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Clinical Characteristics and Mortality of Life-Threatening Events Requiring Cardiopulmonary Resuscitation in Gastrointestinal Endoscopy Units

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Abstract: Little is known about life-threatening events during gastrointestinal endoscopy (GIE). This study aimed to evaluate the clinical characteristics of emergency conditions requiring cardiopulmonary resuscitation (CPR) in GIE units and to assess the risk factors for mortality in these cases.

We retrospectively collected life-threatening cases that occurred in the GIE units of 6 tertiary hospitals from January 2012 to June 2014. Cases were defined as alert calls for resuscitation teams in emergency situations of respiratory failure or cardiac arrest. Demographic data, clinical features, and probable causes were assessed. Factors associated with mortality were elucidated using logistic regression analysis.

Among 263,426 endoscopies, 40 cases of CPR (0.015%) occurred during the period (male 67.5%, median age 62 yr). Gastrointestinal bleeding (GIB), such as hematemesis or melena, was the most common indication for endoscopy (55%). The types of clinical situations encountered were as follows: respiratory insufficiency (47.5%), decreased blood pressure (25%), and cardiac arrhythmia (25%). Although most of these conditions were detected during endoscopy (67.5%), one-third of cases (32.5%) were found before or after procedures. The most frequent probable cause of cases was aggravation of underlying diseases (57.5%), such as uncontrolled bleeding or exacerbation of lung disease. Despite efforts to resuscitate, 18 patients (45%) died. GIB was the single independent risk factor for mortality (odds ratio 28.45, 95% confidence interval 1.55–523.33, $P = 0.024$).

Life-threatening situations requiring CPR can occur during endoscopy, even before or after the procedure. Greater attention should be paid while endoscopy is performed for GIB.

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Abbreviations: ASA = American Society of Anesthesiologists, CI = confidence interval, CPR = cardiopulmonary resuscitation, EGD = esophagogastroduodenoscopy, EMR = endoscopic mucosal resection, ERCP = endoscopic retrograde cholangiopancreatography, ESD = endoscopic submucosal dissection, GIB = gastrointestinal bleeding, GIE = gastrointestinal endoscopy, OR = odds ratio.

INTRODUCTION

Gastrointestinal endoscopy (GIE), which consists of esophagogastroduodenoscopy (EGD) and colonoscopy, has been recognized as a pivotal tool leading to dramatic changes in the diagnosis and treatment of many digestive diseases.[1] Because cancer is the leading cause of death, many countries have attempted to establish national cancer control programs to reduce the incidence of cancer and the number of deaths caused by cancer.[2] For instance, to address the high incidence of stomach cancer, South Korea has operated the National Cancer Screening Program since 1999, with a tremendous volume of EGD procedures performed in clinical practice.[2,3] Demand for colonoscopy has also been on the rise because it is an important mode of screening for colorectal cancer in many developed countries.[4,5]

Although GIE is a safe procedure, patients might have cardiopulmonary events potentially related to mortality while undergoing these procedures.[6–8] Recently published data reported the risk of cardiovascular and cardiopulmonary events caused by GIE at 0.3% and 0.9%, respectively.[6,8] However, these studies defined cardiovascular or cardiopulmonary events across a wide range of severities, from very mild clinical episodes, such as transient hypoxia, low oxygen saturation, all types of arrhythmia, or chest pain, to more serious episodes, such as myocardial infarction or respiratory distress. There have been limited data on life-threatening events requiring cardiopulmonary resuscitation (CPR) in GIE unit.

The aims of this study were to evaluate the clinical characteristics of life-threatening events, known as ''code blue'' cases, that developed in GIE units and to assess the risk factors for mortality in these cases.

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PATIENTS AND METHODS

Case Definition and Data Collection

This study was conducted in 6 tertiary hospitals in the Daegu-Gyeongbuk province in the southeastern part of South Korea. Index cases were retrospectively collected from CPR registry data of all hospitals. The registered CPR data of the hospitals included all patients older than 18 years who experienced cardiac arrhythmia or respiratory failure requiring resuscitation or was in need of immediate medical attention in each hospital. We retrieved these life-threatening cases occurring in the GIE units between January 2012 and June 2014 from the registry. Endoscopic procedures described in this study included EGD, colonoscopy, and therapeutic endoscopies, such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). EGD and colonoscopy consisted of all procedures for diagnosis, simple polypectomy, hemostasis, percutaneous endoscopic gastrostomy, endoscopic ultrasonography, and foreign body removal. EMR and ESD were procedures for removal of the lesions more than 2 cm in size. Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic stent insertion were excluded in the study because most ERCP and stent insertion were performed in the radiology department where fluoroscopic guidance was available, not in the GIE unit.

