

Spectrum of final pathological diagnosis of gastric adenoma after endoscopic resection

Kwan Woo Nam, Kyu Sang Song, Heon Young Lee, Byung Seok Lee, Jae Kyu Seong, Seok Hyun Kim, Hee Seok Moon, Eaum Seok Lee, Hyun Yong Jeong

Kwan Woo Nam, Gastroenterology Center, Sun Hospital, Daejeon 301-725, South Korea

Kyu Sang Song, Pathologic Department, Chung-Nam National University Hospital, Daejeon 301-721, South Korea

Heon Young Lee, Byung Seok Lee, Jae Kyu Seong, Seok Hyun Kim, Hee Seok Moon, Eaum Seok Lee, Hyun Yong Jeong, Gastroenterology Unit of Internal Medicine Department, Chung-Nam National University Hospital, Daejeon 301-721, South Korea

Author contributions: Nam KW and Jeong HY performed the majority of the research; Song KS provided pathologic advises and, along with Jeong HY, was also involved in editing the manuscript; Moon HS, Lee ES, Lee HY, Lee BS, Seong JK and Kim SH provided the collection of all the human material in addition to collecting the medical record reviews and analysis for this work; Jeong HY designed the study and Nam KW wrote the manuscript.

Supported by Chung-Nam National University Hospital Fund
Correspondence to: Dr. Hyun Yong Jeong, Gastroenterology Unit of Internal Medicine Department, Chung-Nam National University Hospital, Daejeon 301-721, South Korea. jeonghy@cnuh.co.kr

Telephone: +82-42-2807159 Fax: +82-42-2544553

Received: September 19, 2010 Revised: January 25, 2011

Accepted: February 2, 2011

Published online: December 21, 2011

Abstract

AIM: To investigate how many discrepancies occur in patients before and after endoscopic treatment of referred adenoma and the reason for these results.

METHODS: We retrospectively reviewed data from 554 cases of 534 patients who were referred from primary care centres for adenoma treatment and treated for endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) at Chungnam National University Hospital, from July 2006 to June 2009. Re-endoscopy was examined in 142 cases and biopsy

was performed in 108 cases prior to treatment. Three endoscopists (1, 2 and 3) performed all EMRs or ESDs and three pathologists (1, 2 and 3) diagnosed most of the cases. Transfer notes, medical records and endoscopic pictures of these cases were retrospectively reviewed and analyzed.

RESULTS: Adenocarcinoma was 72 (13.0%) cases in total 554 cases after endoscopic treatment of referred adenoma. When the grade of dysplasia was high (55.0%), biopsy number was more than three (22.7%), size was no smaller than 2.0 cm (23.2%), morphologic type was depressed (35.8%) or yamada type IV (100%), and color was red (30.9%) or mixed-or-undetermined (25.0%), it had much more malignancy rate than the others ($P < 0.05$). All 18 cases diagnosed as adenocarcinoma in the re-endoscopic forceps biopsy were performed by endoscopist 1. There were different malignancy rates according to the pathologist ($P = 0.027$).

CONCLUSION: High grade dysplasia is the most important factor for predicting malignancy as a final pathologic diagnosis before treating the referred gastric adenoma. This discrepancy can occur mainly through inappropriately selecting a biopsy site where cancer cells do not exist, but it also depends on the pathologist to some extent.

© 2011 Baishideng. All rights reserved.

Key words: Discrepancy; Adenoma; High grade dysplasia; Endoscopic mucosal resection; Endoscopic submucosal dissection

Peer reviewer: Barbara Braden, Professor, Department of Gastroenterology, John Radcliffe Hospital, Headley Way, OX3 9DU Oxford, United Kingdom

Nam KW, Song KS, Lee HY, Lee BS, Seong JK, Kim SH, Moon HS, Lee ES, Jeong HY. Spectrum of final pathological di-

agnosis of gastric adenoma after endoscopic resection. *World J Gastroenterol* 2011; 17(47): 5177-5183 Available from: URL: <http://www.wjnet.com/1007-9327/full/v17/i47/5177.htm> DOI: <http://dx.doi.org/10.3748/wjg.v17.i47.5177>

INTRODUCTION

Since gastric adenoma can progress to higher grade dysplasia or cancer, as shown in long-term follow up studies, it should be treated by endoscopic resection or surgical resection^[1-3]. Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) have been approved as standard treatments for gastric adenoma^[4]. Pathologic results from the mucosectomy specimens taken from endoscopic resection of gastric adenoma can be different from those of an endoscopic forceps biopsy^[5,6]. As endoscopy has been examined more commonly and extensively, prevalence of adenoma referred from a primary care center for endoscopic resection has increased. However, there have been no reports on the histologic discrepancy between the endoscopy-based diagnosis of the referred gastric adenoma and the final pathologic diagnosis, and previous studies did not include analysis of other possible factors for discrepancy^[5-7]. This study aimed to elucidate and analyze possible factors affecting discrepancy for referred gastric adenoma.

