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Original Article

Association of Intensive Endoscopic Burden with Esophageal Cancer Detection: A Nationwide Cohort Study

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Background/Aims: Early diagnosis of esophageal cancer (EC) remains challenging despite the increasing frequency of endoscopic screenings globally. The rapidly increasing number of endoscopic screenings performed over a certain period might influence diagnostic performance. This study evaluated the association between the number of endoscopic screenings and EC detection rates in a nationwide cohort.

Methods: This retrospective population-based study used the Korean National Cancer Screening Program database, comprising 32,774,742 males and females aged ≥40 years between 2015 and 2019. Negative binomial regression model and least-squares mean evaluation were used to assess the association between month of the year and EC detection rates.

Results: This study enrolled 28,032,590 participants who underwent upper endoscopy. The number of participants in the fourth quarter (October to December: 10,923,142 [39.0%]) was 2.1 times higher than that in the first quarter (January to March: 5,085,087 [18.1%]); this trend continued for all 5 years. Contrarily, detection rates for EC in the fourth quarter (0.08/1,000 person) were half that in the first quarter (0.15/1,000 person). The odds of detecting EC were lowest in November; in 2015 the odds were 0.57 (95% confidence interval, 0.41 to 0.79; p=0.001) times lower and in 2016, they were 0.51 (95% confidence interval, 0.37 to 0.68; p<0.001) times lower compared to January. The predicted detection rates showed a decreasing trend toward the end of the year (p>0.05 for all).

Conclusions: The workload of endoscopists increased excessively with the rising number of endoscopies toward the end of the year, which was reflected by the decreased EC detection rates during this period. **(Gut Liver 2025;19:59-68)**

Key Words: Esophageal neoplasms; Upper endoscopy; Detection rate; Endoscopic burden

INTRODUCTION

According to GLOBOCAN 2020, esophageal cancer (EC) is the seventh most common cancer and the sixth leading cause of cancer-related mortality worldwide.[1] Early EC detection is important because its mortality rate increases when diagnosed late.[2,3] The gold standard for diagnosing EC is upper endoscopy with biopsy.[4] For patients who cannot tolerate upper endoscopy, upper gastrointestinal series (UGIS) is an alternative option.[5] However, because upper endoscopy must be performed to confirm the histological diagnosis when EC is suspected in UGIS, the role of endoscopy in EC detection is becoming increasingly important.

The Korean National Cancer Screening Program (KNCSP) provides a biennial gastric cancer screening program with either UGIS or upper endoscopy for individuals aged ≥40 years.[6] Although both diagnostic tools can detect ECs, annual participation rates in the KNCSP and the number of individuals who undergo endoscopy has increased over time.[7] For example, between 2007 and 2016, 72.7% of the invited participants from the KNCSP underwent upper

endoscopy instead of UGIS. Consequently, the workload of endoscopists has increased recently.

Increasing the workload of endoscopists affects examination quality. In index colonoscopy, increased procedural hours negatively correlated with the adenoma detection rate.[8] In a previous study using the KNCSP database, the number of gastric cancer screenings increased from October onward, and the increase in endoscopists' workload at the end of the year was associated with decreased gastric cancer detection rates.[9] The present study hypothesized that the same trend would be observed with EC detection rates, and controlling the number of endoscopic screenings is a modifiable factor that may help improve the EC detection rate. Thus, this study aimed to evaluate the association between the increased number of screening endoscopies and EC detection rate using a large population from the KNCSP database.

MATERIALS AND METHODS

1. Study population and design

This population-based retrospective cohort study used data from the KNCSP database between January 1, 2015, and December 31, 2019. Permission to use the KNCSP database was obtained from the Ministry of Health and Welfare. In total, 32,774,742 individuals participated in the gastric cancer screening program provided by the government. This study linked the data of the enrolled participants to the National Health Insurance Sharing Service–National Health Information Database and tracked their medical records until 2021. Participants were excluded if they had previously been diagnosed with EC or if they chose to undergo UGIS instead of upper endoscopy. The study protocol was approved by the Institutional Review Board of Ajou University Hospital (approval number: AJOUIRB-EXP-2021-306). The need for informed patient consent was waived because the study utilized a de-identified dataset for the analyses. This study followed the Strengthening of the Reporting of Observational Studies in Epidemiology Reporting Guidelines for Cohort Studies.[10]

