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Clinical coding data algorithm to categorize type of gastrointestinal bleeding as a primary reason for massive transfusion: Results from the Australian and New Zealand Massive Transfusion Registry

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ABSTRACT

Background

Management of major gastrointestinal bleeding (GIB) may require massive transfusion (MT), but limited data are available. Upper and lower GIB have different etiologies, prognosis, bleeding patterns and outcomes. Better understanding of current transfusion management and outcomes in these patients is important. We sought to define and validate an algorithm based on clinical coding data to distinguish critical upper and lower GIB using data from the Australian and New Zealand Massive Transfusion Registry (ANZ-MTR).

Study Design and Methods

ANZ-MTR hospital-source data on adult patients receiving a MT (defined as ≥ 5 red cell units within 4 hours) for any bleeding context was used. An algorithm allocating ICD-10-AM codes into 'probable' or 'possible' causes of GIB was developed and applied to the ANZ-MTR. Source medical records of 69 randomly selected cases were independently reviewed to validate the algorithm.

Results

Of 5,482 MT cases available from 25 hospitals, 716 (13%) were identified as GIB with 538/716 (75%) categorized 'probable' and 178/716 'possible' GIB. Upper and lower GIB causes of MT were identified for 455/538 (85%) and 76/538 (14%) 'probable' cases, respectively; 7/538 (1.3%) cases had both upper and lower GIB. Allocation by the algorithm into a 'probable' GIB category had a 95.7% (CI 90-100%) positive predictive value when validated against source medical records.

Conclusion

An algorithm based on ICD-10-AM codes can be used to accurately categorize patients with luminal GIB as the primary reason for MT, enabling further study of this critically unwell and resource-intensive cohort of patients.

KEYWORDS: gastrointestinal, hemorrhage, transfusion, protocol, validation, registry, clinical outcomes

Introduction

Acute gastrointestinal bleeding (GIB) is a common medical emergency, with an estimated incidence of 100-180 per 100,000 adults.[1-3] Management may require a range of health resources including hospital admission, endoscopic intervention and blood transfusion. Bleeding from the upper gastrointestinal tract is the most frequent site of acute GIB and has been reported to account for more than two-thirds of all GIB; lower GIB accounts for approximately 20% of cases, with obscure and small bowel bleeding making up the remaining cases[4].

Management of acute GIB has been reported to utilize around 9-21% of all blood products transfused,[5, 6] and approximately 14% of massive transfusion (MT) events[7]. A restrictive transfusion strategy for acute upper GIB, a concept spearheaded by Duggan,[8, 9] has gained impetus with growing evidence suggesting this approach reduces risk of re-bleeding and mortality[10]; however optimal transfusion practice and clinical outcomes remain undefined. The two largest studies published on restrictive versus liberal transfusion strategies excluded patients with exsanguinating hemorrhage,[11, 12] and thus data on optimal transfusion management in acute upper GIB requiring MT are very limited. The recent International Consensus Conference on patient blood management recommended more research into the transfusion management of patients with acute GIB[13].

To study these events requires a robust classification algorithm that can accurately and reproducibly identify this cohort of patients. Hospital administrative databases contain a range of data on diagnoses, clinical management, outcomes and health care resource utilisation. Although the purpose of these databases is predominantly administrative, they also provide valuable information for medical research. Previous studies have used hospital electronic records and clinical coding classifications (e.g. International Classification of Diseases, 10th edition; ICD-10 codes) to define non-critical upper

GIB[14]. However there are numerous causes of GIB and many of these etiologies, for example gastritis, are not relevant to critical bleeding requiring MT. Understanding the characteristics, management and outcomes of patients with critical GIB requiring MT allows further studies to evaluate whether the significant utilisation of valuable blood products in this clinical setting improves mortality or morbidity of these patients.

The Australian and New Zealand Massive Transfusion Registry (ANZ-MTR) captures hospital-sourced primary data on all adult patients who have received a MT[15]. At the time of this study, data were available from 25 participating hospitals. The ANZ-MTR gathers data from administrative datasets, including hospital diagnostic and procedure codes, laboratory results, detailed blood product use and patient outcomes. This registry provides the unique opportunity to evaluate the utility of diagnostic and procedure codes to identify and classify patients with critical GIB requiring MT, which has not previously been described.

The purpose of this study was to develop and validate an algorithm based on clinical diagnostic and procedure codes that enables identification and classification of GIB as the reason for MT.