General Management of Life-Threatening Cases in Endoscopy Units

In general, all patients were monitored for blood pressure and O_2 saturation with oximetry in the GIE unit. There was a nurse dedicated to monitoring the patients in the endoscopy room and the recovery room of all hospitals. In the cases without sedative agents, respiratory failure was recognized by decreased conscious level with reduction in O_2 saturation or developing cyanosis. In the cases with sedation, it was noticed by reduction in O_2 saturation or developing cyanosis. When this emergency situation was detected, medical personnel in the endoscopy unit immediately announced ''code blue'' to make an alert call for the special resuscitation team, according to each hospital policy. CPR equipment was available in the endoscopy units of all 6 hospitals.

Data of Clinical Characteristics

We assessed the patients' clinical data, such as co-morbidities, American Society of Anesthesiologists (ASA) classification, and initial vital signs at the endoscopy unit while reviewing their medical records. Information on endoscopy included indication, type of endoscopy (EGD, colonoscopy, and EMR/ESD), time of performance of endoscopy (emergency vs nonemergency) and sedative agents used during the procedures (midazolam, propofol, and meperidine). ''Emergency endoscopy'' was defined as endoscopic examination performed within 8 hr from the decision of the endoscopy.[9] For life-threatening situations, the time when the ''code blue'' was announced (before procedure, intra-procedure, and after procedure), the type of ''code blue'' condition, such as respiratory failure, hypotension, and cardiac arrhythmia (bradycardia or arrest), and the probable causes of the situation were evaluated. These probable causes were related to sedative agents; aspiration; aggravation of underlying diseases, such as uncontrolled bleeding, exacerbation of lung disease, or worsening ischemic heart disease; and the procedure itself, for example, perforation. These characteristics were also used as risk factors for mortality in these cases. Two independent clinical experts (E.S.K. and S.M.L.) determined the probable causes of the cases after a thorough review process. When there was a disagreement regarding the decision, discussion was undertaken between the experts and the physician who was responsible for the case in the hospital. The study was approved by the ethics review committees of the institutional review boards of all of the hospitals participating in the study.

Statistical Analysis

The data are demonstrated as case numbers (%) or medians with ranges. For comparisons of continuous variables, the Mann-Whitney test was used. Differences in categorical variables were assessed with Fisher's exact test. To determine the independent risk factors associated with mortality during endoscopy procedures, logistic regression analysis was performed using variables with statistically significant associations identified in univariate analysis. A 2-tailed P value < 0.05 was considered significant. The statistical analysis was performed with SPSS software, version 14.0 (SPSS, Chicago, IL).

RESULTS

Between January 2012 and June 2014, a total of 263,426 endoscopic procedures (EGD 178,624 [67.8%], colonoscopy 67,389 [25.5%], and EMR/ESD 17,413 [6.6%]) were performed in the endoscopy units of 6 tertiary hospitals in the Daegu-Gyeongbuk province of South Korea. During the same period, life-threatening conditions requiring CPR occurred in 40 cases (0.015%) (male 13, median age 61 years old [26–89]). Most of the conditions (33 cases) occurred during EGD procedures (0.018%, 33/178,624), while 5 and 2 cases occurred during colonoscopy (0.007%, 5/67,389) and therapeutic endoscopy (0.015%, 2/17,413), respectively (Fig. 1).

The most common co-morbidity was malignancy (15, 37.5%), followed by liver cirrhosis (14, 35%) and hypertension (8, 20%). More than half of the cases (27, 67.5%) showed an ASA physical classification score ≥ 3 (condition of severe systemic disease). The largest proportion of the patients (28, 70%) consisted of inpatients, and 1 quarter of the patients was referred from the emergency department when the decision for an endoscopic procedure was made. In terms of the endoscopy indications, gastrointestinal bleeding (GIB), such as hematemesis, melena,