2. The KNCSP and screening endoscopy protocol

The KNCSP provides screening services for six common cancers: stomach, liver, colorectum, breast, uterine cervix, and lung cancers. Although the KNCSP does not provide a screening program for EC, its data was used for this study because the esophagus was also evaluated when the participants underwent upper endoscopy. Endoscopic screening involves image acquisition after close observation by an endoscopist. Images of at least eight areas (duodenum, ampulla, antrum, angle, corpus, fundus retroflexion view, esophagogastric junction, and esophagus) were recommended, along with multiple additional images in areas with abnormal lesions. A tissue biopsy was performed when abnormal findings were detected on endoscopic screening. If further evaluation or treatment was needed based on the biopsy or endoscopic findings, the patient was referred to an upper-tier hospital for reexamination. The Korean Ministry of Health and Welfare implemented an endoscopy quality management project for the KNCSP in 2008. The Quality Improvement Committee of the Korean Society for Gastrointestinal Endoscopy developed quality indicators for the endoscopy quality improvement program, which were adopted in all endoscopic screening facilities.[11]

3. Data collection and definitions

The KNCSP data included demographic characteristics, such as age and sex, medical and family history, history of gastric cancer, colon cancer, or gastric disease, collected using a self-administered questionnaire, screening month, and endoscopy results. These data were available in the KNCSP's claims data for 2015 and 2016, patients' medical history was unavailable for 2017, and their sex and age groups were unavailable for 2018 and 2019. Although the required variables differed for each analysis, this study included data from 2015 to 2019 to get more participants. However, the corresponding year was excluded from each analysis if the required variable data were unmet.

Screening results were defined as positive when the endoscopic results indicated a suspected or confirmed diagnosis of EC. After linking the results with the medical records from the National Health Insurance Sharing Service–National Health Information Database, the detected cancer was defined as EC that was screening-positive and confirmed with the diagnosis code for EC (International Statistical Classification of Diseases, Tenth Revision, code C15.xx). Interval cancer was defined as EC confirmed with a diagnosis code of EC (C15.xx) within 1 year of an initial negative screening result.

4. Statistical analysis

Participants' descriptive data were summarized annually using means and standard deviations for continuous variables and numbers and percentages for categorical variables. Each year, the number of participants and detection rates of EC were calculated monthly and visualized. In addition, the overall screening performance for EC was assessed using sensitivity, specificity, detection rate per 1,000 persons, positive predictive value, interval cancer rates per 1,000 persons, and negative and positive rates per

1,000 persons. Logistic regression analysis of participants in 2015 and 2016 was performed to identify factors associated with EC detection among the following covariates: sex, age, screening month, history of gastric and colon cancer, and history of gastric disease, including peptic ulcer, atrophic gastritis, intestinal metaplasia, and gastric polyps. Considering the overdispersed data, the screening month effect was estimated and tested using negative binomial regression, adjusting for age groups. Based on this regression model, the least-squares method was applied to predict the detection rate with a 95% confidence interval for 2015 to 2017.

RESULTS

1. Study population and baseline characteristics

A total of 32,774,742 participants underwent gastric cancer screening using UGIS or upper endoscopy between 2015 and 2019. Of these, 28,032,590 patients who underwent upper endoscopy were included in this study (Fig. 1). The mean age was 56.42±10.61, and 54.34% of the participants (8,957,275) were females. A total of 4,327 participants (0.02%) had positive screening results, and 3,033 (0.01%) were confirmed to have EC. Among the 28,028,263 participants with negative screening results, 3,331 were diagnosed with EC within 1 year. For quarterly screening periods, the number of participants in the fourth quarter (October to December: 10,923,142 [38.97%]) was 2.15 times higher than that in the first quarter (January to March: 5,085,087 [18.14%]). This trend was the same in all 5 years, and the number of upper endoscopies for the fourth quarter of each year was 1.78 to 2.75 times greater than that of the first quarter (Table 1). The overall screening performance for EC between 2015 and 2019 is reported