Materials and Methods

Study cohort

The ANZ-MTR contains data for patients ≥ 18 years of age who received a MT, defined as ≥ 5 red blood cell units within a 4-hour period for any bleeding context[16]. MT cases in the registry have been algorithmically categorized into broad groups of critical bleeding events as previously described[17]. In summary, the critical bleeding categories include trauma, obstetrics, surgical bleeding (cardiothoracic, vascular, liver, other surgery), GIB, cases with both GIB and surgical bleeding, and other medical conditions. Data for 5,482 MT cases that occurred between January 2011 and September 2015, provided by 25 participating hospitals, were available at the time of analysis. For this study, all MT cases allocated to the 'GIB' category by the registry's in-built bleeding context algorithm were selected ($n = 716$ GIB MT cases).

The study was conducted within the existing ethics approval conditions of the ANZ-MTR, approved by the Human Research Ethics Committees of Monash University and participating hospitals.

Data collection

1) ANZ-MTR data

The ANZ-MTR uses electronic data extraction and data linkage methodologies as previously published[15]. Briefly, identifiable patient data from hospital data sources, including Health Information Services databases (patient demographics, admission data and clinical coding data) and Laboratory Information Systems (transfusion history and laboratory results) are electronically extracted by staff at participating hospitals and securely sent to the ANZ-MTR via secure file transfer protocol. Each MT case is assigned a unique identification number by the in-built ANZ-MTR data importation process. In Australia and New Zealand, hospital admission episodes are coded according to the Australian modification of the International Classification of Diseases, 10th Edition codes (ICD-10-AM) and the Australian Classification of Health Intervention (ACHI) [18]. For this study, ICD-10-AM diagnostic and ACHI procedure coding data for each of the GIB MT cases were accessed from the ANZ-MTR.

2) Hospital medical chart review

A standardized validation case report form was specifically developed for this study. A validation sample of 69 GIB MT cases (i.e. approximately 10% of all 716 GIB MT cases) was randomly selected. Hospital clinical staff reviewed source medical records to identify the reason for the MT (i.e. 'upper GIB', 'lower GIB', 'more than one site of bleeding', 'if more than one site of bleeding, the primary site of bleeding that led to massive transfusion' and 'other (non-GI) cause of bleeding') and the intervention performed (i.e. 'gastroscopy', 'more than one gastroscopy', 'colonoscopy', 'radiological embolization for GIB' and 'surgery for GIB').

Case classification

Due to the substantial heterogeneity of etiologies and large number of clinical codes for GIB, other investigators have used a process that grouped ICD-10 codes into categories of 'probable' and 'possible' causes of upper GIB[14]. In this study, a similar approach was used to develop the refined coding algorithm for the GIB MT cohort. 'Probable' cases were those that contained diagnostic ICD-10-AM and procedural codes that clearly defined cause, investigation or therapies for a GIB episode requiring MT and 'possible'

cases were those that did not include any of these diagnostic nor procedure codes, but included less specific, general GIB codes (Table 1). GIB MT cases containing both 'probable' and 'possible' codes were categorised into the 'probable' cohort, however cases with only 'possible' codes in the absence of any 'probable' codes were classified into the 'possible' cohort. The 'probable' cohort was then further divided into upper or lower gastrointestinal causes of GIB MT, based on specific diagnostic and/or procedure codes in the coding records of each case.

Statistical analysis

Descriptive analysis was conducted to provide an indication of the frequency of 'probable' and 'possible' GIB MT cases. The sample size of approximately 10% of total GIB MT cases for the medical record review/validation of the coding algorithm was selected on the basis of providing suitable precision in the estimated positive predictive values. All analyses were conducted using STATA statistical analysis software, version 15.1 (StataCorp, College Station, TX, USA).

Results

Case classification by the refined algorithm

Of the total 5,482 MT cases from 25 hospitals available in the ANZ-MTR at time of this analysis, 716 (13%) were categorized as 'GIB' by the ANZ-MTR's in-built algorithm. Application of the refined classification algorithm to these 716 GIB MT cases, yielded 538/716 (75%) cases that had 'probable' codes and 178/716 (25%) cases that had only 'possible' ICD-10-AM codes (Figure 1).

Of the 'probable' cohort, 455/538 (84.6%) cases were categorized by the refined algorithm as upper gastrointestinal causes of GIB MT and 76/538 (14.1%) cases were lower gastrointestinal causes of GIB MT (Figure 1). There were 7/538 (1.3%) cases with both upper and lower gastrointestinal causes of bleeding identified.

