Difference in F-18 FDG Uptake After Esophagogastroduodenoscopy and Colonoscopy in Healthy Sedated Subjects

Jong-Ryool Oh¹ · Ji-Hyoung Seo² · Woo-Jin Chang³ · Seung-II Bae³ · In-Wook Song³ · Jin-Gu Bong⁴ · Hye-Yeon Jeong⁴ · So-Young Park⁵ · Jeongyup Bae⁶ · Hyundae Yoon³

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Abstract

Purpose We aimed to evaluate the difference in fluorodeoxyglucose (FDG) uptake in sedated healthy subjects after they underwent esophagogastroduodenoscopy (EGD) and colonoscopy procedures.

Methods The endoscopy group ($n = 29$) included healthy subjects who underwent screening via F-18 FDG positron emission tomography/computed tomography (PET/CT) after an EGD and/or colonoscopy under sedation on the same day. The control group ($n = 35$) included healthy subjects who underwent screening via PET/CT only. FDG uptake in the tongue, uvula, epiglottis, vocal cords, esophagus, stomach, duodenum, liver, cecum, colon, anus, and muscle were compared between the two groups.

Results Maximum standardized uptake value (SUVmax) in the tongue, pharynx, larynx, and esophagus did not

significantly differ between the endoscopy and control groups. In contrast, mean SUVmax in the whole stomach was 18 % higher in the endoscopy group than in the control group (SUVmax: 2.96 vs. 2.51, $P = 0.010$). In the lower gastrointestinal track, SUVmax from the cecum to the rectum was not significantly different between the two groups, whereas SUVmax in the anus was 20 % higher in the endoscopy group than in the control group (SUVmax: 4.21 vs. 3.50, $P = 0.002$). SUVmax in the liver and muscle was not significantly different between the two groups. Mean volume of the stomach and mean cross section of the colon was significantly higher in the endoscopy group than in the control group (stomach: 313.28 cm³ vs. 209.93 cm³, $P < 0.001$, colon: 8.82 cm² vs. 5.98 cm², $P = 0.001$).

Conclusions EGD and colonoscopy under sedation does not lead to significant differences in SUVmax in most parts of the body. Only gastric FDG uptake in the EGD subjects and anal FDG uptake in the colonoscopy subjects was higher than uptake in those regions in the control subjects.

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✉ Hyundae Yoon
ynm98@naver.com

Keywords Colonoscopy · Endoscopy · Esophagogastroduodenoscopy · FDG PET/CT

- ¹ Department of Nuclear Medicine, Raphael Hospital, Daegu, Republic of Korea
- ² Department of Nuclear Medicine, Fatima Hospital, Daegu, Republic of Korea
- ³ Department of Internal Medicine, Raphael Hospital, 303, Jungang-daero, Jung-gu, 41968 Daegu, Republic of Korea
- ⁴ Department of Surgery, Raphael Hospital, Daegu, Republic of Korea
- ⁵ Department of Anesthesiology, Raphael Hospital, Daegu, Republic of Korea
- ⁶ Department of Pathology, Raphael Hospital, Daegu, Republic of Korea

Introduction

F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) has become a crucial imaging method for monitoring patients with malignancies. Malignant tissues have high metabolic rates and can take up more FDG than normal tissues. However, tissues affected by inflammation or other stress also show enhanced FDG utilization, which can lead to false-positive results on PET/CT scans. Surgery, chemotherapy, radiotherapy, or other interventional procedures can induce unwanted FDG uptake

in patients with malignancies. Although the optimal timing of a PET/CT scan in relation to those other treatments has not been clearly determined, it has been suggested that PET/CT scans be delayed for at least several weeks to months after those treatments [1–5].

Esophagogastroduodenoscopy (EGD) and colonoscopy are gold standard procedures for evaluating upper and lower gastrointestinal (GI) malignancies. In our institute, PET/CT scans are generally scheduled on a different day from EGD or colonoscopy procedures due to concerns that those procedures or the overnight bowel preparations may induce changes in FDG uptake in the body. If both examinations must be performed on the same day, it is preferred that the PET/CT scan be performed after the endoscopy because of the radiation exposure for the endoscopists. Practical guidelines or PET/CT scan findings after EGD or colonoscopy procedures are lacking. In this study, we aimed to evaluate the differences in F-18 FDG uptake just after EGD and colonoscopy procedures in sedated healthy subjects.