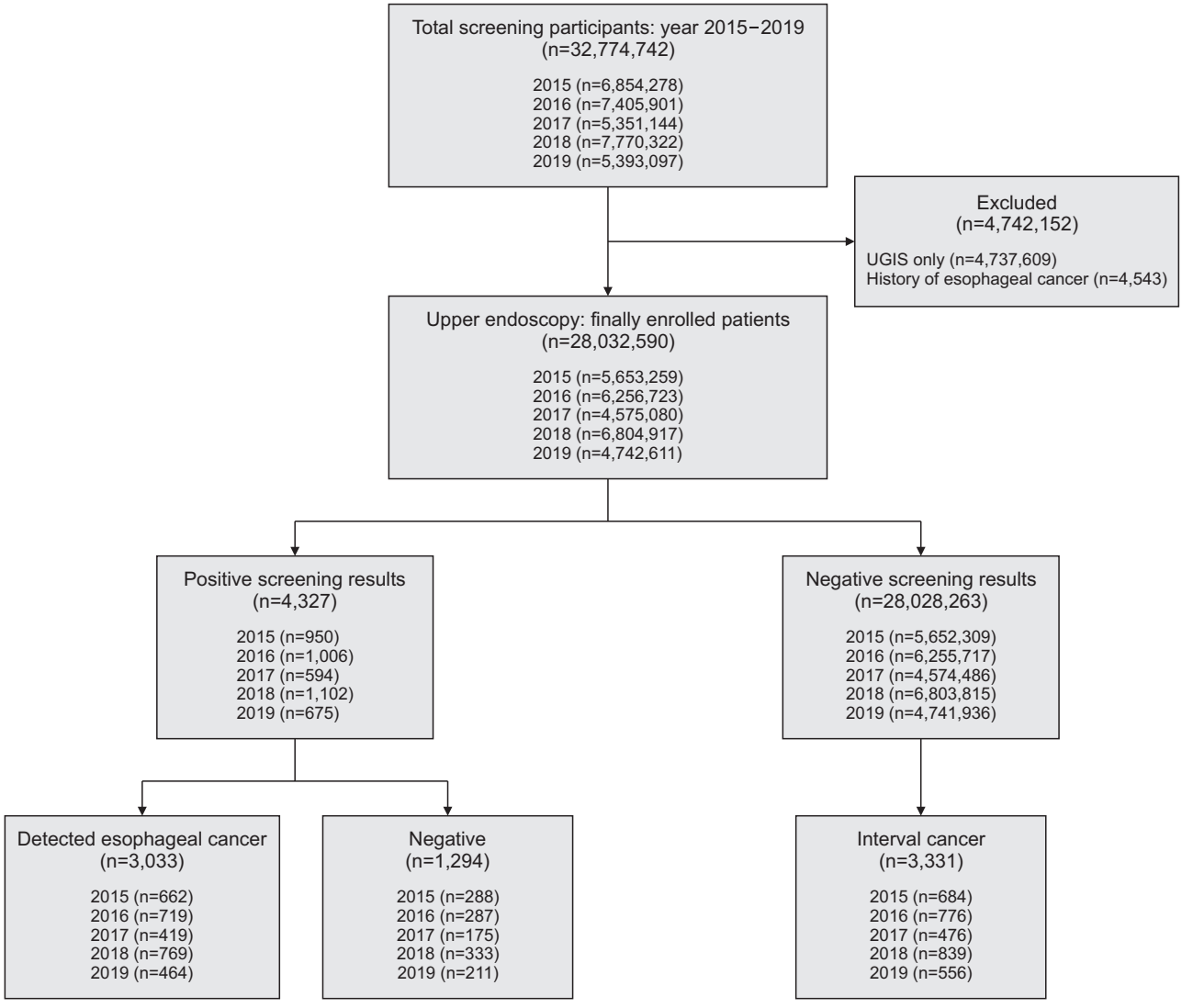

Fig. 1. Flowchart of participant inclusion. UGIS, upper gastrointestinal series.

Table 1. Baseline Characteristics of Enrolled Participants

Characteristic	Total	Screening year				
		2015	2016	2017	2018	2019
No. of screening	28,032,590 (100)	5,653,259 (20.17)	6,256,723 (22.32)	4,575,080 (16.32)	6,804,917 (24.28)	4,742,611 (16.92)
Sex					NA	NA
Male	7,527,787 (45.66)	2,589,853 (45.81)	2,875,381 (45.96)	2,062,553 (45.08)		
Female	8,957,275 (54.34)	3,063,406 (54.19)	3,381,342 (54.04)	2,512,527 (54.92)		
Age, yr	56.42±10.61	55.74±10.65	56.03±10.69	57.78±10.31		
Age group					NA	NA
40–49 yr	4,879,350 (29.60)	1,796,538 (31.78)	1,953,813 (31.23)	1,128,999 (24.68)		
50–59 yr	5,276,572 (32.01)	1,824,161 (32.27)	1,983,297 (31.70)	1,469,114 (32.11)		
60–69 yr	4,028,947 (24.44)	1,308,139 (23.14)	1,482,455 (23.69)	1,238,353 (27.07)		
70–79 yr	1,972,361 (11.96)	623,575 (11.03)	714,873 (11.43)	633,913 (13.86)		
≥80 yr	327,832 (1.99)	100,846 (1.78)	122,285 (1.95)	104,701 (2.29)		
Screening quarter						
January–March	5,085,087 (18.14)	918,454 (16.25)	1,146,680 (18.33)	875,743 (19.10)	1,211,184 (17.80)	933,026 (19.67)
April–June	5,999,278 (21.40)	1,022,290 (18.08)	1,354,463 (21.65)	1,034,742 (22.60)	1,499,277 (22.03)	1,088,506 (22.95)
July–September	6,025,083 (21.49)	1,190,705 (21.06)	1,290,415 (20.62)	1,049,669 (22.90)	1,430,394 (21.02)	1,063,900 (22.43)
October–December	10,923,142 (38.97)	2,521,810 (44.61)	2,465,165 (39.40)	1,614,926 (35.30)	2,664,062 (39.15)	1,657,179 (34.94)
History of gastric cancer	153,296 (0.55)	36,897 (0.65)	41,531 (0.66)	NA	45,923 (0.67)	28,945 (0.61)
History of colon cancer	97,705 (0.35)	20,858 (0.37)	24,734 (0.40)	NA	29,389 (0.43)	22,724 (0.48)
History of gastric disease*	6,134,544 (21.88)	1,245,272 (22.03)	1,412,844 (22.58)	NA	1,689,715 (24.83)	1,342,749 (28.31)

