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Gastrointestinal and non-gastrointestinal complication rates associated with diagnostic esophagogastroduodenoscopy under sedation

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Abstract

Esophagogastroduodenoscopy (EGD) under sedation may result in gastrointestinal (GI) and non-GI complications. However, no previous studies have reported 30-day GI and non-GI complications after diagnostic EGD under sedation.

We conducted a retrospective, observational study of 30-day GI and non-GI complication rates after outpatient diagnostic EGD under sedation in subjects ≥18 years between January 2012 and December 2017 based on a common data model database. Thirty-day complication rates were compared with EGD under sedation or not, type of sedation drugs (midazolam only vs midazolam/propofol) and age groups (18-64 year vs ≥65 year) for GI (bleeding and perforation) and non-GI complications (pneumonia, acute myocardial infarction, congestive heart failure and cerebral stroke).

In total, 39,910 were performed with sedation (midazolam only, n = 16,033 and midazolam/propofol, n = 23,864) and 22,894 were performed without sedation. Elderly patients significantly favored EGD without sedation ($P < .01$). GI and non-GI complication rates were similar between EGD under sedation and without sedation (all $P > .1$) except for acute myocardial infarction rate, which was significantly higher in EGD without sedation than EGD under sedation (1.7/10,000 vs 0.3/10,000 persons, $P = .043$). All GI and non-GI complications were also similar between the midazolam/propofol and midazolam only groups as well as between young and old patients (all $P > .1$).

Outpatient diagnostic EGD under sedation has an excellent safety profile. In addition, it can be safely performed with midazolam only or midazolam/propofol and in young and old patients.

Abbreviations: AMI = acute myocardial infarction, ASGE = American Society for Gastrointestinal Endoscopy, CDM = common data model, EGD = esophagogastroduodenoscopy, EHR = electronic health record, GI = gastrointestinal, SNOMED-CT = Systemized Nomenclature for Medicine-Clinical Terms.

Keywords: common data model, complications, conscious sedation, EGD, safety

1. Introduction

Esophagogastroduodenoscopy (EGD) is a commonly performed gastrointestinal (GI) procedure that is usually performed under sedation.[1] Although EGD under sedation may result in GI and non-GI complications, only a few studies have reported non-GI complications associated with EGD.[2,3] In the Clinical Outcomes Research Initiative database,[2] upper GI procedures were associated with a cardiopulmonary event rate of 1/170 and a mortality rate of 1/10,000.[2] In a claim-based retrospective study for EGD,[3] the major cardiocerebrovascular complication rate was 55.4/10,000. In a prospective study of 14,149 EGD procedures performed at 36 hospitals,[4] the morbidity rate was

1/200 and cardiorespiratory complications were the most common complication type. In a prospective study from the Mayo Clinic, the complication rate related to diagnostic EGD under anesthesia was 1.6/10,000 patients.[5] The variable complication rates associated with EGD under sedation may be explained by many different factors, such as study design (prospective vs retrospective), definitions of complication, data source, patient population, indications for EGD, proportion of sedative endoscopy, and types of sedation drugs used.[2–5]

For sedation of EGD, midazolam only,[6] midazolam/propofol,[7] propofol only,[8,9] or propofol/opiates/benzodiazepines[10] have been used. A prospective randomized study of interventional GI endoscopy revealed similar safety profiles for sedation with midazolam/propofol vs propofol alone.[11] A systemic review and meta-analysis of randomized, controlled trials of routine GI endoscopy under sedation showed similar complication rates for midazolam-based vs propofol-based sedation.[12] Previous studies were limited, however, as heterogeneous endoscopy procedures were analyzed together,[11,12] and their sample sizes were too small to assess the exact magnitude of complications associated with EGD under sedation.[7,9–11] Exact knowledge of potential complications associated with diagnostic EGD under sedation may help to minimize the risk of EGD under sedation, but, no studies has reported 30-day GI and non-GI complications after diagnostic EGD under sedation.

In this context, we aimed to assess GI and non-GI complications associated with diagnostic EGD under sedation using a common data model (CDM).