MATERIALS AND METHODS

A total of 1049 patients with gastric adenoma were endoscopically treated by EMR or ESD between July 2006 and June 2009 at Chungnam National University Hospital. Among these, 534 patients were referred from primary care centres, most of them from the Tae-jeon Chungcheong province in South Korea. Because it was intended for all the referred patients to undergo endoscopic treatment, most patients were treated with EMR or ESD, except for an extreme few who had a tendency toward bleeding, or were untreatable due to size, location, or comorbidity. Endoscopists decided resection methods (EMR or ESD) from clinical information such as age, size, morphology, color, location and pathologic grade, but there were no strict criteria. Transfer notes, medical records, and endoscopic pictures of these cases were retrospectively reviewed and analyzed. One hundred and forty-two cases were examined by re-endoscopy and 108 cases underwent re-biopsy prior to endoscopic resection according to the judgment of the endoscopist. The main reason for pre-evaluations of endoscopic examination and biopsy before the resection was incomplete or confusing referred medical records for determining treatment methods. This is schematically described in Figure 1. Transfer reports were reviewed for information of histologic grade, biopsy number, date of the biopsy, and the name of the referring center. Pathologic reports on 54 patients were written as mild, moderate, or severe grade dysplasia of the adenoma, instead of low or high grade dysplasia. Grad-

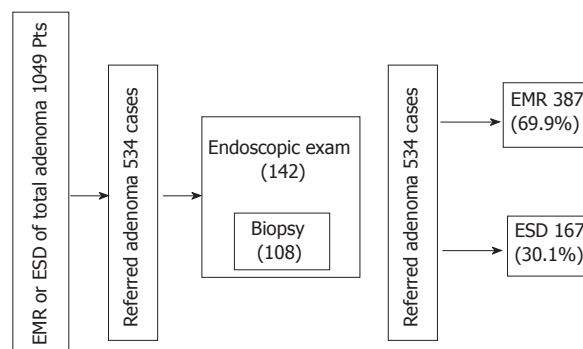


Figure 1 Schematic description of the study design. EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection; Pts: Patients.

ing terms of adenoma required unification for statistical analysis. “Mild grade” or “moderate grade” was classified as low grade and “severe grade” or “moderate to severe grade” was classified as high grade. Three endoscopists performed all EMRs or ESDs and three pathologists diagnosed most of the cases. Endoscopic reports and saved pictures of procedures were reviewed for morphologic type, color, size, and location.

SPSS version 13.0 was used for statistic analysis. The one-way analysis of variance test was used for comparison of continuous variables; for example, age, size, day duration and biopsy number. The χ^2 test was used for other parameters of nominal variables.

RESULTS

Baseline characteristics, endoscopic features and treatment results of referred adenoma

Baseline characteristics and endoscopic features of referred adenomas from primary care centres are shown in Table 1. The mean age of the 554 cases was 66.1 years old. More than 86.4% of cases were located within and under the lower body. Results showed adenomas with no grading record in the transfer note in 92 cases (16.6%), low grade adenomas in 382 cases (69.0%), and high grade adenomas in 80 cases (14.4%). Treatment results of referred adenoma are shown in Table 2. Early gastric cancers were found in 72 cases (13.0%), no adenomatous lesions were found in 56 cases (10.1%), low grade adenomas were found in 356 cases (64.3%), and high grade adenomas were found in 68 cases (12.3%). One case involved mucosa associated lymphatic tissue lymphoma (MALToma) and one complicated case of bleeding were referred. Histologic results of pre-procedure re-endoscopic biopsy were various, from gastritis to adenocarcinoma. In the re-endoscopic biopsy, there were 18 cases (16.7%) of adenocarcinoma and one case of MALToma. The most common complication of EMR and ESD was bleeding (14 cases, 2.5%) which is defined as a case requiring an endoscopic procedure for bleeding control. Perforation (2 cases, 0.4%) and stricture (2 cases, 0.4%) were rare complications of EMR or ESD. There was one case of positive resection margin, in which surgery was