Data are presented as number (%) or mean±SE.
SE, standard error, NA, not available.
*Gastric disease includes the flowing: peptic ulcer, atrophic gastritis, intestinal metaplasia, gastric polyp, and other gastric diseases.

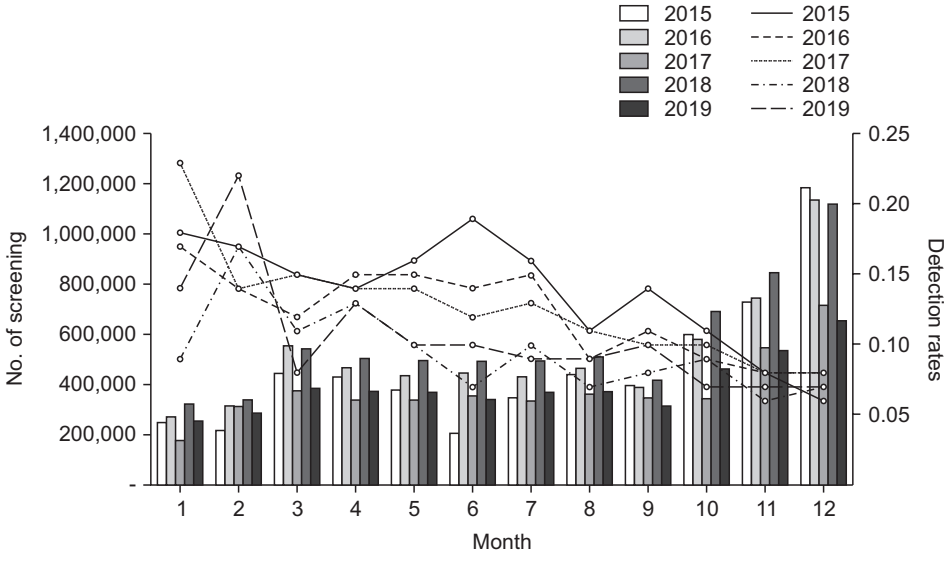

Fig. 2. Changes in the monthly number of screenings and esophageal cancer detection rates between 2015 and 2019.

in Supplementary Table 1.

2. Monthly changes in the number of participants and monthly detection rates for EC

The number of screening endoscopies increased toward the end of the year and was highest every December between 2015 and 2019. For 5 years, 4,819,606 participants (17.19%) underwent screening in December, which was 2.28 times greater than the average number of participants screened between January and November. In other words, the number of individuals participating in the KNCSP were higher at the end of each year. In particular, 4.7 times more participants underwent upper endoscopy in December (1,187,404) than in January (250,604) in 2015. The EC detection rate tended to decrease toward the end of the year. It was lowest in November and December (0.06–0.08 per 1,000 person) when the number of screening endoscopies was the highest (Fig. 2, Supplementary Table 2).

Table 2. Logistic Regression Analysis of Risk Factors for Esophageal Cancer Detection