2. Materials and methods

2.1. Data source

We used a CDM data with 822,180 patients of Kyung Hee University Hospital at Gangdong between January 2006 to December 2017. Electronic health records (EHRs) was converted to CDM version 5.3 in 2018. CDM was developed to standardize EHRs with the same structure to facilitate network analysis among collaborating hospitals.[13–17] EHRs are stored in databases that are built using a wide variety of data models and, often, local terminologies, therefore, an analysis across multiple disparate databases either tailors the analysis to accommodate each of the underlying data models and terminologies or converts the databases to a CDM.[16,17] As CDM was designed to include all observational EHRs, which is not compatible with international coding systems,[16,17] disparate coding systems can be harmonized—with minimal information loss—to a standardized vocabulary in CDM. As our EHR data were initially recorded using International Classification of Diseases, version 10 codes, they were mapped to Systemized Nomenclature for Medicine-Clinical Terms (SNOMED-CT) codes and all conditions were defined using the SNOMED-CT code in the CDM database.[16,17]

2.2. Study design

We conducted a retrospective, observational study to assess 30-day GI and non-GI complication rates after outpatient diagnostic EGD under sedation in all subjects ≥18 years between January 2012 and December 2017. Thirty-day complication rates after diagnostic EGD were compared with or without sedation, and also compared with sedation drugs and age groups. Outpatients older than 18 years who underwent the EGD for the first time in their history were assigned to the outpatient diagnostic EGD cohort. Diagnostic EGD cohort included patients who underwent EGD with or without biopsy, but excluded patients who underwent any type of interventional EGD such as polypectomy or dilatation. For subjects who underwent multiple EGDs, the first EGD encounter was used. To exclude double endoscopy procedures, EGDs performed on the same day or within ± 30 days of colonoscopy or endoscopic retrograde cholangiopanceatography were excluded.

Whether or not sedation during EGDs mostly depends on the patient's own choice in South Korea, because medical cost of EGDs is reimbursed by the National Health Insurance Service but the cost of sedation during EGDs is not reimbursed. According to the American Society for Gastrointestinal Endoscopy (ASGE) guideline[6] and the Korean Society for Gastrointestinal Endoscopy,[18] sedation during EGD is also judged by endoscopists as well as patients based on patient comorbidities. Sedation with midazolam only was defined as a drug exposure to midazolam and no exposure to propofol for the diagnostic EGD, and sedation with midazolam/propofol was defined as a drug exposure to midazolam and propofol simultaneously for the diagnostic EGD. EGD without sedation was defined as no drug exposure to midazolam or propofol. No other type of sedation drugs was used in our hospital during the study period. All EGDs were performed according to ASGE guidelines.[6] Briefly, all EGDs were performed after applying a topical lidocaine spray, and use of antispasmodic medication and simethicone, if not contraindicated. All patients were monitored for blood pressure regardless of sedation, however, oxygen supply and saturation monitoring were provided for only sedative EGDs. Conversion from non-sedative EGDs to sedative EGDs rarely occurred in our center. Variables used in this study were age, age group (young age, 18 to 64 years vs old age, ≥65 years), sex, and sedation drugs (midazolam only vs midazolam/propofol). Old patients were defined as those ≥65 years according to endoscopic practice guidelines for the elderly.[19] This study was approved by the Institutional Review Board of the study institution (KHNMC IRB 2020-08-021).

2.3. Definition of complications

30-day GI and non-GI complication rates of diagnostic EGD were calculated as the number of cases and proportion per 10,000 persons in each group. Concept identification and concept codes for concept sets based on CDM in each cohort are described in Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A993. Thirty-day complications were classified into categories based on SNOMED-CT codes, and defined as complications occurring within 30 days of EGD under sedation resulting in presentation to the emergency department or hospitalization. GI complications included GI bleeding or perforation, whereas non-GI complications included pneumonia, acute myocardial infarction (AMI), congestive heart failure, and cerebral stroke (hemorrhage or infarction). All captured events were defined as a condition occurrence for the first time in the person's history after the index EGD, and the earliest event per person during study period was defined as an initial event.

