Original Article

http://dx.doi.org/10.3349/ymj.2015.56.1.72
pISSN: 0513-5796, eISSN: 1976-2437

Yonsei Med J 56(1):72-81, 2015

YMJ

Efficacy and Safety of Endoscopic Resection Therapies for Rectal Carcinoid Tumors: A Meta-Analysis

Lei He, Tao Deng, and Hesheng Luo

Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, China.

Received: February 18, 2014
Revised: April 21, 2014
Accepted: April 23, 2014
Corresponding author: Dr. Tao Deng,
Department of Gastroenterology,
Renmin Hospital of Wuhan University,
238 Jiefang Road, Wuhan 430060, China.
Tel: 86-27-88041911, Fax: 86-27-88042292
E-mail: dengtao1120@hotmail.com

· The authors have no financial conflicts of interest.

Purpose: Several endoscopic resection therapies have been applied for the treatment of rectal carcinoid tumors. However, there is currently no consensus regarding the optimal strategy. We performed a meta-analysis to compare the efficacy and safety of endoscopic mucosal resection (EMR) or modified EMR (m-EMR) versus endoscopic submucosal dissection (ESD) for the treatment of rectal carcinoid tumors. **Materials and Methods:** PubMed, Web of Science, Medline, Embase and CNKI were searched up to the end of January 2014 in order to identify all studies on the effects of EMR (or m-EMR) and ESD on rectal carcinoid tumors. **Results:** A total of fourteen studies involving 782 patients were included. The pooled data suggested a significantly higher rate of pathological complete resection among patients treated with ESD or m-EMR than those treated with EMR [odds ratio (OR)=0.42, 95% confidence interval (CI): 0.25–0.71; OR=0.10, 95% CI: 0.03–0.33, respectively], while there was no significant difference between the m-EMR group and ESD group (OR=1.19, 95% CI: 0.49–2.86); The procedure time of ESD was longer than EMR or m-EMR groups [mean differences (MD)=-11.29, 95% CI: -14.19 – -8.38, MD= -10.90, 95% CI: -18.69 – -3.11, respectively], but it was insignificance between the EMR and m-EMR groups. No significant differences were detected among the treatment groups with regard to complications or recurrence. **Conclusion:** The results of this meta-analysis suggest that treatment of rectal carcinoid tumors with ESD or m-EMR is superior to EMR, and the efficacy of m-EMR is equivalence to ESD treatment. However, more well-designed studies are needed to confirm these findings.

Key Words: Endoscopic submucosal dissection, endoscopic mucosal resection, rectal carcinoid tumor, meta-analysis

INTRODUCTION

Rectal carcinoid tumors are uncommon neuroendocrine neoplasms and they account for approximately 10% to 17% of all carcinoid tumors.[1,2] Generally, they are found incidentally during colonoscopy as submucosal tumors covered with yellow-discolored mucosa. The number of incidence of carcinoid tumors of the gastrointestinal tract has increased over the past five decades, due in part to rapid advances in screening endoscopy.[3,4] Approximately 80% of rectal carcinoid tumors are smaller than 1 cm in diameter, without invasion or metastasis at the time of di-

© Copyright:
Yonsei University College of Medicine 2015

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

agnosis.[5] Recently, the European Neuroendocrine Tumor Society 2012 Consensus Guidelines suggested that well-differentiated rectal neuroendocrine tumors smaller than 2 cm in diameter without muscularis invasion or lymph node involvement could be endoscopically resected.[6]

To date, various endoscopic techniques have been applied to rectal carcinoid tumors. Such techniques include endoscopic polypectomy, endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Moreover, some new techniques derived from conventional EMR procedures have been developed, which included EMR using a band-ligation device (EMR-B), EMR using a transparent cap (EMR-C), EMR using a dual-channel endoscope (EMR-D), EMR with a ligation device (EMR-L), and endoscopic submucosal resection with a ligation device (ESMR-L). All these techniques share the same step of creating a pseudopedicle before resection, and were classified as modified EMR (m-EMR) in this study.

Recently, several studies have examined the efficacy of endoscopic resection therapies for the treatment of rectal carcinoid tumors.[7-20] However, there is currently no consensus regarding the optimal endoscopic treatment strategy. Therefore, we conducted a meta-analysis of published data in order to evaluate the efficacy and safety of ESD, compared with EMR, for successfully treating rectal carcinoid tumors.