Effect	Year 2015				Year 2016			
	Univariable		Multivariable		Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex								
Female	Ref.		Ref.		Ref.		Ref.	
Male	5.51 (4.66–6.51)	<0.001	5.52 (4.67–6.53)	<0.001	5.87 (4.97–6.92)	<0.001	5.92 (5.01–6.98)	<0.001
Age group								
40–49 yr	Ref.		Ref.		Ref.		Ref.	
50–59 yr	2.86 (2.18–3.75)	<0.001	2.82 (2.15–3.70)	<0.001	2.26 (1.78–2.88)	<0.001	2.30 (1.80–2.93)	<0.001
60–69 yr	6.28 (4.85–8.13)	<0.001	5.97 (4.60–7.74)	<0.001	5.05 (4.02–6.34)	<0.001	5.00 (3.98–6.29)	<0.001
70–79 yr	11.98 (9.23–15.55)	<0.001	11.03 (8.47–14.36)	<0.001	7.33 (5.78–9.29)	<0.001	7.17 (5.64–9.11)	<0.001
≥80 yr	16.81 (12.01–23.53)	<0.001	15.26 (10.87–21.43)	<0.001	14.29 (10.65–19.18)	<0.001	13.79 (10.24–18.59)	<0.001
Month								
January	Ref.		Ref.		Ref.		Ref.	
February	0.93 (0.64–1.36)	0.717	0.93 (0.64–1.36)	0.719	0.60 (0.43–0.85)	0.004	0.61 (0.43–0.86)	0.004
March	0.84 (0.60–1.16)	0.276	0.79 (0.57–1.09)	0.153	0.63 (0.47–0.85)	0.002	0.59 (0.44–0.79)	<0.001
April	0.85 (0.61–1.17)	0.315	0.84 (0.61–1.16)	0.294	0.67 (0.50–0.91)	0.009	0.65 (0.48–0.88)	0.005
May	0.93 (0.67–1.29)	0.650	0.98 (0.71–1.36)	0.904	0.62 (0.45–0.84)	0.002	0.61 (0.44–0.83)	0.002
June	1.20 (0.84–1.71)	0.317	1.26 (0.88–1.79)	0.206	0.56 (0.41–0.76)	<0.001	0.58 (0.42–0.79)	<0.001
July	1.00 (0.72–1.39)	0.988	1.14 (0.82–1.59)	0.430	0.67 (0.49–0.91)	0.010	0.75 (0.55–1.02)	0.063
August	0.68 (0.48–0.95)	0.025	0.87 (0.62–1.22)	0.413	0.53 (0.38–0.72)	<0.001	0.66 (0.48–0.90)	0.010
September	0.73 (0.52–1.03)	0.074	0.88 (0.63–1.25)	0.479	0.48 (0.34–0.68)	<0.001	0.56 (0.40–0.79)	0.001
October	0.59 (0.42–0.81)	0.001	0.69 (0.50–0.96)	0.028	0.56 (0.41–0.75)	<0.001	0.64 (0.47–0.86)	0.003
November	0.44 (0.32–0.62)	<0.001	0.57 (0.41–0.79)	0.001	0.41 (0.31–0.56)	<0.001	0.51 (0.37–0.68)	<0.001
December	0.41 (0.30–0.56)	<0.001	0.58 (0.43–0.79)	0.001	0.38 (0.29–0.50)	<0.001	0.51 (0.38–0.67)	<0.001
History of gastric cancer	1.95 (1.10–3.44)	0.022	0.89 (0.50–1.57)	0.685	1.96 (1.14–3.39)	0.016	0.94 (0.55–1.64)	0.838
History of colon cancer	2.58 (1.34–4.98)	0.005	1.26 (0.65–2.43)	0.492	2.02 (1.01–4.05)	0.047	1.04 (0.52–2.10)	0.905
History of gastric disease*	0.80 (0.68–0.94)	0.008	0.76 (0.65–0.90)	0.001	0.71 (0.61–0.84)	<0.001	0.69 (0.59–0.82)	<0.001

OR, odds ratio; CI, confidence interval; Ref., reference.

*Gastric disease includes the flowing: peptic ulcer, atrophic gastritis, intestinal metaplasia, gastric polyp, and other gastric diseases.

3. Factors related to endoscopic screening sensitivity for EC detection

Logistic regression analysis of risk factors for EC detection was performed in the consequent 2 years because the KNCSP data, including sex, age group, screening month, previous medical history, and endoscopy results, were only fully available in 2015 and 2016. Univariate analysis showed that sex and age were significantly associated with EC detection (p<0.001). October to December was significantly associated with EC detection in 2015 (p<0.05), and all calendar months were significantly associated with EC detection in 2016 (p<0.05 for all). In the multivariate analysis, the overall significance remained similar for both years, except in July 2016. Compared with January, the odds ratio of cancer detection in December was 0.58 (95% confidence interval, 0.43 to 0.79; p<0.001) and 0.51 (95% confidence interval, 0.38 to 0.67; p<0.001) in 2015 and 2016, respectively. While the odds of cancer detection decreased significantly in the last quarter of 2015, they decreased from the beginning of 2016. However, both years clearly demonstrated a decreasing tendency in the odds of cancer detection toward the end of the year (Table 2).