2.4. Sedation policy for diagnostic EGD

All EGDs were performed in an endoscopy room fully equipped for advanced cardiac life support following the sedation protocol of our center,[20] which is in accordance with ASGE guidelines.[21] Briefly, all patients routinely received supplemental oxygen (2 L/min) via a nasal cannula, and their vital signs and oxygen saturation were monitored continuously every 2 minute using pulse oximetry and an automatic blood pressure cuff. An initial dose of sedative drug was given to patients according to an age and weight-based protocol to achieve moderate sedation. In the midazolam-only group, 0.07 mg/kg of midazolam was given initially, and subsequent incremental boluses of 1 to 2 mg of midazolam were allowed to be given every 2 minute at the discretion of the endoscopist. In the midazolam/propofol group, 2 mg of midazolam and 20 to 30 mg of propofol (20 mg for patients ≥ 65 years and 30 mg for patients 18-64 years) were given intravenously initially. Subsequent incremental boluses of 1 mg of midazolam and 10 mg propofol were allowed to be given every 2 minute at the discretion of the endoscopist. Sedation level was evaluated using the Modified Observer's Assessment of Awareness/Sedation score.[22]

2.5. Statistical analysis

We used ATLAS version 2.7.6 (https://api.feedernet.co.kr/atlas/v2.7.6/7/43/0/#/home), which is an open source application developed as a part of CDM database intended to provide a unified interface to patient level data and analytics. Analysis was based on the platform of "Federated E-health Big Data for Evidence Renovation Network (FEEDER-NET)", which is a health big-data platform based on CDM supported by the Bio Industrial Strategic Technology Development Program.[23] Data are presented as means ± standard deviations (SD) for normally distributed continuous variables and as numbers (percentages) for categorical variables. Comparative analysis was done using the Chi-squared test or Fisher exact test for proportions, and Student t test or nonparametric Mann–Whitney U test for means. All P values were two tailed, and values less than .05 were considered statistically significant. All statistical analyses were performed using SAS software (SAS 9.4; SAS Institute, Cary, NC).

3. Results

3.1. Demographic characteristics of the study population

Demographic characteristics of patients who underwent EGD are summarized in Table 1. CDM database includes data from 74,059 patients who underwent EGD procedures. Of these EGD procedures, 39,910 were performed under sedation (midazolam only, n = 16,033 and midazolam/propofol, n = 23,864) and 22,894 were performed without sedation. Elderly patients significantly favored EGD without sedation ($P < .01$), and male patients significantly preferred EGD without sedation ($P < .01$).

3.2. Thirty-day complication rates of EGD under sedation

Table 2 shows the 30-day GI and non-GI complication rates for EGD with or without sedation. AMI rate was significantly higher after EGD without sedation than EGD under sedation (1.7/10,000 vs 0.3/10,000 persons, $P = .043$). Other complication rates, including bleeding, perforation, pneumonia, congestive heart failure, and cerebral stroke, were not significantly different between EGD with or without sedation.

3.3. Thirty-day complication rates of EGD according to sedation drugs and age group

Table 3 shows the 30-day complication rates of EGD under sedation according to types of sedation drugs used. All GI and non-GI complications were similar between midazolam only and the midazolam/propofol groups (all $P > .1$). Table 4 shows the 30-day complication rates of EGD under sedation according to age group. All GI and non-GI complication rates were also similar between young and old patients (all $P > .1$).

4. Discussion

GI and non-GI complications are inherent when performing EGDs; however, they are not consistently defined or reported. In this study, we evaluated 30-day GI and non-GI complications after diagnostic EGDs using a well-defined CDM database over a 12-year period. The most important finding of this study is that 30-day GI and non-GI complication rates were not significantly different between EGD under sedation and EGD without sedation, except higher AMI rate in EGD without sedation. All GI and non-GI complication rates were also similar between midazolam only and the midazolam/propofol groups and between young and old patients. Our findings support an excellent safety profile of outpatient diagnostic EGD under sedation. Complication rates of EGD in previous studies were limited, as the vast majority of published studies had a small sample size, heterogeneous endoscopy procedures were analyzed together,[11,12] and individual GI and non-GI complications were not analyzed in detail.[24,25] In a population-based study from Korea,[3] the 14-day major cardiocerebrovascular complication (including AMI, cardiac arrest, stroke) rate was 31.4/10,000 after outpatient EGD under sedation. This claim-based data is limited because sedation for EGD is not reimbursed by the medical insurance program in Korea and their figures are higher than our usual experiences in daily clinical practice.[3]