The ICD-10-AM diagnostic codes used in the refined classification algorithm to define the 'probable' cohort, divided into upper and lower GIB etiologies, and the frequency of each of these codes in the GIB cohort, are shown in Table 2. The most common diagnostic GIB ICD-10-AM code was 'I983 - Oesophageal varices with bleeding in

diseases classified elsewhere' (n = 118), followed by 'K264 - Chronic or unspecified duodenal ulcer with haemorrhage' (n = 109). The ACHI procedure codes used in the classification algorithm, in conjunction with the listed ICD-10-AM diagnostic codes, are shown in the online Supplementary Tables S1 and S2.

The frequency of non-specific ICD-10-AM codes indicative of GIB (i.e. hematemesis, melena and gastrointestinal hemorrhage unspecified) in the 'probable' compared with 'possible' cohort are shown in Table 3. There was a much higher occurrence of these codes used in the 'possible' cohort compared to the 'probable' cohort.

Validation

Completed case report forms were received for all 69 randomly selected cases. In 66/69 (95.6%) cases, medical chart review was concordant with the classification assigned by the refined classification algorithm; 34/36 upper GIB (94.4% concordance), 10/10 lower GIB (100% concordance) and 22/23 'possible' GIB (95.7% concordance). For the two cases incorrectly allocated by the algorithm to upper GIB, medical record review identified the source of bleeding in the jejunum (1 case) and bleeding from stoma varices (1 case). Medical chart review of the 'possible' cases confirmed that 22 cases were not luminal GIB, including, but not limited, to gastrointestinal surgical and anastomotic bleeds and incomplete data. The one remaining 'possible' case, which only had limited and non-specific coding data available, was identified by medical chart review to be an elderly patient with a massive GIB at hospital arrival; blood was transfused, but the patient was palliated in the emergency department.

Compared to the source medical records, the algorithm had strong positive predictive values (PPV) of 95.7% (CI 90.0 – 100%) and 95.7% (CI 87.3 – 100%) for the 'probable' and 'possible' cohorts, respectively (Table 4).

Discussion

This study demonstrated that our refined classification algorithm, based on ICD-10-AM diagnostic and procedure codes, when applied to hospital clinical coding data, can accurately categorize patients with primary upper and lower GIB requiring MT. The algorithm allows delineation of the clinical profiles of these specific groups of critically

ill GIB patients, and informs review of therapeutic and blood transfusion interventions and outcomes.

Hospital administrative databases have previously been used to describe cohorts of patients with GIB[14, 19]; however whether coding data can accurately categorize patients with primary GIB requiring MT has not previously been evaluated. Identification and classification of GIB using ICD-10-AM codes from administrative datasets is complicated by the substantial heterogeneity of ICD-10-AM codes and etiologies for GIB. Upper GIB related ICD-10 codes have previously been published[14, 19]; however these lists could not be used for the purpose of this study, as the lists included ICD-10 codes for GIB etiologies that would not cause GIB requiring MT (e.g. gastritis [K29], esophagitis [K20]) and other broad criteria such as codes for blood transfusion or cross matching. Similarly, causes of lower GIB such as malignancy, colonic angiodysplasia, ischemic colitis and bleeding secondary to inflammatory bowel disease are unlikely to cause GIB requiring MT. The caveats to this include lower GIB from Crohn's disease, endoscopic mucosal resection post-polypectomy bleeding or colonic Dieulafoy lesions; however on review of the diagnostic and procedure codes of all 716 GIB MT cases, there were no coding data to suggest these were the cause of any of the GIB events. Thus although possible, these lower GIB events are rare and unable to be clearly delineated as the cause of bleeding requiring MT. Consequently, new criteria were required for a list of codes that would differentiate primary GIB as the reason for MT from cases where GIB was a consequence of contemporaneous or previous interventions, or the available coding data was too non-specific.

Of the total GIB cohort in the ANZ-MTR, 75% of cases were identified by the refined classification algorithm as being 'probable' primary GIB requiring MT; of these 85% had an upper GIB etiology and 14% had a lower GIB etiology. These proportions of upper and lower GIB are consistent with previously published reports.⁴ Validation of these assignments by comparing with source medical records demonstrated a 95.7% accuracy of this classification algorithm, with 66/69 of the randomly selected validation cases confirmed as correctly categorized into 'probable' upper GIB, 'probable' lower GIB or 'possible' GIB. Strong PPVs were demonstrated in this study by the refined classification algorithm compared to the source medical records, with PPV of 95.7% (CI 90.0 – 100%) and 95.7% (CI 87.3 – 100%) for the 'probable' and 'possible' cohorts respectively. These findings are similar to a Danish study that compared PPV of ICD-10 codes for classification of peptic ulcers validated against the endoscopic findings; the PPV of ICD-10

codes for peptic, gastric and duodenal ulcer diagnosis was found to be 95.6%, 90.3% and 94.4% respectively[20].