Table 1 The baseline characteristics and endoscopic features of referred adenomas *n* (%)

No. of cases	554
No. of patients	534
Age (yr), mean ± SD	62.1 ± 9.6
Male:female	372:182 (2.04:1)
Histologic grade	
Adenoma (no grading)	92 (16.6)
Low grade	382 (69.0)
High grade	80 (14.4)
No. of referring hospitals	116
No. of Bx, mean ± SD	2.24 ± 1.75
Mean duration between biopsy and procedure	40.7 d
Information of endoscopic photo	449 (81.0)
Size (cm), mean ± SD	1.2 ± 0.8
Morphologic type	
Elevated	275 (49.6)
Flat	206 (37.2)
Depressed	67 (12.1)
Y-IV	6 (1.1)
Color	
Whitish	332 (59.9)
Reddish	94 (17.0)
Mixed or undetermined	128 (23.1)
Longitudinal location	
Antrum	298 (53.8)
Angle	57 (10.3)
Body	191 (34.4)
High	12 (2.2)
Middle	55 (9.9)
Lower	124 (22.4)
Cardia or fundus	8 (1.5)
Circular location	
Anterior	123 (22.2)
Posterior	119 (21.5)
Lesser curvature	193 (34.8)
Greater curvature	113 (20.4)

Bx: Biopsy; Y-IV: Yamada type IV.

performed for completion of treatment. Sixteen patients had multiple adenomas, 12 patients had 2 adenomas and 4 patients had 3 adenomas (Table 2).

Agreement and discrepancy of histologic diagnosis

Comparison of histologic diagnoses between local clinic endoscopic biopsy and repeat endoscopic biopsy and post-procedure specimens are described in Table 3. The rate of discrepancy between primary care center and repeat biopsy was 42.4% (39 cases/92), 38.1% (176 cases/462) between primary care center and post procedure specimens, and 29.6% (32 cases/108) between repeat biopsy and post procedure specimens. The rate of complete agreement was 57.6% (53 cases/108), 61.9% (286 cases/554), and 70.4% (76 cases/108), respectively. In all comparisons, the discrepancy rate of high grade dysplasia was higher than that of other forms of adenomas.

Although the histologic diagnosis of referred adenoma was as low grade dysplasia, it could be high grade (11.0%) or adenocarcinoma (5.8%) in the post procedure. High grade adenoma of the primary care center could also be low grade adenoma (27.5%) or early gastric cancer (55.0%) as a final pathologic diagnosis.

Table 2 Treatment results of referred adenomas *n* (%)

Repeat endoscopy	142 (25.6)
Repeat biopsy	108 (19.5)
No. of biopsy, mean ± SD	2.4 ± 1.0
Histologic results of repeat biopsy	
Low grade adenoma	73 (67.6)
High grade adenoma	9 (8.3)
Adenocarcinoma	18 (16.7)
Gastritis	7 (6.5)
Others	1 (0.9) (MALToma)
Endoscopist	
1	462 (83.4)
2	64 (11.6)
3	28 (5.1)
Pathologist	
1	340 (61.4)
2	124 (22.4)
3	83 (15.0)
Others	8 (1.1)
Histologic type; tubulovillous adenoma	10 (1.8)
Type of procedure	
EMR	387 (69.9)
ESD	167 (30.1)
Histologic results of post-procedure	
Low grade adenoma	356 (64.3)
High grade adenoma	68 (12.3)
EGC	72 (13.0)
No adenomatous lesion	56 (10.1)
Others	2 (0.4) (MALToma: 1, transfer by Cx: 1)
Complication	
Bleeding	14 (2.5)
Perforation	2 (0.4)
Stricture	2 (0.4)
Cases with multiple adenoma	
2 adenoma in a patient	12 patients/534 (2.2)
3 adenoma in a patient	4 patients/534 (0.7)

MALToma: Mucosa associated lymphoid tissue lymphoma; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection; EGC: Early gastric cancer; Cx: Complication.

Consistent high grade adenoma was only 15.0% between local clinics and post procedure biopsy. All adenocarcinomas of repeat endoscopic biopsies were early gastric cancer in the post procedure, except for one case, which had no adenomatous lesion. When this one case was reviewed with pathologists, the specimen from the repeat endoscopic biopsy was not enough for adenocarcinoma. There were only a few atypical glands, but this could still be suggestive of malignancy (Table 3).