In our study, AMI rate was significantly higher in non-sedative EGD group than sedative EGD group ($P = .043$). The higher incidence of cardiac events in the non-sedative EGD could be secondary to a higher comorbidity in these patients. According to ASGE guidelines,[6] all patients undergoing EGDs required pre-procedural evaluation to assess their risk for sedation and to manage potential problems related to preexisting comorbidities. As a result, nonsedative EGD group may be associated with higher cardiac comorbidities than those in sedative EGD group. On the contrary, the stress of nonsedative EGDs, which is more than that of sedative EGD, may impact on the development of cardiac events. However, this possibility is thought to be extremely low because the examination time of EGDs is only 3 to 4 minutes in routine diagnostic procedures. In addition, moderate sedation of EGD may have little impact on cardiovascular function, as this level of sedation targets maintaining cardiovascular function according to ASGE guideline.[6] Until now, there has been few studies on the cardiovascular complications after diagnostic EGDs. In 21,899 EGDs performed at a tertiary academic center, cardiovascular complications were reported in only 0.02% of cases.[26] However, this study analyzed therapeutic and diagnostic EGDs together. In a prospective study for sedative

Table 1

Demographic characteristics of the study population.

| Demographic characteristics | EGD with sedation | | EGD without sedation |
	Midazolam only	Midazolam/propofol	
Total number of patients	16,033	23,864	22,894
Age (yrs), m±SD	47.1±12.5	47.4±13.8	47.9±14.6
Age (yrs) group, n (%)			
Young age (18-64 yr)	14,537 (90.7)	21,087 (88.4)	19,514 (85.2)
Old age (≥65 yr)	1,496 (9.3)	2,777 (11.6)	3,380 (14.8)
Sex, n (%)			
Male	7,555 (47.1)	11,413 (47.8)	11,162 (48.8)
Female	8,478 (52.9)	12,451 (52.2)	11,731 (51.2)

m = mean, SD = standard deviation.

diagnostic EGD in 10,662 adults, no cardiovascular complication was reported.[8]

In the era of EGD under sedation, midazolam is traditionally used, but propofol has been increasingly used since the 2000s due to its rapid onset and offset of sedation, shortened recovery time, and normalization of neuropsychiatric function.[6,12,27–29] However, the combination of midazolam/propofol is also widely used in clinical practice,[7,9–12,30,31] as propofol has a narrow therapeutic window and no pharmacological antagonists.[12,27,32] Only a handful of studies have compared safety profiles between midazolam/propofol vs midazolam for GI endoscopy.[10,30] In a randomized trial of diagnostic EGDs,[10] immediate complication rates were similar between the midazolam/propofol group and midazolam group. In a recent study of therapeutic EGDs,[30] cardiopulmonary complication rates were not statistically different between the midazolam/ propofol group and midazolam group. In a prospective observational study,[33] the 1-day respiratory infection rate after outpatient EGD was not statistically different between midazolam/propofol and propofol groups. In a meta-analysis of routine endoscopy including EGD and colonoscopy,[12] the

incidence of hypoxemia was similar between midazolam/ propofol group and midazolam or propofol only groups. In a nationwide population-based study, 14-day cardiocerebrovascular complication rates were higher in the EGD under sedation than EGD without sedation.[3] However, risk of sedation must be interpreted cautiously as most prior studies focused on sedation efficacy rather than safety profile and short-term complications with a small sample sizes. We found that GI and non-GI complications were very low and similar between EGD with midazolam/propofol and with midazolam only. Previous studies have found that old age is a risk factor for complications associated with EGD, and age itself increases sedation-related complications.[3,6,18,24] In our study, most complication rates were higher in old age group than young age group without statistical significance. We used the cut-off age for defining old age with 65 years according to endoscopic practice guidelines[19]; however, cut-off age may be reconsidered for the complication study of EGD as physical performance in this age is much improved in recent years compared with the past and other variable cut-off ages were used in the literature.[34] For example, the complication rates of diagnostic endoscopy were about 6-

Table 2

Comparison of 30-day complication rates between EGD with or without sedation.