MATERIALS AND METHODS

Search strategy

A literature search was conducted using PubMed, Web of Science, Medline, Embase and CNKI up to January 2014 without language restrictions. Relevant studies were identified using the following terms: "endoscopic submucosal dissection or ESD", "endoscopic mucosal resection or EMR", and "rectal carcinoid tumor or rectal neuroendocrine tumor". The search was restricted to human subjects. Additional studies were identified using a hand search of references of original or review articles and international conferences on this topic, primarily including Asian Pacific Digestive Week, United European Gastroenterology Week and American Gastroenterological Association Digestive Disease Week.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: 1) including patients with rectal carcinoid tumors, 2) including a comparison of EMR or m-EMR therapy with ESD for rectal carcinoid tumors, and 3) presenting detailed outcomes of two groups or including such data for calculation in the article text. Meanwhile, the major exclusion criteria were: 1) an unclear study population or trial size, 2) study without extractable data, and 3) case reports, editorials, commentaries, reviews or abstracts only.

Data extraction

Two investigators (He L and Deng T) independently extracted the data and reached a consensus for all items. If the investigators generated different results, they checked the data again and had a discussion in order to reach an agreement. If they were unable to reach an agreement, an expert was invited to join the discussion. The following data were extracted from the selected studies: the first author's name, year of publication, country of origin, treatment, patients in the two groups, age, gender, tumor size limit, mean size of the tumor (endoscopic and pathological), numbers of complete resections (endoscopic and pathological), procedure time, numbers of bleeding, perforation, recurrence, and follow-up time.

Statistical analysis

The efficacy and safety of ESD therapy compared with EMR or m-EMR for the treatment of rectal carcinoid tumors was estimated for each study using the odds ratio (OR) and 95% confidence interval (95% CI). The mean differences (MD) with 95% CI were used for continuous variables (tumor size and procedure time). The χ^2-test-based Q statistic test was performed to assess the between-study heterogeneity.[21] We also quantified the effect heterogeneity according to the I^2 test. When a significant Q test ($p<0.05$) or I^2 >50% indicated heterogeneity across studies, the random effects model was used.[22] Otherwise, the fixed effects model was applied.[23] An analysis of sensitivity was performed in order to evaluate the stability of the results. Finally, potential publication bias was investigated using Begg's funnel plot and Egger's regression test.[24,25] A p value of <0.05 was regarded as being statistically significant.

All statistical analyses were performed using the Cochrane Collaboration RevMan 5.2 and STATA package version 12.0 (Stata Corporation, College Station, TX, USA).

RESULTS

Study characteristics

A total of 637 citations were identified in the search. Accord-

ing to the inclusion criteria, fourteen studies with 782 patients were included in the meta-analysis.[7-20] The characteristics of the selected studies are summarized in Table 1. Of the fourteen eligible studies, nine were from Korea,[7,8,10-14,17,18] three were from China,[9,19,20] and two were from Japan;[15,16] twelve studies were published in English, one in Chinese,[9] and one in Korean.[10]

Quantitative data synthesis

Complete resection rate

Ten studies with available data reported pathologically complete resection rate and pooled data suggested a significantly higher rate of complete resection among patients treated with ESD or m-EMR than among those treated with EMR (OR=0.42, 95% CI: 0.25–0.71; OR=0.10, 95% CI: 0.03–0.33, respectively), while there was no significant difference between the m-EMR group and ESD group (OR=1.19, 95% CI: 0.49–2.86) (Table 2, Fig. 1).

Twelve studies with available data reported endoscopically complete resection rate. The results showed that the complete resection rates were significantly higher in the ESD or m-EMR group compared with the EMR group (OR=0.28, 95% CI: 0.11–0.70; OR=0.33, 95% CI: 0.14–0.76, respectively),