Detection of adenocarcinoma in re-endoscopic repeat biopsy prior to the procedure

Histologic results of re-endoscopic biopsy (108 cases) are shown in (Table 4), according to the endoscopists and pathologists. All of the adenocarcinoma biopsies were performed by endoscopist 1 (*P* < 0.001). Pathologist 1 diagnosed a much larger number of adenocarcinomas than pathologist 2 (*P* = 0.048).

Risk factors for predicting malignancy of referred adenoma

There was no difference between the malignancy group

Table 3 Comparisons of histologic diagnoses *n* (%)

	LG	HG	EGC	NAL	Others	Total	Agreement	Discrepancy
Between local clinic biopsy and repeat biopsy								
Adenoma	11 (68.8)	3 (18.8)	0 (0)	1 (6.3)	1 (6.3)	16 (100)		
LG	51 (83.6)	4 (6.6)	2 (3.3)	4 (6.6)	0 (0)	61 (100)	51 (83.6)	10 (16.4)
HG	11 (35.5)	2 (6.5)	16 (51.6)	2 (6.5)	0 (0)	31 (100)	2 (6.5)	29 (93.5)
Total	73 (67.6)	9 (8.3)	18 (16.7)	7 (6.5)	1 (0.9)	108 (100)	53 (57.6)	39 (42.4)
Between local clinic and post procedure								
Adenoma	60 (65.2)	14 (15.2)	6 (6.5)	11 (12.0)	1 (1.1)	92 (100)		
LG	274 (71.7)	42 (11.0)	22 (5.8)	43 (11.3)	1 (0.3)	382 (100)	274 (71.7)	108 (28.3)
HG	22 (27.5)	12 (15.0)	44 (55.0)	2 (2.5)	0 (0)	80 (100)	12 (15.0)	68 (85.0)
Total	356 (64.3)	68 (12.3)	72 (13.0)	56 (10.1)	2 (0.4)	554 (100)	286 (61.9)	176 (38.1)
Between repeat forcep biopsy and post procedure								
LG	52 (71.2)	1 (15.1)	6 (8.2)	3 (4.1)	1 (1.4)	73 (100)	52 (71.2)	21 (28.8)
HG	3 (33.3)	4 (44.4)	2 (22.2)	0 (0)	0 (0)	9 (100)	4 (44.4)	5 (45.6)
Adenocarcinoma	0 (0)	0 (0)	17 (94.4)	1 (5.6)	0 (0)	18 (100)	17 (94.4)	1 (5.6)
Benign lesion	3 (42.9)	0 (0)	2 (28.6)	2 (28.6)	0 (0)	7 (100)	2 (28.6)	5 (71.4)
Others	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)	1 (100)	0 (0)
Total	58 (53.7)	15 (13.9)	27 (25.0)	6 (5.6)	2 (1.9)	108 (100)	76 (70.4)	32 (29.6)

LG: Low grade; HG: High grade; NAL: No adenomatous lesion; EGC: Early gastric cancer.

Table 4 Results of re-endoscopic forceps biopsy according to endoscopists and pathologists *n* (%)

	LG	HG	Ade	NAL	Others	Total
Endoscopist						
1	34 (54.0)	6 (9.5)	18 (28.6)	4 (6.3)	1 (1.6)	63
2	36 (92.3)	3 (7.7)	0	0	0	39
3	3 (50.0)	0	0	3 (50.0)	0	6
Pathologist						
1	40 (64.5)	4 (6.5)	15 (24.2)	2 (3.2)	1 (1.6)	62
2	20 (66.7)	4 (13.3)	2 (6.7)	4 (13.3)	0	30
3	8 (80.0)	1 (10.0)	1 (10.0)	0	0	10
Others	5 (83.3)	0	0	1 (16.7)	0	6
Deletion of minority						
	Adenocarcinoma		Non-adenocarcinoma		<i>P</i> value	
Endoscopist						
1	18 (28.6)		45 (71.4)		< 0.001	
2	0 (0)		39 (100)			
Pathologist						
1	15 (24.2)		47 (77.8)		0.048	
2	2 (6.7)		15 (93.3)			

Ade: Adenocarcinoma; LG: Low grade; HG: High grade; NAL: No adenomatous lesion.

and the non-malignancy group as a final pathologic diagnosis with regard to age, sex, histologic type, duration between local clinic biopsy and procedure, longitudinal and circular location, endoscopist, local clinics, and multiplicity. There was a difference with regard to histologic grade, number of biopsies, size, morphologic type, color, type of procedure, examination of repeat endoscopy, pathologist, and complications (Table 5).