Materials and Methods

Subjects

Healthy subjects included in this single-institution study underwent endoscopy and FDG PET/CT screening from January 2013 to November 2015. The endoscopy group included subjects who underwent PET/CT scanning just after EGD and/or colonoscopy on the same day. The control group included healthy subjects who underwent PET/CT scanning within the 6 months before or after, but not within 1 week after, endoscopy. All subjects with a previous history of malignancy, GI surgery, or any endoscopic evidence of tumorous or active inflammatory lesions in the GI track were excluded from both groups. All subjects with active GI symptoms, such as diarrhea or abdominal pain, on the day of the PET/CT examination were excluded from the control group. Because of high physiologic FDG uptake in the intestines, diabetic patients who are taking metformin were also excluded from the analysis [6]. The local ethics committee approved this study, and all enrolled subjects gave written informed consent for participation in the study and for the evaluation of their clinical information.

Endoscopy

Endoscopies were performed with a forward-viewing endoscopy by two experienced endoscopists. A video endoscope (GIF-H260Z, GIF-Q260J; Olympus, Tokyo, Japan) equipped with a 4-mm transparent cap (D-201-11804; Olympus) was used. For the EGD, 8–14 ml of propofol was injected prior to the procedure to achieve adequate sedation. The endoscope was

introduced up to the second portion of the duodenum. After the EGD, 2–4 mg of midazolam and 50 mg of pethidine were injected before and during colonoscopy. The scope was introduced into the terminal ileum. During the withdrawal, all colon segments were assessed for a minimum of 7 min. In the colonoscopy group, bowel preparation was performed with 2 L of polyethylene glycol solution given one day before the procedure or a split dose of the solution one day before and on the day of the examination.

PET/CT

Scanning was performed on a Biograph mCT PET/CT system (Siemens, Erlangen, Germany). All subjects fasted for at least 6 h prior to the intravenous administration of FDG. Their blood glucose levels were measured before the FDG was injected. If their blood glucose level was ≥ 8.3 mmol/l, PET/CT was deferred. The FDG dose that was injected was determined based on the subject's body weight (4.44–5.55 MBq/kg). Image acquisitions started approximately 60 min after FDG injection. Just prior to image acquisitions, all subjects drank 500 mL of water for gastric filling and voided for bladder emptying. No oral or intravenous contrast material was administered. CT images were acquired from the skull base to the upper thigh with subjects in the supine position and their arms down. The CT parameters were 120 kV, automated from 10 to 130 mA, 0.5 s/rotation, field of view (FOV) of 50 cm, scan length of 22 s, and slice thickness of 3.75 mm. Immediately following CT acquisition, PET data were acquired in the same anatomic locations with a 15.7-cm axial FOV and was acquired in the two-dimensional mode with 2 min/bed position. The CT data were used for attenuation correction. The images were reconstructed using a conventional iterative algorithm.

Data Analysis

Image display and analysis was performed using workstation software (Siemens TrueD, Erlangen, Germany). SUVmax and volume/cross section of target organ was measured by one experienced nuclear medicine physician who was board-certified with 9 years PET/CT experience. Lesions were measured in subjects who underwent both EGD and colonoscopy in the endoscopy group and all subjects in the control group. The lower GI track was excluded from analysis for subjects who underwent EGD only and the upper GI track (including the tongue, pharynx, and larynx) was excluded in subjects who underwent colonoscopy only in the endoscopy group.