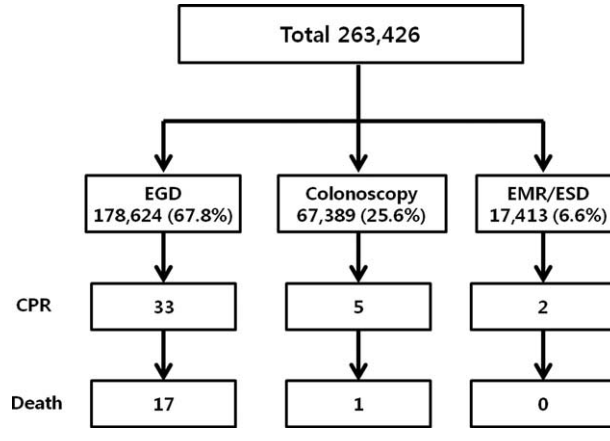

FIGURE 1. Flow chart of the patients. CPR = cardiopulmonary resuscitation, EGD = esophagogastroduodenoscopy, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection.

and hematochezia, accounted for 55% (22 cases), while abdominal pain and therapeutic endoscopy, such as EMR/ESD, accounted for 10% (4 cases) and 5% (2 cases), respectively. Other indications included percutaneous endoscopic gastrostomy, esophageal foreign body, dysphagia, constipation, workup for ovarian cancer, and screening purposes comprising 22.5% (9 cases) of the cases. Twenty-three cases (57.5%) occurred during nonemergency endoscopy (≥8 hr from the decision of the endoscopy) and 17 (42.5%) during emergency endoscopy (<8 hr from the decision of the endoscopy). One-half of the patients (21, 52.5%) were administered sedative agents. The baseline characteristics of the patients are described in Table 1.

TABLE 1. Baseline Characteristics of the Patients

Variables	N = 40
Male, n (%)	13 (32.5)
Age, yr, median (range)	61 (26–89)
Co-morbidities, n (%)	
Malignancy	15 (37.5)
Liver cirrhosis	14 (35)
Hypertension	8 (20)
Diabetes mellitus	7 (17.5)
Cerebrovascular accident	5 (12.5)
Ischemic heart disease	3 (7.5)
Respiratory disease	3 (7.5)
Heart failure	2 (5)
Chronic kidney disease	2 (5)
Body mass index, median (range)	22 (15.1–29.3)
History of abdominal surgery, n (%)	11 (27.5)
Patient status, n (%)	
Inpatient	28 (70)
Outpatient	2 (5)
Emergency room	10 (25)
ASA classification, n (%)	
I	3 (7.5)
II	10 (25)
III	23 (57.5)
IV	4 (10)
Unstable systolic blood pressure (<90 mm Hg), n (%)	11 (27.5)
Unstable pulse rate (>100/min), n (%)	16 (40)
Indication of endoscopy, n (%)	
Hematemesis	17 (42.5)
Melena	3 (7.5)
Hematochezia	2 (5)
EMR/ESD	2 (5)
Epigastric pain/abdominal pain	4 (10)
Anemia	1 (2.5)
Nausea/vomiting	1 (2.5)
Diarrhea	1 (2.5)
Others*	9 (22.5)
Type of endoscopy, n (%)	
Esophagogastroduodenoscopy	33 (82.5)
Colonoscopy	5 (12.5)
EMR/ESD	2 (5)
Time of endoscopy, n (%)	
Emergency endoscopy	17 (42.5)
Nonemergency endoscopy	23 (57.5)
Sedative agent, n (%), median dose	
Propofol	17 (42.5), 80 mg
Midazolam	8 (20), 2.25 mg
Meperidine	3 (7.5), 25 mg

ASA = American Society of Anesthesiologists, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection.

* Others included percutaneous endoscopic gastrostomy, esophageal foreign body, dysphagia, constipation, workup for ovarian cancer, and screening purposes.

Clinical Characteristics of the Life-Threatening Cases in the Endoscopy Unit

Most of the life-threatening situations (27, 67.5%) were recognized during the endoscopic procedure, while 6 cases (15%) and 7 cases (17.5%) were detected pre and postendoscopic procedure, respectively (Table 2). Apparent respiratory failure (19, 47.5%) was the most frequent type of life-threatening case, followed by hypotension (10, 25%) and cardiac arrhythmia (10, 25%). The probable causes of the cases were as follows: aggravation of underlying disease (23, 57.5%) such as uncontrolled bleeding and exacerbation of lung disease; adverse effects of sedative agents (11, 27.5%); aspiration (3, 7.5%); and procedure-related causes (1, 2.5%). This last case directly caused by the procedure was cardiac arrest, likely associated with compression of the inferior vena cava resulting in reduced venous return due to excessive intraperitoneal air distension caused by luminal perforation during gastric ESD.

