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Original Article

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Role of Upper Gastrointestinal Endoscopy in Patients with Human Immunodeficiency Virus Infection in the Era of Combination Antiretroviral Therapy

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ABSTRACT

Background: Gastrointestinal (GI) diseases are common in patients with human immunodeficiency virus (HIV) infection. There are few reports on the epidemiology and endoscopic findings of gastric cancer in patients with HIV infection in the era of combination antiretroviral therapy (cART). We retrospectively analyzed upper GI endoscopic findings in patients with HIV infection and investigated their role as gastric cancer screening.
Materials and Methods: We retrospectively investigated endoscopies conducted in Korean patients with HIV infection referred for endoscopy at a tertiary hospital between January 2004 and December 2018. Endoscopic and pathologic findings were analyzed according to the reason for endoscopy, patient age, and cART duration. All endoscopic findings were reevaluated by gastroenterologists.
Results: Three hundred ten endoscopies in 201 patients with HIV infection were investigated. Of these, 118 (38.1%) endoscopies in 81 (40.1%) patients were performed for cancer screening purposes. Gastric cancer was found in 4 patients (2.0%); one of them presented with gastric cancer at the time of HIV diagnosis, and the other 3 patients were diagnosed with early gastric cancer on screening endoscopy, which was cured with endoscopic submucosal dissection or surgery. The prevalence of gastric cancer in screening endoscopies was 3.7%. Atrophic gastritis was a more common finding in screening endoscopies than in diagnostic endoscopies (P <0.001), and was significantly associated with longer durations of cART (P <0.001). The overall prevalence of gastric cancer, atrophic gastritis, and intestinal metaplasia was 2.0, 57.8, and 25.4%, respectively. The prevalence of atrophic gastritis and intestinal metaplasia increased with age.
Conclusion: Regular gastric cancer screening might be useful for early diagnosis and treatment of gastric cancer in patients with HIV infection.

Keywords: Human immunodeficiency virus; Endoscopy; Gastric cancer; Cancer screening; Antiretroviral therapy

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INTRODUCTION

Gastrointestinal (GI) diseases are common in patients with human immunodeficiency virus (HIV) infection and have been attributed to opportunistic diseases that resulted from advanced immunosuppression in the era before combination antiretroviral therapy (cART) was available [1]. With the advent of potent cART, the spectrum of GI diseases has changed in these patients, requiring a broader range of diagnostic considerations. As cART utilization has increased the life expectancy of patients with HIV infection, malignancies, particularly non-acquired immune deficiency syndrome (AIDS)-defining cancers, have become a growing cause of death in this population [2, 3]. Cancer screening is now considered an important component of health maintenance in HIV clinical practice.

Several studies have reported cancer epidemiology and screening interventions in patients with HIV infection [4-8]. However, gastric cancer data have been too limited to allow specific screening recommendations. Recent studies showed that the incidence of gastric cancer in patients with HIV infection was 1.8-1.9 times higher than that in the general population [9, 10]. Although there have been studies of upper GI endoscopic findings in symptomatic patients with HIV infection [1, 11-13], few studies have investigated endoscopic findings for gastric cancer in those receiving cART.

In the general population of Korea, gastric cancer is the second most common cancer after thyroid cancer [14], and *Helicobacter pylori* infection is found in approximately 60% of adults [15]. The National Cancer Screening Program (NCSP) of the National Health Insurance Service (NHIS) in Korea provides upper GI series or endoscopy for gastric cancer screening every 2 years for individuals aged ≥40 years [16]. Previous studies on Korean patients with HIV infection have reported that gastric cancer accounted for 3.1% of 32 cancers and 6.3% of 48 cancers [17, 18]. However, there are limited data on upper GI endoscopic findings and gastric cancer incidence in Korean patients with HIV infection. In this study, we retrospectively analyzed upper GI endoscopic findings in patients with HIV infection and investigated their role as gastric cancer screening.