4. Association between detection rates and calendar month

Different age groups prefer different calendar months for endoscopic screening;[9] therefore, each age group was added as a covariate in the model along with the screening month. The KNCSP data for sex, age group, and screening month are available for 2015, 2016, and 2017. A negative binomial model was tested to estimate the effect size of the screening month for each of the 3 years. Age group was a significant factor for each year, except in those aged 70 to 79 years, and the EC detection rate was higher in the older age group. After adjusting for age group, the detection rate was tested according to the calendar month, and the estimated coefficient showed a decreasing trend toward the end of the year. However, the difference was not significant (Table 3). Therefore, the EC detection rate was predicted using the least-squares mean based on the negative binomial regression model. The calendar month was adjusted according to age groups, and the predicted detection rates showed a decreasing trend toward the end of the year compared to the rate at the beginning of the year in 2015, 2016, and 2017 (Table 4).

Table 3. Estimation of the Effect Size of Screening Month by Negative Binomial Regression*

	Year 2015				Year 2016				Year 2017			
	Estimate	Standard error	Wald chi-square	p-value	Estimate	Standard error	Wald chi-square	p-value	Estimate	Standard error	Wald chi-square	p-value
Intercept	−0.99	0.41	6.01	0.014	−0.94	0.35	7.15	0.008	−0.98	0.54	3.29	0.070
Month												
January	0.55	0.49	1.26	0.261	0.82	0.43	3.62	0.057	−0.54	0.69	0.61	0.435
February	0.20	0.49	0.17	0.680	0.04	0.43	0.01	0.931	0.57	0.70	0.66	0.415
March	0.46	0.49	0.91	0.340	0.42	0.43	0.95	0.331	0.23	0.71	0.11	0.744
April	0.09	0.49	0.03	0.861	0.41	0.43	0.88	0.348	−0.06	0.68	0.01	0.928
May	0.73	0.49	2.23	0.136	0.49	0.44	1.25	0.263	0.25	0.70	0.12	0.726
June	0.81	0.49	2.76	0.097	0.34	0.43	0.62	0.433	0.07	0.70	0.01	0.924
July	0.66	0.49	1.81	0.178	0.41	0.43	0.91	0.339	0.22	0.70	0.10	0.753
August	0.27	0.49	0.31	0.579	0.40	0.43	0.85	0.357	−0.26	0.68	0.14	0.703
September	0.47	0.49	0.94	0.333	0.08	0.43	0.03	0.860	−0.29	0.68	0.18	0.672
October	0.36	0.49	0.53	0.466	0.14	0.43	0.10	0.753	−0.15	0.68	0.05	0.831
November	0.33	0.49	0.47	0.492	−0.35	0.43	0.66	0.417	−0.19	0.69	0.08	0.781
December	0.00	0.00	-	-	0.00	0.00	-	-	0.00	0.00	-	-
Age group												
40–49 yr	−3.94	0.33	144.17	<0.001	−3.67	0.28	166.83	<0.001	−4.21	0.50	71.56	<0.001
50–59 yr	−1.98	0.32	39.21	<0.001	−1.97	0.28	49.32	<0.001	−2.31	0.44	27.12	<0.001
60–69 yr	−1.12	0.32	12.58	<0.001	−0.94	0.28	11.15	<0.001	−0.96	0.45	4.64	0.031
70–79 yr	−0.30	0.32	0.91	0.339	−0.50	0.28	3.16	0.075	−0.47	0.44	1.11	0.292
≥80 yr	0.00	0.00	-	-	0.00	0.00	-	-	0.00	0.00	-	-
Dispersion	0.59	0.11			0.46	0.09			1.15	0.21		

*The negative binomial regression model was fit with the number of screenings as an offset term. Overdispersion was tested based on scaled Pearson chi-square analysis. The covariance matrix was multiplied by a factor of deviance/degree of freedom.

Table 4. Predicted Detection Rate Calculated with the Least-Squares Mean Based on Negative Binomial Regression

	Predicted detection rate (95% confidence interval)		
	Year 2015	Year 2016	Year 2017
Month			
January	0.15 (0.08–0.29)	0.22 (0.12–0.39)	0.04 (0.02–0.12)
February	0.10 (0.05–0.21)	0.10 (0.05–0.18)	0.14 (0.05–0.35)
March	0.14 (0.07–0.27)	0.14 (0.08–0.26)	0.10 (0.04–0.26)
April	0.09 (0.05–0.18)	0.14 (0.08–0.26)	0.07 (0.03–0.19)
May	0.18 (0.09–0.35)	0.15 (0.08–0.28)	0.10 (0.04–0.26)
June	0.19 (0.10–0.37)	0.13 (0.07–0.24)	0.08 (0.03–0.21)
July	0.16 (0.08–0.32)	0.14 (0.08–0.26)	0.10 (0.04–0.25)
August	0.11 (0.06–0.22)	0.14 (0.08–0.26)	0.06 (0.02–0.15)
September	0.14 (0.07–0.27)	0.10 (0.06–0.19)	0.06 (0.02–0.15)
October	0.12 (0.06–0.24)	0.11 (0.06–0.20)	0.07 (0.03–0.17)
November	0.12 (0.06–0.23)	0.07 (0.04–0.12)	0.06 (0.02–0.16)
December	0.09 (0.04–0.17)	0.09 (0.05–0.17)	0.08 (0.03–0.20)
Age group			
40–49 yr	0.01 (0.01–0.02)	0.01 (0.01–0.02)	0.01 (0–0.01)
50–59 yr	0.08 (0.05–0.12)	0.07 (0.05–0.10)	0.04 (0.02–0.07)
60–69 yr	0.18 (0.12–0.28)	0.20 (0.14–0.29)	0.14 (0.08–0.26)
70–79 yr	0.41 (0.27–0.64)	0.31 (0.21–0.45)	0.23 (0.13–0.43)
≥80 yr	0.56 (0.36–0.87)	0.51 (0.34–0.75)	0.37 (0.20–0.70)