Measurement of SUVmax

The volume of interest (VOI) in each target organ was manually drawn in the fused PET/CT images, and the maximum

standardized uptake value (SUVmax) was automatically calculated based on body weight by the attenuation-corrected PET data (Supplementary Fig. 1). If the fusion image was misregistered due to intestinal movement, the VOI was drawn in the PET-only images. If the target organ had a symmetric structure, the arithmetic mean of the SUVmax in the right and left organ was recorded. The tongue VOI was drawn in the coronal view; the genioglossus (2.0 cm diameter sphere) was measured at the level of the anterior end of the hyoid bone and the styloglossus (1.5 cm diameter sphere) was at the level of the apex of the orbital cavity. VOIs of the uvula (1.0 cm diameter sphere), epiglottis (1.0 cm diameter sphere), vocal cords (2.0 cm diameter sphere), and esophagus were drawn in the sagittal view; the cervical esophagus (2.5 cm high ellipsoid, cross section: variable) was measured at the level just above the sternal notch and the thoracic esophagus (2.5 cm high ellipsoid, cross section: variable) was just below the tracheal bifurcation. VOIs of the gastroesophageal junction (2.5 cm diameter sphere), fundus (4.0 cm diameter sphere), greater curvature, lesser curvature, antrum, pylorus, duodenum (3.0 cm high ellipsoid, cross section: variable), liver (2.5 cm diameter sphere), and lower gastrointestinal track (from cecum to descending colon, 3.0 cm high ellipsoid, cross section: variable) were drawn in the coronal view. FDG uptake in the greater and lesser curvature was measured at the level of maximum diameter of the stomach in the coronal view. Duodenal uptake was measured in the second portion of the duodenum. Uptake in the ascending, transverse, and descending colon were measured in the median portion of each segment of the bowel. Hepatic uptake was measured at the level of the portal vein. VOIs of the sigmoid colon, rectum (3.0 cm high ellipsoid, cross section: variable), and anus (3.0 cm diameter sphere) were drawn in the sagittal view. The sigmoid colon was measured in the horizontal portion above the bladder. The rectum was measured in front of the coccyx. VOIs of the rectus abdominis (1.0 cm diameter sphere) and psoas muscle (2.0 cm diameter sphere) were drawn in the axial view at the level of the upper end of the iliac crest. Mean gastric uptake was an arithmetic mean of SUVmax in the gastroesophageal junction, fundus, greater curvature, lesser curvature, antrum, and pylorus. Mean colon uptake was an arithmetic mean of SUVmax in the ascending colon, transverse colon, descending colon, sigmoid colon, and rectum.

Measurement of Volume and Cross Section

VOI in the stomach was manually drawn in the fused PET/CT images, and then volume (cm³) of the stomach was automatically calculated. If the fusion image was misregistered, the VOI was drawn in the PET-only images. Because the colon is a long and winding organ, extent of distension in the colon was evaluated with cross section (cm²) instead of volume.

Cross section of the ascending, transverse, descending, sigmoid colon, and rectum was automatically calculated through the VOI drawn for the measurement of SUVmax in the previous section. Mean cross section of the colon was an arithmetic mean of cross section in the ascending colon, transverse colon, descending colon, sigmoid colon, and rectum.

Statistical Analysis

Clinical parameters and SUVmax/volume/cross section in the corresponding organ were statistically compared using independent t-tests. The Pearson correlation coefficient was used for assessment of correlations between the SUVmax and volume of the stomach, and the SUVmax and cross section of the colon. A *P*-value <0.05 was considered to indicate a statistically significant difference.

Results

Patient Characteristics

A total of 29 subjects were included in the endoscopy group and 35 subjects were in the control group. In the endoscopy group, 22 of the subjects received both an EGD and a colonoscopy, six subjects received an EGD only, and one patient received a colonoscopy only. FDG was injected a mean of 82 ± 45 min after EGDs and 84 ± 40 min after colonoscopies. There were no significant differences in gender, mean age, body weight, body mass index (BMI), serum glucose level before the FDG injection, and the dose of FDG injected between the endoscopy and control groups (Table 1).