MATERIALS AND METHODS

1. Study population and data collection

We retrospectively reviewed the medical records of patients with HIV infection who underwent upper GI endoscopy at Pusan National University Hospital (Busan, Korea) between January 2004 and December 2018. This hospital is a 1,450-bed university-affiliated teaching hospital and provides HIV care for patients with HIV infection in the southeastern region of Korea. Patients were excluded from analysis if they had undergone gastric resection for gastric cancer treatment before presentation to the study hospital. Ethnic minorities and patients with unsuccessful endoscopy were also excluded.

We collected data on patient characteristics, including age, sex, timing of diagnosis, HIV status, CD4 cell count, viral load, use of antiretroviral therapy, presence of GI symptoms, purpose of endoscopy, and endoscopic and pathologic findings. Each endoscopic examination was classified as either diagnostic or screening endoscopy. Screening endoscopy included endoscopies performed as part of the NCSP of the NHIS or the health check program (HCP) of the health promotion center (HPC) of the study hospital. Endoscopic

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examinations performed owing to the presence of GI symptoms were classified as diagnostic endoscopy. Endoscopic findings were reviewed by 2 gastroenterologists, and all diagnoses were made on the basis of minimal standard terminologies for GI endoscopy [14]. Atrophic gastritis was assessed endoscopically using the Kimura-Takemoto classification [15]. Intestinal metaplasia was diagnosed either endoscopically by visualizing whitish plaque-like elevations in the gastric antrum and/or body or pathologically. Endoscopic biopsy specimens were graded using the Sydney system. *H. pylori* infection was assessed using the rapid urease test or biopsy results.

To examine the influence of the duration of cART on the endoscopic findings, we stratified the patients who received cART for at least 6 months and whose time to follow-up loss was less than 10% of the total follow-up duration into 4 groups according to the duration of therapy: 1) ≤6 months of cART, 2) 6 months to 5 years after cART initiation, 3) 5 to 10 years after cART initiation, and 4) >10 years after cART initiation. Similar findings with no significant change in multiple endoscopies within each period were not duplicated.

To determine the role of upper GI endoscopy as gastric cancer screening, we analyzed the incidence of gastric cancer in patients with HIV infection who underwent upper GI endoscopy for screening purpose. The incidence was computed as events per 1,000 person-years (PYs). The observation periods were measured from the date of the first visit to the study hospital to either the last date on which upper GI endoscopy was performed or the date of endoscopic gastric cancer diagnosis, whichever was earlier.

2. Statistical analysis

Statistical analyses were performed using SPSS for window version 25.0 (SPSS Inc., Chicago, IL, USA). All continuous variables were summarized as median and interquartile range (IQR). Categorical variables were described using frequencies and percentiles. Categorical variables were compared using Pearson's $\chi 2$ test or Fisher's exact test, whereas noncategorical variables were tested using the t-test or one-way ANOVA. All results were considered significant by $P<0.05$.

3. Ethics statement

The study protocol was approved by the institutional review board of Pusan National University Hospital (IRB No C-1802-012-064), which recommended waiver of informed consent.

RESULTS

During the study period, 1,139 patients with HIV infection visited the study hospital. Three hundred thirty-four upper GI endoscopies were performed in 210 patients (18.4%). Of these, 4 patients were excluded from the analysis owing to gastric resection before enrollment (1.9%); further, 1 ethnic minority patient (0.5%) and 4 patients with unsuccessful endoscopy (1.9%) were also excluded. The remaining 310 endoscopies in 201 patients were included in the analysis; the baseline characteristics and endoscopic findings are presented in **Tables 1** and **2**, respectively. The median age at the time of endoscopy was 52.5 years (IQR, 44–60 years). The median number of endoscopies per patient was 1 (IQR, 1–2). The average number of endoscopies per patient was 1.5; 32.8% of the patients underwent more than 2 endoscopies. The median follow-up was 4.6 years (IQR, 0.6–8.8 years).

