either an incomplete or no procedure performed. Many of these patients needed to undergo other imaging or interventional (eg, ERCP) procedures, with some experiencing subsequent complications. Despite the fact that no cost analysis was undertaken in the current study, our findings indicate that the work-up of patients with failed procedures probably involves significant healthcare resources. This is in keeping with a previous report showing that 3.6% of patients undergoing ERCP had a failed procedure, which had important financial and clinical implications.³¹ Although some of the unplanned events may be difficult to predict and avoid (eg, some adverse events), the risk of some others occurring may be easier to minimise. In particular, patient discomfort or restlessness (accounting for 31% of all unplanned events in our cohort, especially in Afro-Caribbean patients) could probably be avoided by the use of propofol sedation. Propofol administration has been shown to be superior to other agents with regard to recovery time and physician as well as patient satisfaction.^{32–34} Previous studies have also demonstrated a high level of safety for propofol monotherapy and combination therapy in gastrointestinal endoscopy.³⁵

Certain limitations should be taken into consideration when interpreting the results of the current study. Firstly, although unplanned events were registered prospectively, the study was otherwise retrospective. Thus patients were not followed-up systematically to ensure complications manifesting after the first hours post-EUS were identified. Secondly, most patients were referred from other institutions so the implications of unplanned events remain unknown for a large proportion of the cohort. Lastly, the current study was performed in a single centre which accepts tertiary

referrals for EUS and, despite its large size, conclusions may not be generalised to other practice settings.

In conclusion, the proportion of EUS procedures complicated by unplanned events was 4.1% in a tertiary referral centre. Unplanned events were mainly due to anatomical reasons and restlessness, despite adequate sedation, and they were related to upper gastrointestinal cancer staging, inpatient procedures and Afro-Caribbean patient origin. Unplanned events commonly resulted in incomplete examinations and, thus, seemed to have significant clinical implications.

Competing interests None.

Ethics approval This study was conducted with the approval of the institutional review board.

Provenance and peer review Not commissioned; externally peer reviewed.

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