Risk Factors for Mortality in the Life-Threatening Cases in the Endoscopy Unit

Although every effort was undertaken to rescue the patients, 18 (45%) of them ultimately died. Univariate analysis found that co-morbidity of liver cirrhosis, a high level of ASA classification (III, IV), initial unstable systolic blood pressure (<90 mm Hg), emergency endoscopy, and GIB as an indication for endoscopy were significantly associated with high mortality risk (Table 3). In multivariate analysis, only GIB as an indication for endoscopy (odds ratio 28.45, 95% confidence interval 1.55–523.33, $P = 0.024$) was identified as a significantly independent risk factor for mortality in these patients (Table 4).

DISCUSSION

This study demonstrated that critical events requiring CPR occurred in GIE unit at a rate of 15 per 100,000 cases (40/263,426). We found that approximately half of these patients (45%, 18/40) died despite efforts at resuscitation, resulting in an overall mortality rate from life-threatening events in GIE unit of 6 per 100,000 individuals (18/263,426), and GIB as an indication for endoscopy was significantly related to this risk. To the best of our knowledge, this study was the first to evaluate the clinical characteristics and mortality of life-threatening cases observed in GIE units.

One study retrospectively reviewing the largest multicenter endoscopic database, ''the CORI project,'' reported 6.3 cases of CPR per 100,000 GI endoscopic procedures.[8] However, this study was different from ours in that the authors of that study only included cases using conscious sedation. In addition, they did not describe the clinical characteristics of these life-threatening cases. Because nonuniversity practice sites were also included in the CORI database, whereas we only studied tertiary hospitals, the clinical severity of the patients might have been different between the studies.

TABLE 2. Clinical Data on the Life-Threatening Events in Gastrointestinal Endoscopy Units

Variables	N = 40
Timing of call for code blue, n (%)	
Before endoscopy	6 (15)
Before sedation	3 (7.5)
After sedation	3 (7.5)
During endoscopy	27 (67.5)
After endoscopy	7 (17.5)
Situation on call for code blue, n (%)	
Respiratory insufficiency	19 (47.5)
Hypotension	10 (25)
Cardiac arrhythmia	10 (25)
Others	1 (2.5)
Probable causes of code blue, n (%)	
Aggravation of underlying disease	23 (57.5)
Sedative drug related	11 (27.5)
Aspiration	3 (7.5)
Procedure related	1 (2.5)
Others	2 (5)

McLernon et al reported that the EGD-attributed death rate was 1 in 9000 and that GIB, such as melena or hematemesis, was found to be associated with this mortality, similar to our results.[7] However, this study evaluated only the outcomes of EGD, so it is difficult to extrapolate the results to general GI endoscopic procedures. In addition, McLernon et al estimated 30-day mortality after EGD using 3 different databases: an endoscopy database, a death registry, and the Scottish Morbid Record National Database. Therefore, it may have been difficult to confirm the causes of death during endoscopic procedures. In contrast, our cases included only events that occurred in endoscopy units, enabling us to obtain an accurate measurement of cardiopulmonary events associated with GIE.

One of the important findings of the present study was that one-third of the life-threatening events (13, 32.5%) were detected before (6, 15%) or after procedures (7, 17.5%) in GIE units. Three cases were found even before the administration of sedative agents, while awaiting the procedure in the unit. Two of the cases showed deteriorating blood pressure due to severe variceal bleeding associated with liver cirrhosis, and the other presented with arrhythmia that was probably related to acute cerebral infarction. Three cases with respiratory failure provoked by the administration of sedative agents were recognized before initiating the endoscopic procedure. Most of the cases (5 of 7) detected after procedures and during the recovery phase in the GIE unit showed hypovolemic shock related to uncontrolled bleeding. This result emphasized the importance of close monitoring of patients, even before and after procedures in the preparation and recovery rooms of the endoscopy unit and particularly when managing patients with GIB.

Although there have been no studies of the survival rate with CPR in the endoscopy unit, survival with CPR in the hospital has been reported at 41% to 49.3% in general.[10–12] In our study, the survival rate after CPR in the GIE unit was 55%, which was slightly better than that in previous studies. There are several plausible explanations for the superior survival rate observed in our study. First, most of the cases in our study had potentially reversible causes of cardiopulmonary events, such as hypoxemia or hypovolemia. Second, the intervals

TABLE 3. Univariate Analysis of the Risk Factors for Mortality of the Life-Threatening Events in Gastrointestinal Endoscopy Units