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Table 1. Clinical characteristics of the 310 endoscopies in the 201 patients with human immunodeficiency virus

Characteristics	No. (%)
No. of endoscopy per patient	
One	135 (67.2)
Two or more	66 (32.8)
Time of endoscopy	
Before cART	59 (19.0)
After cART	251 (81.0)
Reason of endoscopic prescription	
Screening examination	118 (38.1)
Diagnostic purpose	192 (61.9)
Abdominal pain/discomfort	28 (14.6)
Nausea/Vomiting/Anorexia	22 (11.5)
Dysphagia	21 (10.9)
GI bleeding (melena, hematemesis, hematochezia)	19 (10.0)
Heartburn	15 (7.8)
Anemia evaluation	11 (5.7)
Dyspepsia	11 (5.7)
Diarrhea	7 (3.6)
Other	58 (30.2)

cART, combination antiretroviral therapy; GI, gastrointestinal.

Of the total of 310 endoscopies in 201 patients, 192 (61.9%) endoscopies in 142 patients were performed for diagnostic purposes. Their most commonly reported GI symptom was abdominal pain (14.6%), followed by nausea/vomiting/anorexia (11.5%) and dysphagia (10.9%); 30 (15.7%) endoscopies were performed to evaluate GI bleeding, including active bleeding and anemia. Atrophic gastritis (34.9%) was the most common endoscopic finding,

Table 2. Clinical characteristics and endoscopic findings according to purpose of endoscopies in the patients with human immunodeficiency virus infection

Characteristics	Total (N = 310)	Screening endoscopy (N = 118)	Diagnostic endoscopy (N = 192)	*P*-value[a]
Age at the time of endoscopy, No. (%)				<0.001
<40 years	39 (12.6)	5 (4.2)	34 (17.7)	
40–59 years	182 (58.7)	69 (58.5)	113 (58.9)	
≥60 years	89 (28.7)	44 (37.3)	45 (23.4)	
Median CD4 cell count/mm^3 (IQR)	457.0 (217.3–667.3)	590.5 (426.3–793.3)	338.5 (68.5–595.5)	<0.001
Median HIV RNA virus, log/mL, (IQR)	0 (0–4.2)	0 (0–0)	2.1 (0–5.0)	<0.001
Median observation period to endoscopy, years (IQR)	4.6 (0.6–8.8)	7.7 (4.4–11.4)	2.5 (0.1–6.0)	<0.001
Endoscopies after cART, No. (%)	251 (81.0)	110 (93.2)	141 (73.4)	<0.001
Median cART period to endoscopy, years (IQR)	3.7 (0.2–7.8)	7.5 (4.1–11.0)	1.4 (0–5.6)	<0.001
Endoscopic findings, No. (%)				
Opportunistic infection	36 (11.6)	4 (3.4)	32 (16.7)	<0.001
Esophagus				
Reflux esophagitis	70 (22.6)	21 (17.8)	49 (25.5)	0.114
Esophageal candidiasis	33 (10.6)	4 (1.8)	29 (15.1)	0.001
Esophageal ulcer	19 (6.1)	1 (0.8)	18 (9.4)	0.002
CMV esophagitis	5 (1.6)	0 (0)	5 (2.6)	0.161
HSV esophagitis	2 (0.6)	0 (0)	2 (1.0)	0.527
Stomach				
Erosive gastritis	66 (21.3)	30 (25.4)	36 (18.8)	0.163
Gastric ulcer	30 (9.7)	10 (8.5)	20 (10.4)	0.574
Atrophic gastritis	133 (42.9)	66 (55.9)	67 (34.9)	<0.001
Intestinal metaplasia	60 (19.4)	28 (23.7)	32 (16.7)	0.126
Gastric cancer	4 (1.3)	3 (2.5)	1 (0.5)	0.156
Kaposi sarcoma	1 (0.3)	0 (0)	1 (0.5)	1.000
Duodenum				
Duodenitis	22 (7.1)	9 (7.6)	13 (6.8)	0.776
Duodenal ulcer	6 (1.9)	3 (2.5)	3 (1.6)	0.677

[a]Comparison between screening endoscopy and diagnostic endoscopy
IQR, interquartile range; HIV, human immunodeficiency virus; cART, combination antiretroviral therapy; CMV, cytomegalovirus; HSV, herpes simplex virus.