DISCUSSION

The exact pathogenesis of EC is yet to be established, and effective interventions to prevent its onset are unclear. Hence, early detection through repetitive endoscopic evaluation is the most effective preventive measure. Previous studies have discussed the benefits and role of endoscopic screening for EC.[12,13] Endoscopic screening is important because the disease can be diagnosed and treated only after visualizing the lesion endoscopically and confirming it histologically. Thus, upper endoscopy is the most important test for early detection of EC. Some Asian countries have implemented national endoscopic cancer screening programs for gastric cancer, which have been reported to lower gastric cancer-related mortality.[14,15] Furthermore, endoscopic screening during regular checkups has increased the detection of gastric and EC.[16,17] Thus, endoscopy plays an increasingly important role in preventing and diagnosing EC, and the burden on endoscopists has intensified proportionally. Our previous study reported an association between the number of endoscopic screenings and gastric cancer detection rate.[9] Since the endoscopy protocol in the KNCSP for gastric cancer includes esophageal observation, the present study examined the relationship between endoscopic frequency and EC detection rates. Thus, the study analyzed approximately 30 million individuals who underwent upper endoscopy and the association between calendar months and the number of endoscopic screenings over 5 years. The results indicated that the number of endoscopic screenings increased dramatically toward the end of the year. In contrast, the EC detection rate dropped dramatically toward the end of the year. In particular, 17.19% of all endoscopic screenings were performed in December, which was 4.74-fold higher than the number of screenings in January. Age can also influence the incidence of cancer.[18] Age-adjusted analysis showed that the estimated coefficient declined toward the end of the year but was not statistically significant. Thus, the predicted detection rate was calculated using the least-squares method. The analysis included age- and sex-adjusted calendar months, and the results showed that the predicted detection rate of EC decreased toward the end of the year. Thus, this study's results suggest that endoscopic workload can influence EC detection.

EC tends to be diagnosed late because it is often asymptomatic in the early stages.[19] In Korea, over the past two decades, the proportion of EC cases diagnosed at an early stage has increased gradually, and the 5-year survival rate of EC has also improved.[20] This may have been due to the introduction of a gastric cancer screening program under the KNCSP in 2002,[7] as the esophagus was also evaluated when participants underwent screening. While UGIS only provides superficial images with contrast and requires retesting with endoscopy and biopsy when EC is suspected, upper endoscopy allows direct inspection of suspected lesions, and biopsy can be performed immediately for confirmation. In addition, endoscopy has a higher detection rate, sensitivity, and specificity and a lower interval cancer rate than UGIS. Therefore, an increasing number of participants choose to undergo screening with upper endoscopy

instead of UGIS.[7]

The present study, as well as previous studies using the KNCSP database,[9] reported a dramatic increase in the number of endoscopic screenings at the end of the year, which was associated with a decreased cancer detection rate. The reason for this increase is unclear. However, it can be deduced that the monthly variation in the number of endoscopies might be due to a psychological tendency to postpone the endoscopy date as much as possible because many individuals undergo it solely for screening purposes. The KNCSP is concerned about this issue and has recently started reporting the monthly number of available screenings to its participants. Moreover, attempts have been made to distribute participants accordingly. Due to the lack of studies on the relationship between the rapid increase in the number of examinations and the quality of the tests, several factors must be considered when setting the endoscopic number considering the appropriate endoscopic workload. Therefore, this study is expected to provide important data for the KNCSP and countries preparing to introduce national cancer screening programs.