Variables	Death 18 (45%)	Survival 22 (55%)	*P* Value
Age, median, yr	62	60	0.577
Male, n (%)	3 (16.7)	10 (45.5)	0.09
Co-morbidities, n (%)			
Liver cirrhosis	10 (55.6)	4 (18.2)	0.021
Malignancy	8 (44.4)	7 (31.8)	0.517
Hypertension	3 (16.7)	5 (22.7)	0.709
Diabetes mellitus	4 (22.2)	3 (13.6)	0.68
Cerebrovascular accident	2 (11.1)	3 (13.6)	1.0
Ischemic heart disease	1 (5.6)	2 (9.1)	1.0
Respiratory disease	1 (5.6)	2 (9.1)	1.0
Heart failure	0	2 (9.1)	0.492
Chronic kidney disease	0	2 (9.1)	0.492
Body mass index, median	22	23	0.577
History of abdominal surgery, n (%)	7 (38.9)	4 (18.2)	0.173
Patient location, n (%)			0.104
Inpatient	11 (61.3)	17 (77.3)	
Outpatient	0	2 (9.1)	
Emergency room	7 (38.9)	3 (13.6)	
ASA classification, n (%)			0.016
I, II	2 (11.1)	11 (50)	
III, IV	16 (88.9)	11 (50)	
Unstable systolic blood pressure (<90 mm Hg), n (%)	8 (44.4)	3 (13.6)	0.04
Unstable pulse rate (>100/min), n (%)	9 (50)	7 (31.8)	0.335
Type of endoscopy, n (%)			0.177
Esophagogastroduodenoscopy	17 (94.4)	16 (72.7)	
Colonoscopy	1 (5.6)	4 (18.2)	
EMR/ESD	0	2 (9.1)	
Time of endoscopy, n (%)			<0.001
Emergency endoscopy	14 (77.8)	3 (13.6)	
Nonemergency endoscopy	4 (22.2)	19 (86.4)	
Bleeding as an indication, n (%)	17 (94.4)	5 (22.7)	<0.001
Use of sedative agents, n (%)	2 (11.1%)	19 (86.4%)	<0.001

ASA = American Society of Anesthesiologists, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection.

TABLE 4. Multivariate Analysis of the Risk Factors for Mortality of the Life-Threatening Events in Gastrointestinal Endoscopy Units

Variables	Odds Ratio	95% Confidence Interval	*P* Value
Liver cirrhosis	4.13	0.29–59.14	0.296
Unstable systolic blood pressure	5.58	0.45–69.08	0.181
Bleeding as an indication	28.45	1.55–523.33	0.024
Emergency endoscopy	3.98	0.28–56.66	0.308
ASA III and IV	2.43	0.21–28.49	0.479

ASA = American Society of Anesthesiologists.

between the events and CPR might have been short because all of the patients were monitored and there were CPR equipment and supplies in each endoscopy unit. A short interval between patient collapse and CPR and monitoring before cardiopulmonary events have been identified as variables associated with an increased likelihood of survival after CPR.[11,13–15]

Only bleeding as an indication for procedures was found to be a significant risk factor for mortality after CPR in the endoscopy units on multivariate analysis in the present study. Generally, mortality due to upper GIB remains high, ranging from 10% to 14%, despite technical advancements in therapeutic endoscopy.[16,17] Therefore, this result confirms that close monitoring is warranted, and significant warnings should be given in cases of endoscopy for patients with GIB.

Given that sedation causes central cardiorespiratory depression, it is widely recognized that sedation is associated with the risk of cardiopulmonary events, leading to morbidity and mortality during GIE.[18,19] Interestingly, however, we found that the use of sedative agents was significantly less associated with the risk of mortality on univariate analysis. We presumed that sedative agents tended to be avoided at the endoscopist's discretion in clinically serious patients who might be more susceptible to the risk of death. Therefore, we excluded this variable from multivariate analysis of the risk of mortality.

This study had several limitations. First, because of its retrospective design, some cases might have been missed during data collection. However, we used prospectively registered data from CPR cases in each hospital to reduce the selection bias. Second, only tertiary hospitals were involved in the study, so a greater frequency of patients with serious clinical status may have been included. Third, ERCP which has a high complication rate[20,21] was not included in this study. Fourth, portable endoscopic procedures for patients in serious condition such as in the intensive care unit were not included. Therefore, the risks of procedures might have been underestimated. Finally, we could not obtain the conscious level of the patients before the endoscopy which might be related with risk of mortality because of the retrospective design of the study.

In conclusion, life-threatening events requiring CPR can occur in the GIE unit, even before or after procedures. Greater attention should be paid while performing endoscopy for patients with GIB because they show a high risk of mortality when life-threatening events occur.

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