Before the resection, predictive factors for a malignant result were high grade dysplasia (55.0%), a biopsy number of more than three (22.7%), a size of no less than 2.0 cm (23.2%), a morphologic type of depressed (35.8%) or yamada type IV (100%), and a red (30.9%) or mixed-or-undetermined (25.0%) coloration. There was no statistical significance between less than 1.0 cm and

no less than 1.0 cm ($P = 0.124$).

Cases of ESD, repeat endoscopy, or complicated cases had many more malignant results than cases of EMR or direct procedures without re-endoscopy or non-complicated cases. The rate of malignancy was different according to the pathologist ($P = 0.027$). Mean duration from local clinic biopsy to endoscopic treatment did not differ between the malignancy group and the non-malignancy group. There was also no difference between cases (26 cases) with duration of no more than 14 d and cases (33 cases) of duration of more than 90 d. High grade dysplasia showed the highest odds ratio (19.5) with regard to risk factors for malignancy (Table 6).

DISCUSSION

Histologically, gastric adenomas are composed of cells with hyperchromatic, elongated nuclei arranged in a picket-fence pattern with cystic glands and nuclear atypia being occasionally present^[8,9]. The malignant potential of adenomas has been demonstrated in long term follow up studies, even in low grade dysplasia, therefore, resection is recommended^[3,10]. Since the introduction of EMR in Japan, techniques for endoscopic resection have been continuously advancing; therefore, EMR and ESD are now approved for use in standard treatment of gastric adenoma^[4,11,12].

Predictive factors for malignancy

In univariate analysis, risk factors for malignant transformation included location, histologic type (tubulovillous), redness, and high grade dysplasia in the study by Park *et al*^[5], and depressed type, high grade dysplasia, redness, ulceration in the study by Jung *et al*^[6] in the univariate analysis. In multivariate analysis, only high grade dysplasia had a significant relationship with malignant transformation in the two studies. In our study, predictive factors for

Table 5 Comparison of the non-malignancy group and the malignancy group *n* (%)

	Non-malignancy group	Malignancy group	<i>P</i> value	
No. of cases	482 (87.0)	72 (13.0)		
No. of patient	462 (86.5)	72 (13.5)		
Age (yr), mean ± SD	61.8 ± 9.8	63.7 ± 9.0	0.132	
Sex				
Male	320 (86.0)	52 (14.0)	0.350	
Female	162 (89.0)	20 (11.0)		
Histologic grade				
Adenoma	86 (93.5)	6 (6.5)	< 0.001	
Low grade	360 (94.2)	22 (5.8)		
High grade	36 (45.0)	44 (55.0)		
Histologic type				
Tubulovillous	7 (7.0)	3 (3.0)	0.129	
Tubular	475 (83.3)	69 (12.7)		
No. of Bx, mean ± SD	2.1 ± 1.6	2.9 ± 2.2	< 0.001	
No. of biopsy				
Undetermined	111 (86.0)	18 (14.0)	< 0.001	
1	47 (92.2)	4 (7.8)		
2	117 (94.4)	7 (5.6)		
3	105 (92.1)	9 (7.9)		
4	47 (72.3)	18 (27.7)		
5	25 (80.6)	6 (19.4)		
6	12 (70.6)	5 (29.4)		
7	1 (33.3)	2 (66.7)		
8	1 (33.3)	2 (66.7)		
3	269 (93.1)	20 (6.9)		
4	86 (72.3)	33 (27.7)		
Mean duration between Bx and procedure (d)	40.9	39.3		0.869
Duration between biopsy and procedure				
14 d	24 (92.3)	2 (7.7)		0.658
90 d	29 (87.9)	4 (12.1)		
Size (cm), mean ± SD	1.2 ± 0.8	1.5 ± 1.1	0.003	
< 1.0	201 (89.7)	23 (10.3)	0.010	
> 1.0, < 2.0	218 (87.9)	30 (12.1)		
> 2.0	63 (76.8)	19 (23.2)		
Morphologic type				
Elevated	252 (91.6)	23 (8.4)	< 0.001	
Flat	187 (90.8)	19 (9.2)		
Depressed	43 (64.2)	24 (35.8)		
Y-IV	0 (0)	6 (100)		
Color				
Whitish	321 (96.7)	11 (3.3)	< 0.001	
Reddish	65 (69.1)	29 (30.9)		
Mixed or undetermined	96 (75.0)	32 (25.0)		
Longitudinal location				
Antrum	255 (85.6)	43 (14.4)	0.291	
Angle	47 (82.5)	10 (17.5)		
Body	173 (90.6)	18 (9.4)		
Cardia or fundus	7 (87.5)	1 (12.5)		
Circular location				
Anterior	104 (84.6)	19 (15.4)	0.573	
Posterior	107 (89.9)	12 (10.1)		
Lesser curvature	171 (88.6)	22 (11.4)		
Greater curvature	95 (84.1)	18 (15.9)		
Type of procedure				
EMR	371 (95.9)	16 (4.1)	< 0.001	
ESD	111 (66.5)	56 (33.5)		
Repeat endoscopy				
Yes	110 (77.5)	32 (22.5)	< 0.001	
No	372 (90.3)	40 (9.7)		
Endoscopist				
1	397 (85.6)	65 (14.1)	0.204	
2	60 (93.8)	4 (6.3)		
3	25 (89.3)	3 (10.7)		