This study has several limitations. The ANZ-MTR relies on coding data performed by hospitals predominantly for administrative and funding purposes, rather than primarily for medical or research purposes. ICD-10 coding accuracy has been estimated to be between 83 – 87%[21]. There is a risk that the ‘probable’ list of codes used for our refined classification algorithm was too restrictive with associated selection bias. However, applying an algorithm that is too broad could result in capturing a cohort that includes cases in which GIB requiring MT was a consequence of other significant co-morbidities and procedures, such as surgery or other medical indications.

The ‘possible’ cohort may contain *bona fide* primary GIB MT cases, but without a precise cause of GIB documented in the hospital’s clinical codings, these cases would not be captured into the ‘probable’ cohort; for example, the single case identified in the validation process in which no specific etiology was recorded and death occurred quickly due to uncontrollable GIB despite MT. Furthermore, the cases in the ANZ-MTR relate only to patients who reached hospital and received a MT there. In a recently published study of major hemorrhage-related fatalities reported to the coroner, GIB accounted for 28% of all such deaths, of which only 13% survived to reach hospital and/or receive any transfusion[22].

The strength of this refined classification algorithm is that it accurately defined a large sample of 538 cases with primary luminal GIB that required MT of ≥ 5 red cell units within 4 hours – truly acute GIB and a patient cohort for which limited data are available. The data were obtained from a large and diverse group of 25 hospitals from around Australia and New Zealand, and the validation group was randomly selected. Therefore, our results are likely generalizable to other settings, with potential to apply this algorithm to other clinical databases world-wide that capture transfusion data.

In summary, we have shown that ICD-10-AM diagnostic and procedure coding data can be used to accurately classify cause of GIB in patients receiving a MT. This is important, as GIB is one of the most common indications for MT (i.e. approximately 13% of cases in the ANZ MTR), and more research is needed. Identification of this important group of patients with GIB requiring MT allows further research into evaluation of current therapeutic management strategies, intensive care unit utilization, predictors and risk of

mortality. This will inform future therapeutic strategies and allocation of health care resources.

Contributors

SK, ZM and EW conceived the study. SK, ZM and EW designed the study. SK and RS acquired the data. MT analysed the data. SK, ZM, EW, RS and MT interpreted data. SK drafted the manuscript. SK, RS, ZM, MT, PG, GB and EW revised the manuscript. All authors approved the final version.

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Table 1. Categories of ICD-10-AM and procedural codes that may be associated with a GIB requiring a massive transfusion

Study categorization: 'probable' or 'possible'	Criteria for study categorization
Probable	ICD-10-AM codes for upper or lower GIB diagnosis that could require massive transfusion (see Table 2)
	Upper gastrointestinal endoscopy codes (see Supplementary Table S1)
	Any procedural code for an upper or lower gastrointestinal procedure plausible for managing a

	bleeding episode (see Supplementary Table S2)
Possible	Any general ICD-10-AM code for GIB e.g. 'K92.2 gastrointestinal haemorrhage unspecified'
	ICD-10-AM codes for symptoms indicating a GIB e.g. melena, hematemesis
	ICD-10-AM codes for upper gastrointestinal pathology that might be associated with GIB but would not require massive transfusion e.g. esophagitis, gastritis

Table 2. The frequency of diagnostic ICD-10-AM codes used to define upper and lower GIB requiring massive transfusion in the total 'probable' GIB cohort

Diagnosis group	ICD-10-AM	ICD-10-AM description	Frequency,* n
Upper GIB, n = 455	K226	Gastro-oesophageal laceration-bleeding syndrome	18
	I850	Oesophageal varices with bleeding	18
	I859	Oesophageal varices without bleeding	6
		Oesophageal varices without bleed in	18
	I982	diseases classified elsewhere	
		Oesophageal varices with bleeding in	118
	I983	diseases classified elsewhere	
	I864	Gastric varices	27
	K250	Gastric ulcer acute with bleeding	42
	K251	Gastric ulcer acute with perforation	2
		Acute gastric ulcer with haemorrhage	0
	K252	and perforation	
		Chronic or unspecified gastric ulcer	56
	K254	with haemorrhage	
		Chronic or unspecified gastric ulcer	0
	K255	with perforation	