Complications	EGD with sedation	EGD without sedation	P value
GI complications			
Bleeding	39,877	22,887	.159
Cases, n	7	1	
Proportion per 10,000 persons	1.8	0.4	
Perforation	39,895	22,892	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Non-GI complications			
Pneumonia	39,858	22,871	-
Cases, n	2	0	
Proportion per 10,000 persons	0.5	0.0	
Acute myocardial infarction	39,886	22,889	.043
Cases, n	1	4	
Proportion per 10,000 persons	0.3	1.7	
Congestive heart failure	39,895	22,893	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Cerebral stroke	40,009	22,877	.738
Cases, n	1	1	
Proportion per 10,000 persons	0.2	0.4	

GI = gastrointestinal.

Table 3

Comparison of 30-day complication rates of EGD with sedation according to sedation drugs.

Complications	EGD with midazolam only	EGD with midazolam/propofol	*P* value
GI complications			
Bleeding	16,028	23,849	.450
Cases, n	4	3	
Proportion per 10,000 persons	2.5	1.3	
Perforation	16,033	23,862	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Non-GI complications			
Pneumonia	16,020	23,838	1.000
Cases, n	1	1	
Proportion per 10,000 persons	0.6	0.4	
Acute myocardial infarction	16,030	23,856	.402
Cases, n	1	0	
Proportion per 10,000 persons	0.6	0.0	
Congestive heart failure	16,033	23,862	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Cerebral stroke	16,025	23,984	.401
Cases, n	1	0	
Proportion per 10,000 persons	0.6	0.0	

GI = gastrointestinal.

fold higher in very old (≥85 years) patients compared to younger (40s) patients.[34]

One strength of our study is its large sample size, which was a limitation of prior studies.[7,10,30,31] Previous studies also tended to focus on immediate complications only or had a primary endpoint other than complications of diagnostic EGD. Our study, however, also had several limitations. First, we were not able to assess the extract information about endoscopists or obtain detailed clinical data. In addition, there were inevitable data quality issues due to conversion of EHRs to CDM as data collection was retrospective. However, the data quality in the CDM database has recently been shown to be of excellent quality.[13,14] Second, the 30-day post-procedure observation period is arbitrary, but is based on previous literature.[35] And finally, we only focused on outpatient diagnostic EGD and out definition may not include some patients with comorbid diseases. But, the safety profiles of outpatient diagnostic EGD may be better represented by our working definition.

In conclusion, our findings highlight the excellent safety profile of diagnostic EGD under sedation as it can be safely performed with midazolam only or midazolam/propofol and in young and old patients.

Table 4

Comparison of 30-day complications of EGD with sedation according to age groups.

Complications	Young age (18-64 yrs)	Old age (≥65 yrs)	*P* value
GI complications			
Bleeding	35,610	4,267	.547
Cases, n	6	1	
Proportion per 10,000 persons	1.7	0.2	
Perforation	35,622	4,273	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Non-GI complications			
Pneumonia	35,597	4,261	.202
Cases, n	1	1	
Proportion per 10,000 persons	0.3	2.3	
Acute myocardial infarction	35,616	4,270	.203
Cases, n	0	1	
Proportion per 10,000 persons	0.0	2.3	
Congestive heart failure	35,623	4,272	-
Cases, n	0	0	
Proportion per 10,000 persons	0.0	0.0	
Cerebral stroke	35,608	4,268	.107
Cases, n	0	1	
Proportion per 10,000 persons	0.0	2.3	

GI = gastrointestinal.

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Author contributions

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