Differences in SUVmax

SUVmax in the tongue, pharynx, larynx, and esophagus was not significantly different between the endoscopy and control groups (Fig. 1 and Table 2). In contrast, SUVmax in the GE junction, fundus, greater curvature, and lesser curvature was significantly higher in the endoscopy group than in the control group. Although differences were not statistically significant, SUVmax in the antrum, pylorus, and duodenum was also higher in the endoscopy group (Fig. 1 and Table 2). Among the lower GI track, SUVmax from the cecum to the rectum was not significantly different between two groups, whereas SUVmax in anus was 20 % higher in the endoscopy group than in the control group (SUVmax: 4.21 vs. 3.50, *P* = 0.002). SUVmax in the liver and muscle was not significantly different between the two groups (Fig. 1 and Table 2).

Table 1 Patient characteristics

	Endoscopy group (n = 29)	Control group (n = 35)	P value
Gender (M:F)	19:10	20:15	0.100
Mean age (years)	49 ± 11	51 ± 11	0.541
Body weight (kg)	70 ± 9	67 ± 11	0.264
Body mass index (kg/m ²)	24.3 ± 2.2	24.7 ± 5.0	0.559
Blood glucose (mmol/L)	5.6 ± 0.8	5.6 ± 0.9	0.652
Injected FDG dose (MBq)	344 ± 45	347 ± 63	0.848
Endoscopy (n)			
EGD + Colonoscopy	22		
EGD only	6		
Colonoscopy only	1		
Interval between;			
EGD and FDG injection (min)	82 ± 45		
Colonoscopy and FDG injection (min)	84 ± 40		

EGD esophagogastroduodenoscopy

Correlation Between Volume/Cross Section and SUVmax

Volume of the stomach was significantly higher in the endoscopy group compared with the control group (313.28 cm³ vs. 209.93 cm³, $P < 0.001$, Table 3). Mean SUVmax in the whole stomach was 18 % higher in the endoscopy group than in the control group (SUVmax: 2.96 vs. 2.51, $P = 0.010$). Mean cross section of the colon was also significantly higher in the endoscopy group compared with the control group (8.82 cm² vs. 5.98 cm², $P = 0.001$; Table 3). However, mean SUVmax in the colon was not significantly different between two groups (SUVmax: 2.56 vs. 2.74, $P = 0.470$). Among the correlations between volume/cross section and SUVmax in the stomach and colon, only SUVmax in the sigmoid colon and rectum of the endoscopy group was negatively correlated with cross section of the sigmoid colon and rectum (Table 4).

Discussion

Endoscopic procedures under sedation did not lead to significant differences in FDG uptake in most parts of the body. SUVmax in the stomach and anus was higher by 18 and 20 % in the endoscopy group, respectively. Negative endoscopic findings can guarantee the absence of true tumor lesions that can be masked by enhanced FDG uptake. In terms of quantifying FDG uptake in known malignant lesions, physicians should be aware that FDG uptake in the stomach and anus can be overestimated when PET/CT is performed just after endoscopy under sedation.

Introducing the scope via the mouth in EGD may lead to physiological stress in the oral cavity, pharynx, and larynx. However, FDG uptake changes in those organs were minimal under sedation. When evaluating patients that have

Fig. 1 Difference in distribution of FDG uptake between the endoscopy and control groups

Table 2 Comparison of FDG uptake (SUVmax) between the endoscopy and control groups