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Table 3. Characteristics of human immunodeficiency virus-infected patients who were diagnosed with gastric cancer

	Case 1	Case 2	Case 3	Case 4
Sex/age	45/M	M/58	M/54	M/56
CD4 cell count/mm^3	361	670	1,080	1,310
HIV RNA virus, log/mL	6.0	Not detect	Not detect	Not detect
Observation period (years)	0	4.5	7.3	12.0
cART period (years)	0	4.3	6.0	11.9
Purpose of endoscopy	Diagnostic	Screening	Screening	Screening
No. of endoscopes until cancer detection	1	1	5	7
Endoscopic findings	EGC IIa+IIc	EGC IIc	EGC IIc	EGC IIc
Histopathology	Differentiated-type adenocarcinoma	Differentiated-type adenocarcinoma	Differentiated-type adenocarcinoma	Differentiated-type adenocarcinoma
Depth of invasion	Submucosa (1375 μm from muscularis mucosa)	Submucosa (500 μm/1875 μm)	Submucosa (125 μm/625 μm)	Mucosa
Atrophic gastritis	Present	Present	Present	Present
Intestinal metaplasia	Present	Present	Present	Present
Helicobacter pylori infection	Negative	Negative	Positive	Negative
Treatment	Surgery	Surgery after ESD	ESD	ESD

HIV, human immunodeficiency virus; yrs, years; cART, combination antiretroviral therapy; EGC, early gastric cancer; ESD, endoscopic mucosal dissection.

followed by reflux esophagitis (25.5%), erosive gastritis (18.8%), and intestinal metaplasia (16.7%) (**Table 2**). Gastric cancer was found in 1 patient (0.5%). The patient was presented with early gastric cancer (EGC, type IIa+IIc, differentiated-type adenocarcinoma with atrophic gastritis and intestinal metaplasia on histologic examination) and diagnosed with HIV in the preoperative assessment. He was surgically cured (**Table 3**).

One hundred eighteen (38.1%) endoscopies in 81 patients were performed for cancer screening purposes; 103 (87.3%) for the NCSP of the NHIS; and 15 (12.7%) for the HCP of the study hospital's HPC (**Table 1**). Their observation period was 728.1 years. Atrophic gastritis (55.9%) was the most common endoscopic finding, followed by erosive gastritis (25.4%), intestinal metaplasia (23.7%) and reflux esophagitis (17.8%) (**Table 2**). Gastric cancer was found in 3 patients (2.5%) and their median observation period until cancer detection was 7.3 years (**Table 3**). Their median number of endoscopies performed until cancer detection was 5 (range, 1–7). All 3 patients were diagnosed as EGC (type IIc and differentiated-type adenocarcinoma with atrophic gastritis and intestinal metaplasia on histologic examination) and underwent endoscopic submucosal dissection (ESD). Two patients received curative resection; however, 1 patient underwent additional distal gastrectomy with lymph node dissection because of confirmed submucosal invasion on pathologic examination for ESD (**Table 3**). On follow-up endoscopy, low-grade dysplasia was found in 1 patient who underwent curative ESD, which was treated with additional ESD. The incidence of gastric cancer was 4.1 per 1,000 PYs in 81 HIV-infected patients who undertaken upper GI endoscopy for gastric cancer screening purpose.

The patients who underwent screening endoscopy were older (56 *vs.* 50 years, P <0.001), immunologically more stable (CD4 cell count, 590.5 *vs.* 338.5, P <0.001), and more commonly diagnosed with atrophic gastritis (55.9% *vs.* 34.9%, P <0.001) than the patients who underwent diagnostic endoscopy (**Table 2**).