	Chronic or unspecified gastric ulcer	6
K256	with haemorrhage and perforation	
K270	Peptic ulcer acute with bleeding	0
K271	Peptic ulcer acute with perforation	0
	Acute peptic ulcer with haemorrhage	0
K272	and perforation	
	Chronic or unspecified peptic ulcer	6
K274	with haemorrhage	
	Chronic or unspecified peptic ulcer	0
K275	with perforation	
	Chronic or unspecified peptic ulcer	0
K276	with haemorrhage and perforation	
	Gastrojejunal ulcer chronic or	3
K284	unspecified with haemorrhage	
	Gastrojejunal ulcer chronic or	2
K285	unspecified with perforation	
	Gastrojejunal ulcer chronic or	0
K286	unspecified with haemorrhage and	
	perforation	
K260	Duodenal ulcer acute with bleeding	26
K261	Duodenal ulcer acute with perforation	1
	Acute duodenal ulcer with	7
K262	haemorrhage and perforation	
	Chronic or unspecified duodenal ulcer	6
K265	with perforation	
	Duodenal ulcer chronic or unspecified	29
K266	with haemorrhage and perforation	
	Chronic or unspecified duodenal ulcer	109
K264	with haemorrhage	
	Acute gastrojejunal ulcer with	1
K280	bleeding	
	Acute gastrojejunal ulcer with	0
K281	perforation	
	Acute gastrojejunal ulcer with	0
K282	haemorrhage and perforation	

Lower GIB, n = 76	K570	Diverticular disease of small intestines with perforation and abscess	0
	K221	Ulcer of oesophagus	24
	C15	Malignant neoplasm of oesophagus	6
	C16	Malignant neoplasm of stomach	3
	C17	Malignant neoplasm of small intestine	4
	C22	Malignant neoplasm liver intrahepatic bile duct	8
	K5701	Diverticulitis small intestine with perforation and abscess with bleeding	0
	K5721	Diverticulitis large intestine with perforation and abscess with bleeding	3
	K5741	Diverticulitis both small and large intestines with perforation and abscess with bleeding	0
	K5781	Diverticulitis intestine, part unspecified, with perforation and abscess with bleeding	0
	K5731	Diverticulosis large intestine without perforation or abscess with bleeding	33
	K5733	Diverticulitis large intestine without perforation or abscess with bleeding	5
	K5711	Diverticulosis small intestine without perforation or abscess with bleeding	6
	K5713	Diverticulitis small intestine without perforation or abscess with bleeding	0
	K5751	Diverticulosis both small and large intestine without perforation or abscess with bleeding	0
	K5753	Diverticulitis both small and large intestine without perforation or abscess with bleeding	1
	K5791	Diverticulosis of intestine, part unspecified, without perforation or	3

*Note, some 'probable' GIB MT cases were coded with more than one of the listed codes. Other cases, mostly lower GIB cases, did not have any of the listed diagnostic codes, but rather had non-specific GIB diagnostic codes (see Table 3) and/or specific procedure codes (see Supplementary Tables S1 and S2) that determined categorization by the classification algorithm.

Table 3. Frequency of non-specific GIB ICD-10-AM codes in the 'probable' cohort and 'possible' GIB MT cohort

ICD-10-AM code	ICD-10-AM description	Frequency	
		'Probable' cohort n = 538	'Possible' cohort n = 178
K920	Haematemesis	26	23
K921	Melaena	42	57
K922	Gastrointestinal haemorrhage unspecified	83	138
Total		151	218

Table 4. Positive predictive values of the algorithm to identify 'probable' and 'possible' causes of GIB requiring massive transfusion versus validated data from source medical records.

Algorithmic classification of GIB	Validated confirmation of GIB		Positive predictive value (95% CI)
	Yes	No	
'Probable' upper GIB	34	2	94.4% (87.0% - 100%)
'Probable' lower GIB	10	0	100%

Total 'probable'	44	2	95.7% (90.0% - 100%)
Total 'possible'	22	1	95.7% (87.3% - 100%)

CI – Confidence Interval

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Figure Legends

Figure 1.

Flow chart of categorization of gastrointestinal bleeding (GIB) cases from the Australian and New Zealand Massive Transfusion Registry (ANZ-MTR) cohort by the refined classification algorithm. The algorithm assigned cases based on data from hospital diagnostic and procedure databases. The 'probable' cohort were cases that had specific coding data indicative of intestinal site of bleeding and primary GIB as the most likely reason for massive transfusion; the 'possible' cohort were cases that had coding data less definitive of site or cause of GIB as the reason for massive transfusion.

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