Pathologist			
1	284 (83.5)	56 (16.5)	0.027
2	117 (94.4)	7 (5.6)	
3	74 (89.2)	9 (10.8)	
Others	6 (100)	0 (0)	
Local clinics (> 30 cases)			
1	39 (95.1)	2 (4.9)	0.224
2	37 (90.2)	4 (9.8)	
3	35 (97.2)	1 (2.8)	
4	28 (84.8)	5 (15.2)	
Complication			
Bleeding	9 (64.3)	5 (35.7)	0.005
Perforation	1 (50)	1 (50)	
Stricture	1 (50)	1 (50)	
Total complications	11 (61.1)	7 (38.9)	
No complications	471 (87.9)	65 (12.1)	
Multiplicity			
Patient of single case	449 (86.7)	69 (13.3)	0.464
Patient of multiple cases	13 (81.3)	3 (18.8)	

Bx: Biopsy; Y: Yamada type; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection.

Table 6 Odds ratio of risk factors for malignancy as a final diagnosis

	Odds ratio
High grade dysplasia	19.5
Biopsy number ≥ 4	5.1
Size ≥ 2.0 cm	2.4
Depressed or Y-III, Y-IV	7.3
Reddish or undetermined	11.1
ESD	11.7
Repeat endoscopy	2.7
Pathologist 1	2.4
Complications	4.6

ESD: Endoscopic submucosal dissection; Y: Yamada type.

malignancy as a final diagnosis included histologic grade, biopsy number, size, morphologic type and color. High grade dysplasia was the most important risk factor for malignancy, as in previous studies^[5,6], with the highest odds ratio (Table 6).

Three out of ten cases (30%) of tubulovillous adenoma were malignancies, compared to only 69/475 cases (12.7%) of tubular adenoma, although this was not statistically significant. Cases with more than three biopsies were more often malignant than cases with fewer biopsies. This might be explained by the assumption that the endoscopist has taken more biopsies when he suspected a malignancy. ESD, re-endoscopy, and complicated groups had more many malignancies than EMR, direct procedure without re-endoscopy, and non-complicated groups, but those are not the cause of malignancy, but the result of strict treatment. Other possible factors affecting malignancy will be discussed below.

Possible causes affecting malignant discrepancy: (1) geographic variety of histology; forceps biopsy can be done only on the adenoma site, when cancer cells are mixed in the same lesion; (2) chronological difference between the time of forceps biopsy and the time of

resection; adenoma can be transformed to malignancy; (3) different criteria of pathologist with regard to malignancy; and (4) different location between forceps biopsy and resection.