H. pylori tests were performed on 86 endoscopies in 73 patients. Of these, 30 (41.1%) patients had confirmed *H. pylori* infection. The prevalence of atrophic gastritis increased with age, from 25.8% in the patients younger than 39 years to 59.5% in the patients aged 40-60 years and to 66.1% in the patients older than 60 years (P = 0.001) (**Table 4**). The prevalence of

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Table 4. Prevalence of gastric cancer and its precursor lesions according to age

	≤39 years	40–59 years	≥60 years	*P*-value
Total endoscopies, No.	31	126	59	
Gastric cancer, No. (%)	0 (0)	4 (3.2)	0 (0)	0.352
Intestinal metaplasia, No. (%)	0 (0)	33 (26.2)	20 (33.9)	0.001
Atrophic gastritis, No. (%)	8 (25.8)	75 (59.5)	39 (66.1)	0.001
Screening endoscopies, No.	5	53	30	
Gastric cancer, No. (%)	0 (0)	3 (5.7)	0 (0)	0.623
Intestinal metaplasia, No. (%)	0 (0)	12 (23.6)	13 (43.3)	0.060
Atrophic gastritis, No. (%)	2 (40)	35 (66.0)	22 (73.3)	0.392

intestinal metaplasia also increased with age, from 26.2% in the patients aged 40-60 years to 33.9% in the patients older than 60 years ($P = 0.001$) (**Table 4**).

The clinical characteristics and endoscopic findings of the patients with good adherence to cART, according to the duration of cART, are summarized in **Table 5**. Opportunistic infections were common in the early cART period, and their prevalence gradually decreased thereafter. The prevalence of atrophic gastritis significantly increased with longer durations of cART ($P < 0.001$). Although that of intestinal metaplasia tended to increase over time, it was not statistically significant.

DISCUSSION

The life expectancy of patients with HIV infection has dramatically increased since more potent cART has become available. As the lifespan of these patients is extended, an increasing number are at a risk of developing non-AIDS-defining cancers that typically occur at older ages [16-18].

Table 5. Clinical characteristics and endoscopic findings according to combination antiretroviral therapy duration in the patients with good adherence

	≤6 M (N = 58)	>6 M ~ ≤5 Y (N = 60)	>5 Y ~ ≤10 Y (N = 55)	>10 Y (N = 27)	*P*-value
Age, years, median (IQR)	47.5 (39.8–55.5)	53 (43.3–60)	55 (50–62)	59 (54–67)	<0.001
Male sex, No. (%)	49 (84.5)	53 (88.3)	48 (87.3)	23 (85.2)	0.931
CD4 cell count/mm^3, median (IQR)	107.5 (36.5–296.0)	457 (262.5–610.8)	612 (464.5–793.3)	595 (530–852)	<0.001
CD4 cell count <200/ mm^3, No. (%)	33 (56.9)	7 (11.7)	2 (3.6)	0 (2.9)	<0.001
HIV RNA virus, log/mL, median (IQR)	5 (2.8–5.5)	0 (0–0)	0 (0–0)	0 (0–0)	<0.001
The median observation period, years (IQR)	0.1 (0–0.3)	3.0 (1.5–4.2)	7.6 (5.2–18.8)	12.0 (11.2–13.8)	<0.001
The median cART period, years (IQR)	0 (0–0.1)	2.5 (1.2–3.6)	6.7 (5.1–9.7)	11.5 (10.9–13.0)	<0.001
Endoscopic finding, No. (%)					
Opportunistic infection	16 (27.6)	5 (8.3)	0 (0.0)	2 (7.4)	<0.001
Esophagus					
Reflux esophagitis	15 (25.9)	16 (26.7)	20 (36.4)	4 (14.8)	0.217
Esophageal candidiasis	14 (24.1)	5 (8.3)	0 (0.0)	2 (7.4)	<0.001
Esophageal ulcer	8 (13.8)	3 (5.0)	1 (1.8)	0 (0.0)	0.035
CMV esophagitis	4 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)	0.020
Stomach					
Atrophic gastritis	26 (44.8)	32 (53.3)	39 (70.9)	22 (81.5)	0.002
Erosive gastritis	10 (17.2)	13 (21.7)	20 (36.4)	10 (37.0)	0.056
Erythematous gastritis	22 (37.9)	19 (31.7)	13 (23.6)	4 (14.8)	0.119
Intestinal metaplasia	11 (19.0)	15 (25.0)	19 (34.5)	8 (29.6)	0.293
Gastric ulcer	8 (13.8)	4 (6.7)	7 (12.7)	3 (11.1)	0.619
Gastric cancer	0 (0.0)	1 (1.4)	1 (1.7)	1 (2.9)	0.486
Kaposi sarcoma	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Duodenum					
Duodenal ulcer	1 (1.7)	1 (1.7)	1 (1.8)	2 (7.4)	0.467
Duodenitis	7 (12.1)	3 (5.0)	3 (5.0)	0 (0.0)	0.202