	Endoscopy group (<i>n</i> = 29)	Control group (<i>n</i> = 35)	<i>P</i> value
Tongue			
Genioglossus muscle	1.58 ± 0.52	1.52 ± 0.50	0.630
Styloglossus muscle	4.07 ± 1.67	3.92 ± 1.71	0.720
Pharynx and larynx			
Uvula	2.83 ± 0.70	3.13 ± 0.94	0.159
Epiglottis	2.57 ± 1.28	2.70 ± 1.22	0.665
Vocal cords	3.29 ± 1.21	3.02 ± 0.97	0.330
Upper GIT*			
Cervical esophagus	2.43 ± 0.42	2.28 ± 0.26	0.101
Thoracic esophagus	2.36 ± 0.43	2.27 ± 0.49	0.468
Gastroesophageal junction	3.02 ± 0.78	2.67 ± 0.52	0.047 ^a
Fundus	3.29 ± 0.89	2.77 ± 0.79	0.017 ^a
Greater curvature	2.62 ± 0.81	1.99 ± 0.72	0.002 ^a
Lesser curvature	2.72 ± 0.77	2.25 ± 0.70	0.013 ^a
Antrum	2.98 ± 1.27	2.70 ± 0.70	0.355
Pylorus	3.10 ± 0.84	2.68 ± 0.83	0.053
Duodenum	2.51 ± 0.63	2.24 ± 0.47	0.064
Liver			
Right hepatic lobe	3.05 ± 0.36	2.88 ± 0.44	0.100
Left hepatic lobe	3.06 ± 0.36	2.95 ± 0.51	0.327
Lower GIT			
Cecum	2.86 ± 0.90	2.72 ± 0.86	0.540
Ascending colon	2.39 ± 0.97	2.57 ± 1.51	0.571
Hepatic flexure	2.04 ± 0.88	2.21 ± 0.96	0.493
Transverse colon	1.81 ± 0.48	2.19 ± 1.13	0.083
Splenic flexure	1.80 ± 0.56	2.10 ± 0.88	0.120
Descending colon	2.11 ± 0.80	2.31 ± 1.02	0.442
Sigmoid colon	2.94 ± 0.89	3.35 ± 1.85	0.262
Rectum	3.54 ± 1.27	3.27 ± 1.56	0.491
Anus	4.21 ± 0.80	3.50 ± 0.83	0.002 ^a
Muscle			
Rectus abdominis	0.81 ± 0.19	0.86 ± 0.19	0.341
Psoas	1.01 ± 0.28	0.93 ± 0.20	0.199

GIT gastrointestinal track

^a *P* < 0.05

malignancies in the oral cavity, pharynx, or larynx, PET/CT can be performed on the same day as endoscopic procedures under sedation.

In the upper and lower GI tracks, FDG uptake in the stomach was higher in the endoscopy group, whereas FDG uptake in the colon did not differ between the groups. Uptake in the colon was lower in the endoscopy group, but this difference did not reach statistical significance. The difference is probably due to the anatomical differences between the stomach and the colon. The GI wall consists of four layers from the lumen outward: the mucosa, submucosa, muscular layer, and adventitia. The muscular wall consists of smooth muscle that is usually arranged as an inner circular and outer longitudinal

layer [7]. In the stomach only, there is an additional inner oblique layer of muscle, which is responsible for creating the motion that churns and physically breaks down the food [7]. On the contrary, the colon has tenia coli, which are longitudinal muscular fibers that limit excess dilatation of the colon. Therefore, the stomach distends to a greater extent than the colon, which results in physical stress that might lead to muscle hyperactivity and enhanced secretion from the gastric mucosa [8]. The relatively lower colonic FDG uptake in the colonoscopy group was probably due to the bowel cleansing preparation, as one possible cause of colonic FDG uptake is bacterial overgrowth in the stool [9]. Our results indicate that the bowel preparation did not increase FDG uptake in the

Table 3 Differences of mean volume/cross section and SUVmax in the stomach and colon between the endoscopy and control groups

	Endoscopy group	Control group	P value
Volume of the stomach (cm ³)	313.28 ± 93.23	209.93 ± 76.99	<0.001 ^a
Mean SUVmax of the stomach ^b	2.96 ± 0.69	2.51 ± 0.64	0.010 ^a
Mean cross section of the colon (cm ²) ^c	8.82 ± 3.58	5.98 ± 1.30	0.001 ^a
Ascending colon	9.70 ± 6.34	8.71 ± 3.39	0.499
Transverse colon	8.17 ± 3.57	4.46 ± 1.75	<0.001 ^a
Descending colon	7.64 ± 3.44	4.49 ± 1.70	<0.001 ^a
Sigmoid colon	8.95 ± 3.51	5.38 ± 2.09	<0.001 ^a
Rectum	9.62 ± 8.51	6.87 ± 3.88	0.157
Mean SUVmax of the colon ^d	2.56 ± 0.62	2.74 ± 1.27	0.470

SUVmax maximum standardized uptake value

^a $P < 0.05$

^b an arithmetic mean of SUVmax in the gastroesophageal junction, fundus, greater curvature, lesser curvature, antrum, and pylorus

^c an arithmetic mean of cross section in the ascending colon, transverse colon, descending colon, sigmoid colon, and rectum

^d an arithmetic mean of SUVmax in the ascending colon, transverse colon, descending colon, sigmoid colon, and rectum

colon. High anal uptake was probably due to physical stress during the bowel preparation and/or scope insertion via the sphincter muscle surrounding the anal canal. FDG uptake in reference lesions, the liver and muscles, was not different between the endoscopy and control groups.