Geographic variety of histology

Because relatively small forceps biopsy foci of the polyp cannot represent the entire lesion, there can be a discrepancy between the forceps biopsy and resection specimen of the polyp^[13]. Discrepancies before and after endoscopic resection in adenoma are mainly due to the geographic distribution of malignant cells within the adenoma^[5,6,14], which means that the discrepancy depends on the location of the initial endoscopic forceps biopsy. It is noteworthy that all of the adenocarcinomas (18 cases) in the re-endoscopic forceps biopsy before the procedure were performed by endoscopist 1, although there was no difference in the discrepancy rate between primary care center and post-treatment according to the endoscopist (Table 4). This may be due to the experience of the endoscopist. An expert endoscopist who can reduce the rate of discrepancy has the ability to determine the location of the cancer cells grossly, approximately to the real histology. A similar two studies on malignant transformation of adenoma presented different discrepancy rates in spite of similar study designs^[5,6]. The rate of malignant transformation of adenoma was 6.8% (8/118) in the study by Park *et al*^[5] and 55.3% (63/114) in the study by Jung *et al*^[6]. These large differences can be understood in the same context.

Chronological difference between the time of forceps biopsy and the time of resection

Gastric adenoma can progress to early gastric cancer, as shown in long term follow-up studies^[3,10,15]; even low grade dysplasia has malignant potential. This change can occur over a long period of time. Yamada *et al*^[3] reported on one case of 37 low grade dysplasia and one case of 10 high grade dysplasia that progressed to invasive carcinoma over a period of 212 mo and 55 mo, respectively. In our study, duration from the time of initial biopsy to the time of resection was not different between the malignant group and the nonmalignant group. Statistically, the rate of malignancy was also not different between fewer than two weeks (7.7%, 2 cases/33) and fewer than 90 d (12.1%, 4 cases/26) in duration. This means that a treatment delay of roughly three months is not a problem.

Different criteria of pathologist with regard to malignancy

Because criteria between Japanese and Western pathologists are different, international workshops have been steadily and persistently organized in an effort to establish a consensus^[16-18]. In 1996, eight pathologists from Japan and Western countries met in Tokyo and individually reviewed a set of 35 gastric biopsy and resection specimens of lesions with potential early neoplasias^[16]. There was agreement between Japanese and Western viewpoints in only 11 of the 35 specimens. A different

diagnosis can be made for the same specimen, even by an intraobserver in the time interval of three years^[19]. Table 5 shows that the malignant discrepancy rate of pathologist 1 is approximately three times greater than that of pathologist 2. The rate of adenocarcinoma diagnosis for re-endoscopic forceps biopsy is also higher for pathologist 1 than pathologist 2 (Table 4). Although the forceps biopsy specimen was not reviewed, it can be assumed that forceps biopsy by the primary care center can be underestimated by the pathologist. However, no difference in the malignant discrepancy rate was observed between primary care centers (Table 5). It is a limitation of our study that the same specimens were not reviewed by pathologists.

Different location between forceps biopsy and resection

Logically, it is possible that either the patient or the sample changed, or that a different mucosectomy site was selected from the diagnostic biopsy site; however, this was not included in the discussion.

COMMENTS

Background

Endoscopic examination is performed more commonly in the primary care center, and gastric adenoma is more frequently referred to tertiary care units.

Research frontiers

There have been so many embarrassing events when previous and post-procedure diagnoses have been different. This research is performed to predict the treatment result and to discover the reasons for these events.

Innovations and breakthroughs

There have been no reports about the discrepancy of referred gastric adenoma and diverse predictive factors, and possible causes are included in this study.

Applications

The results of this study will help endoscopists to predict the results of treatment and to decide the proper treatment option.

Peer review

The authors studied various predictive factors for discrepancy of gastric adenoma and deeply analyzed possible causes of discrepancy.

REFERENCES

- 1 **Kamiya T**, Morishita T, Asakura H, Miura S, Munakata Y, Tsuchiya M. Long-term follow-up study on gastric adenoma and its relation to gastric protruded carcinoma. *Cancer* 1982; **50**: 2496-2503
- 2 **Farinati F**, Rugge M, Di Mario F, Valiante F, Baffa R. Early and advanced gastric cancer in the follow-up of moderate and severe gastric dysplasia patients. A prospective study. I.G.G.E.D.--Interdisciplinary group on gastric epithelial dysplasia. *Endoscopy* 1993; **25**: 261-264
- 3 **Yamada H**, Ikegami M, Shimoda T, Takagi N, Maruyama M. Long-term follow-up study of gastric adenoma/dysplasia. *Endoscopy* 2004; **36**: 390-396
- 4 **Lambert R**. Treatment of esophagogastric tumors. *Endoscopy* 2003; **35**: 118-126
- 5 **Park DI**, Rhee PL, Kim JE, Hyun JG, Kim YH, Son HJ, Kim JJ, Paik SW, Rhee JC, Choi KW, Oh YL. Risk factors suggesting malignant transformation of gastric adenoma: univariate and multivariate analysis. *Endoscopy* 2001; **33**: 501-506
- 6 **Jung MK**, Jeon SW, Park SY, Cho CM, Tak WY, Kweon YO, Kim SK, Choi YH, Bae HI. Endoscopic characteristics of gastric adenomas suggesting carcinomatous transformation. *Surg Endosc* 2008; **22**: 2705-2711