M, month; Y, year; IQR, interquartile range; HIV, human immunodeficiency virus; cART, combination antiretroviral therapy; CMV, cytomegalovirus.

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Reports on the epidemiology of gastric cancer in patients with HIV infection are very limited. There are also significant differences in the incidence of gastric cancer by region. Herein, we analyzed the endoscopic findings in patients with HIV infection and investigated the prevalence and incidence of gastric cancer on screening endoscopy in Korea, which has a high incidence of gastric cancer. Our study is the first report on the endoscopic findings and their role as gastric cancer screening in Korean patients with HIV infection.

In a recent study conducted in Japan, a country with a high incidence of gastric cancer, 11 gastric cancers developed in 1,001 patients with HIV infection during a median follow-up of 9 years. This incidence was 1.8 times higher than that in an age- and sex-matched general population [9]. Although cancer screening is currently considered an important component of health maintenance in patients with HIV infection, it is still unclear whether screening specifically for gastric cancer is also helpful in these patients, even in a country with a high incidence of gastric cancer. In Korea, gastric cancer was the third leading cause of cancer death in 2015, with an age-standardized incidence of 33.8 per 100,000 PYs (male sex; 49.3 per 100,000 PYs) [19]. Population-based screening for gastric cancer has been in place since 1999 in Korea. Upper GI series or endoscopy is recommended every 2 years for individuals aged 40-75 years [20]. In a study conducted at 40 hospitals in Korea, the prevalence of gastric cancer was 0.25% among 25,536 individuals who underwent gastric cancer screening [21]. In our study, 3 patients were diagnosed with gastric cancer through screening endoscopy; the prevalence of gastric cancer was 3.7%, it seemed that the prevalence of gastric cancer was somewhat higher than that of the general population. All 3 patients were diagnosed with EGC, which was cured with ESD or surgery. This suggests that gastric cancer screening might be helpful in detecting gastric cancer at an early curable stage in patients with HIV infection, at least in a country with a high incidence of gastric cancer.

We also found that as the duration of cART increased, the prevalence of atrophic gastritis increased over time, from 44.8% in the patients who received cART for ≤6 months to 70.9% in those who received cART for >5 years. The prevalence of intestinal metaplasia also showed an increasing trend with increasing cART duration. Atrophic gastritis and intestinal metaplasia are considered precursor lesions of gastric cancer [22-25]. Gastric cancer was found to develop 10.9 times more frequently in the presence of intestinal metaplasia in Korea [26], and several studies have reported atrophic gastritis as a risk factor for gastric tumorigenesis in Korea [22, 23]. On screening endoscopy of the general population in Korea, the prevalence of atrophic gastritis was reported to be 27.1% and 40.7%, and that of intestinal metaplasia was 7.1% and 12.5% in 2 separate studies [27, 28]. In 25,536 subjects who underwent health check-ups in Korea, the prevalence of atrophic gastritis increased with age, from 14.9% in the subjects aged <40 years to 28.9% in those aged 40-59 years and to 43.5% in those aged >60 years. The prevalence of intestinal metaplasia also increased with age, from 7.9% in those aged <60 years to 12.3% in those aged >60 years [27]. In our study, the prevalence of atrophic gastritis and intestinal metaplasia showed a similar tendency, increasing from 66.0% and 23.6% in those aged 40-59 years to 73.3% and 43.3% in those aged >60 years, respectively. However, the overall prevalence of atrophic gastritis and intestinal metaplasia was somewhat higher than that of the general population. These results support the idea that gastric cancer screening might be helpful for patients with HIV infection in Korea.