An increase in the workload of endoscopists affects their performance in detecting gastric and colon cancers.[8,9,21] However, this trend has not been evaluated for EC yet. In fact, there are only a limited number of studies analyzing EC compared to gastric or colon cancer because the incidence of EC accounts for only 1.1% of all malignancies.[22] Previous studies have analyzed the incidence and survival rates of EC using a population-based database[23] and demonstrated that the gastric cancer screening program reduced EC mortality.[24] To our knowledge, this is the first study to assess the impact of endoscopic frequency on the EC detection rate. Furthermore, the study has important implications because it utilized extensive data from 28 million patients in a national cohort.

A negative binomial model was used to estimate the association between the detection rate and calendar months. Although the result was not statistically significant, the estimated coefficient showed a decreasing trend toward the end of the year. The least-squares mean was calculated to verify this trend, and the predicted detection rate was observed to decrease significantly at the end of the year. In addition, the odds of cancer detection decreased significantly in the logistic regression analysis. Calendar months were significantly associated factor in the logistic regression model, but not in the negative binomial model because the number of detected cancer cases was very low due to the low incidence of EC. This is because the dependent variable in the negative binomial model detects cancer/number of endoscopies and does not detect cancer.

In our study, 3,033 EC cases and 3,331 interval cancer cases were detected. Few studies of interval EC have been conducted in nationwide cohorts because of the lack of screening programs; therefore, it is difficult to validate these numbers. However, a study was conducted in the United States that used a large, population-based cancer registry and reported an EC interval cancer rate of 6.2%.[25] In our study, the number of interval cancers was close to that of the detected cancers; however, the interval cancer rate was 0.01% (3,331 cases in 28,028,263 participants). We believe that these numbers are likely because the incidence of EC was much lower than that of other gastrointestinal cancers, and our study included approximately 30 million participants. Interval EC has not been well studied to date. The efficacy of screening endoscopy for EC has not yet been validated, making it difficult to conduct such a study. Although our findings do not focus on interval cancer, we expect that they will serve as a reference for future studies on interval EC.

This study had several limitations. First, although the study used the real-world data of 28 million individuals from the KNCSP, the number of ECs detected by endoscopic screening was only approximately one-third of the number of patients diagnosed with EC annually.[26] This gap might be because symptomatic and older patients at high risk of screening endoscopy visit tertiary hospitals directly and are therefore not included in our study population. Therefore, the study's findings may not sufficiently represent the general population, and additional studies assessing an entire cohort of individuals undergoing upper endoscopy may be necessary to clarify the study outcomes. Second, because baseline characteristics were only fully available in 2015 and 2016, and few variables were deficient in residual years, statistical analyses were performed with limited information. Smoking and alcohol are well-known risk factors for EC.[27] However, in our study, we could not obtain patient-level risk factors due to the nature of the database; therefore, these risk factors could not be included in the baseline characteristics and further analysis. Additionally, variables, such as patient symptoms, comorbidities, hospital type, and residency, which can influence the EC detection rate, were unavailable for the logistic regression analysis. Third, because the purpose of our study was to investigate EC detection in upper endoscopy, we did not have follow-up data for 1,294 cases in which the screening results were positive but the final results were negative. Fourth, we did not examine changes in interval cancer by quarter or month. Fifth, we checked the overall screening performance for the years used in the analysis but did not provide data on the quarterly or monthly performance. Sixth, in our study, the following factors were not considered in the analysis, and further studies that include them

are necessary: the quality of the endoscopist, the actual number of endoscopic procedures performed by each endoscopist, observation time during endoscopy, and biopsy rates. Seventh, cancer characteristics and stages were not included in the analysis. The histological findings of cancer detected through endoscopy were not provided because of privacy issues with the KNCSP data. However, the most common pathology of EC in Korea is squamous cell carcinoma (96.9%), with only 3.1% of cases being adenocarcinomas.[28] Finally, this study used the KNCSP database for gastric cancer and thus could not evaluate the effects of EC screening.

In conclusion, using population-based data from the KNCSP database, a decrease in the EC detection rate toward the end of the year was observed as the number of endoscopic screenings increased rapidly. These findings suggest that policies such as limiting the number of endoscopic examinations in a specific period, can help improve cancer detection rates.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Study concept and design: C.K.N., K.M.L. Data acquisition: E.L. Data analysis and interpretation: E.L., B.P. Drafting of the manuscript: Y.L., E.L., C.K.N., K.M.L. Critical revision of the manuscript for important intellectual content: C.K.N. Statistical analysis: E.L., B.P. Obtained funding: Y.L. Administrative, technical, or material support; study supervision: G.H.L., S.G.L., S.J.S. Approval of final manuscript: all authors.

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at https://doi.org/10.5009/gnl240111.

DATA AVAILABILITY STATEMENT

The datasets analyzed in this study cannot be shared publicly because of national legislation for protection of personal information. However, data are available from the Korea National Health Insurance Sharing Service (https://nhiss.nhis.or.kr) for those authorized to access the confidential data.

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