- 7 **Muehldorfer SM**, Stolte M, Martus P, Hahn EG, Ell C. Diagnostic accuracy of forceps biopsy versus polypectomy for gastric polyps: a prospective multicentre study. *Gut* 2002; **50**: 465-470
- 8 **Ming SC**, Goldman H. Gastric polyps; a histogenetic classification and its relation to carcinoma. *Cancer* 1965; **18**: 721-726
- 9 **Tomasulo J**. Gastric polyps. Histologic types and their relationship to gastric carcinoma. *Cancer* 1971; **27**: 1346-1355
- 10 **Fertitta AM**, Comin U, Terruzzi V, Minoli G, Zambelli A, Cannatelli G, Bodini P, Bertoli G, Negri R, Brunati S. Clinical significance of gastric dysplasia: a multicenter follow-up study. Gastrointestinal endoscopic pathology study group. *Endoscopy* 1993; **25**: 265-268
- 11 **Tada M**, Murakami M, Karita H, Yanai H, Okita K. Endoscopic resection of early gastric cancer. *Endoscopy* 1993; **25**: 445-450
- 12 **Inoue H**, Takeshita K, Hori H, Muraoka Y, Yoneshima H, Endo M. Endoscopic mucosal resection with a cap-fitted panendoscope for esophagus, stomach, and colon mucosal lesions. *Gastrointest Endosc* 1993; **39**: 58-62
- 13 **Yoon WJ**, Lee DH, Jung YJ, Jeong JB, Kim JW, Kim BG, Lee KL, Lee KH, Park YS, Hwang JH, Kim JW, Kim N, Lee JK, Jung HC, Yoon YB, Song IS. Histologic characteristics of gastric polyps in Korea: emphasis on discrepancy between endoscopic forceps biopsy and endoscopic mucosal resection specimen. *World J Gastroenterol* 2006; **12**: 4029-4032
- 14 **Park EH**, Kang KT, Kim BH, Kim KT, Lee SW, Lee JH, Roh MH, Han SY, Choi SR, Jeong JS, Jang JS. The histologic discrepancy before and after endoscopic submucosal dissection of gastric adenoma and early gastric cancer. *Korean J Gastrointest Endoc* 2007; **34**: 125-131
- 15 **Coma del Corral MJ**, Pardo-Mindan FJ, Razquin S, Ojeda C. Risk of cancer in patients with gastric dysplasia. Follow-up study of 67 patients. *Cancer* 1990; **65**: 2078-2085
- 16 **Schlemper RJ**, Itabashi M, Kato Y, Lewin KJ, Riddell RH, Shimoda T, Sipponen P, Stolte M, Watanabe H, Takahashi H, Fujita R. Differences in diagnostic criteria for gastric carcinoma between Japanese and Western pathologists. *Lancet* 1997; **349**: 1725-1729
- 17 **Schlemper RJ**, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, Dixon MF, Fenoglio-Preiser CM, Fléjou JF, Geboes K, Hattori T, Hirota T, Itabashi M, Iwafuchi M, Iwashita A, Kim YI, Kirchner T, Klimpfinger M, Koike M, Lauwers GY, Lewin KJ, Oberhuber G, Offner F, Price AB, Rubio CA, Shimizu M, Shimoda T, Sipponen P, Solcia E, Stolte M, Watanabe H, Yamabe H. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000; **47**: 251-255
- 18 **Schlemper RJ**, Kato Y, Stolte M. Review of histological classifications of gastrointestinal epithelial neoplasia: differences in diagnosis of early carcinomas between Japanese and Western pathologists. *J Gastroenterol* 2001; **36**: 445-456
- 19 **Palli D**, Bianchi S, Cipriani F, Duca P, Amorosi A, Avellini C, Russo A, Saragoni A, Todde P, Valdes E. Reproducibility of histologic classification of gastric cancer. *Br J Cancer* 1991; **63**: 765-768

S- Editor Sun H L- Editor Rutherford A E- Editor Li JY