Yingbing et al. evaluated physiologic FDG uptake in normal tissues [10]. The reference ranges of SUVmax was 1.66–4.66 in the oropharynx, 1.58–6.81 in soft palate, 0.90–7.69 in the tongue, 1.13–3.23 in the esophagus, 0.76–11.51 in the stomach, 1.49–4.66 in the liver, and 0.49–7.41 in the colorectum. Our results are generally comparable with those data. Mean gastric uptake in the endoscopy group (mean SUVmax: 2.96, range: 1.94–5.00) was lower than the previous result by Yingbing et al. [10]. Because our study excluded the

patients having active inflammatory disease in the stomach, the range is lower than the previous study that performed with unselected patients.

The degree of gastric and colonic FDG uptake can be influenced by the degree of the distension. Gastric filling just before image acquisition can be performed to decrease physiologic gastric uptake and to enhance the differences in FDG uptake between malignancy and normal gastric wall [11, 12]. SUVmax in the normal gastric wall was decreased from 3.1 to 1.6 in a previous study [11]. Presently, both volume and SUVmax in the stomach of the endoscopy group were higher than those of the control group. The authors of the prior study used intravenous injection of 20 mg of hyoscine-N-butylbromide (Buscopan®) to inhibit gastric movement, but

Table 4 Correlation between volume/cross section and SUVmax in the stomach and colon in the endoscopy and control groups

	Endoscopy group		Control group	
	Correlation coefficient (r)	Significance level (P)	Correlation coefficient (r)	Significance level (P)
Correlation between volume (cm ³) and SUVmax				
Stomach	0.072	0.717	−0.315	0.065
Correlation between cross section (cm ²) and SUVmax				
Ascending colon	−0.382	0.079	0.021	0.905
Transverse colon	−0.266	0.219	−0.232	0.180
Descending colon	−0.078	0.723	−0.180	0.302
Sigmoid colon	−0.537	0.008 ^a	0.231	0.181
Rectum	−0.456	0.029 ^a	−0.275	0.110

SUVmax maximum standardized uptake value

^a $P < 0.05$

we did not. Based on the previous and our results, we can assume that metabolic activity in the stomach is closely related to the muscle activity. SUVmax and cross-section in the sigmoid colon and rectum of the control group showed negative correlation. However, correlations between SUVmax and degree of distension in other parts of the control group and all parts of the endoscopy group were not significant.

We acknowledge that our study has several limitations. First, all subjects received endoscopy under sedation. EGD without sedation causes gag-reflex and retching that may enhance physiologic FDG uptake in the related muscles. FDG uptake can change when subjects undergo procedures without anesthesia. Second, although the control group included only subjects without clinical symptoms on the day of examination and without endoscopic abnormality within 6 months, we cannot completely rule out the possibility that subjects might have had subclinical disease on the day of the examination. Third, while the target VOIs were in the least variable portions of each organ or segment, those portions might not represent all of the metabolic activity of the target organ or segment.

Conclusion

EGD and colonoscopy under sedation did not lead to significant differences in FDG uptake in most parts of the body. It is practical to perform an FDG PET/CT on the same day after an EGD and colonoscopy, as long as physicians are aware that gastric FDG uptake after an EGD and anal FDG uptake after a colonoscopy are increased by 18 and 20 %, respectively.

Compliance with Ethical Standards

Conflict of Interest Authors JR Oh, JH Seo, WJ Jang, SI Bae, IW Song, JG Bong, HY Jeong, SY Park, J Bae, and H Yoon declare that they have no conflict of interest.

Ethics Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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