H. pylori infection is an important risk factor for gastric cancer, and its prevalence is very high in Korea [29]. Some studies reported the prevalence of *H. pylori* infection in patients with HIV infection and GI symptoms [30, 31]. However, there is no report of its prevalence in patients

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with HIV infection in Korea. In this study, only 1 patient with gastric cancer had *H. pylori* infection. The false negative results of the rapid urease test are related to the presence of severe atrophic gastritis and proton pump inhibitor or antibiotic use [32]. Further evaluation of *H. pylori* infection in patients with HIV infection is needed in areas with a high prevalence of gastric cancer and *H. pylori* infection.

In this study, the patients who received cancer screening endoscopy were older and more virologically and immunologically stable. In Korea, upper GI endoscopy is provided free of charge by the government for public health promotion. There may have been some patients who received the national cancer screening even though GI symptoms were present. However, regardless of GI symptoms, the prevalence of gastric ulcer and reflux esophagitis was higher than that in subjects who underwent health check-ups (gastric ulcer: 3.3% and reflux esophagitis: 7.9%) [21]. Therefore, even if symptoms are not present, screening endoscopy is important for the diagnosis of GI diseases in patients with HIV infection in the cART era.

This study has some limitations. First, this study was a single-center cohort study, and we could not enroll all patients with HIV infection who underwent endoscopy. Some patients underwent endoscopy in other centers, which is difficult to identify. In addition, many patients do not receive endoscopy because of confidentiality concerns regarding their disease owing to associated stigma. There is a possibility that the prevalence rate is underestimated. On the other hand, the prevalence rate can be overestimated because people with HIV infection received regularly check-up by doctors, so some patients may have had easier access to endoscopy and may have been diagnosed early with gastric cancer. Further studies on cancer screening rates of patients with HIV infection are needed. Second, study subjects were relatively small, we did not perform age- and sex-matched analysis in the assessment of gastric cancer incidence. So, the incidence of gastric cancer in patients with HIV infection was not comparable with that of the general population. Third, routine biopsy and *H. pylori* tests were not performed on all patients. The rapid urease test was performed only for indications allowed by insurance standards, and we did not include the urea breath test or serum *H. pylori* antibody test. This limited our ability to evaluate *H. pylori* infection. Fourth, the longer the cART duration, the older the patients; however, we could not adjust for age in comparing the prevalence of GI diseases according to the duration of cART. Finally, we have some limitations due to retrospective study. We were unable to assess the extent of atrophic gastritis. All cases of intestinal metaplasia and atrophic gastritis were not confirmed on biopsy. Thus, their prevalence may be overestimated or underestimated. Further, we were unable to investigate other risk factors of gastric cancer, such as alcohol use, smoking, and family history of gastric cancer.

In conclusion, we found the prevalence of gastric cancer in screening endoscopies was 3.7%. All gastric cancers confirmed on cancer screening endoscopy were in the early stage. Our study revealed that precursor lesions of gastric cancer, including intestinal metaplasia and atrophic gastritis, as well as other GI diseases were common even in the patients with HIV infection without GI symptoms. However, many patients do not receive periodic endoscopy. Therefore, regular gastric cancer screening might be useful in the early detection of gastric cancer and management of GI diseases in patients with HIV infection even without symptoms.

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