Table 1. Characteristics of the Included Studies

Study	Yr	Country	Treatment	Patients	No. of treated tumors	Age, mean±SD, yr	Gender (male/female)	Size limit (mm)	Mean size of the tumor, mean±SD, mm	
									Endoscopic	Pathological
Baek[7]	2010	Korea	EMR	9	9	47.6 (32–64)	7/2	10	8.8 (5–13)	NR
			ESD	3	3		2/1			
Choi, et al.[8]	2013	Korea	EMR-B	29	29	47.75±11.73	15/14	10	4.34±1.75	NR
			ESD	31	31	48.29±14.44	20/11		5.22±2.09	NR
Dou, et al.[9]	2013	China	EMR	24	26	49.0±8.3	15/9	20	5.6±1.2	NR
			ESD	19	20	48.6±9.0	10/9		7.4±5.3	NR
Kim, et al.[10]	2008	Korea	EMR-C	6	6	46.7±10.8	3/3	15	5.5±2.3	NR
			ESD	2	2	46.0±11.3	1/1		6.5±4.9	NR
Kim, et al.[11]	2012	Korea	EMR	55	55	48.8±13.9	35/20	10	6.3±2.5	6.5±3.2
			ESMR-L	45	45	53.5±10.4	31/14		5.9±2.0	5.8±2.4
Kim, et al.[12]	2013	Korea	EMR	31	31	47.74±11.52	20/11	10	6.77±1.75	4.84±2.05
			ESMR-L	40	40	48.15±8.87	23/17		6.33±1.75	3.97±1.93
			ESD	44	44	47.18±10.22	32/12		5.91±1.83	4.27±1.88
Lee, et al.[13]	2010	Korea	EMR	28	28	49.0±10.3	14/14	15	NR	5.7±4.0
			ESD	46	46	48.6±12.0	21/25		NR	6.2±3.1
Lee, et al.[14]	2013	Korea	EMR-D	44	44	51.4±12.3	25/19	16	6.4±2.7	NR
			ESD	26	26	47.4±10.6	22/4		6.2±4.1	NR
Niimi, et al.[15]	2012	Japan	EMR-L	11	11	45.5±10.6	8/3	10	5.7±2.05	4.4±2.2
			ESD	13	13	55.3±8.6	9/4		5.4±1.4	5.5±2.1
Onozato, et al.[16]	2010	Japan	Two-channel EMR	24	26	58.3 (31–87)	18/6	10	6.6±2.1	NR
			ESD	9	9		7/2		7.7±1.0	NR
Park, et al.[17]	2010	Korea	EMR	62	62	51±12	42/20	16	7.3±2.2	7.1±2.3
			ESD	31	31	50±8	18/13		6.8±2.4	6.5±2.6
Sung, et al.[18]	2012	Korea	EMR	14	14	52.3±12.0	48/29*	15	7.0±2.8	NR
			Two-channel EMR	58	58					
			ESD	5	5					
Zhao, et al.[19]	2012	China	EMR	10	10	54.04±11.58	21/9*	10	NR	NR
			EMR-C	10	10				NR	NR
			ESD	10	10				NR	NR
Zhou, et al.[20]	2010	China	EMR	23	23	50.3±13.6	14/9	10	6.7±2.1	NR
			ESD	20	20	47.6±18.5	12/8		7.2±1.9	NR

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; EMR-B, EMR using a band-ligation device; EMR-C, EMR using a transparent cap; EMR-D, EMR using a dual-channel endoscope; EMR-L, EMR with a ligation device; ESMR-L, endoscopic submucosal resection with a ligation device; NR, not reported.
*No. of all groups.

Table 2. Efficacy and Safety of ESD or EMR (m-EMR)

Study	Yr	Country	Treatment	Patients	No. of treated tumors	No. of complete resections, n (%)		Margin involvement, n (%)			Procedure time (mins)
						Endoscopic	Pathological	Lateral	Vertical	Both	
Baek[7]	2010	Korea	EMR	9	9	NR	9 (100)	0 (0)	0 (0)	0 (0)	NR
			ESD	3	3	NR	3 (100)	0 (0)	0 (0)	0 (0)	NR
Choi, et al.[8]	2013	Korea	EMR-B	29	29	NR	24 (82.8)	2 (6.9)	1 (3.4)	2 (6.9)	6.37±3.52
			ESD	31	31	NR	25 (80.6)	0 (0)	6 (19.4)	0 (0)	15.09±5.73
Dou, et al.[9]	2013	China	EMR	24	26	26 (100)	26 (100)	0 (0)	0 (0)	0 (0)	8.9±6.3
			ESD	19	20	20 (100)	19 (95)	0 (0)	1 (5)	0 (0)	32.6±10.5
Kim, et al.[10]	2008	Korea	EMR-C	6	6	6 (100)	NR	1 (16.7)	-	-	NR
			ESD	2	2	2 (100)	NR	1 (50)	-	-	NR
Kim, et al.[11]	2012	Korea	EMR	55	55	50 (91)	36 (65.5)	3 (5.5)	19 (34.5)	-	5.0±0.8
			ESMR-L	45	45	45 (100)	42 (93.3)	1 (2.2)	2 (4.4)	-	4.8±0.9
Kim, et al.[12]	2013	Korea	EMR	31	31	24 (77.4)	24 (77.4)	1 (3.2)	7 (22.6)	-	3.50±2.06
			ESMR-L	40	40	38 (95)	40 (100)	0 (0)	0 (0)	-	11.75±4.58
			ESD	44	44	43 (97.7)	43 (97.7)	0 (0)	1 (2.3)	-	9.38±4.09
Lee, et al.[13]	2010	Korea	EMR	28	28	25 (89.3)	18 (64.3)	2 (7.1)	8 (28.6)	-	12.0±12.9
			ESD	46	46	46 (100)	38 (82.6)	0 (0)	7 (15.2)	-	18.9±7.3
Lee, et al.[14]	2013	Korea	EMR-D	44	44	44 (100)	38 (86.3)	1 (2.3)	4 (9.1)	1 (2.3)	9.75±7.11
			ESD	26	26	26 (100)	23 (88.4)	0 (0)	3 (11.5)	0 (0)	22.38±7.56
Niimi, et al.[15]	2012	Japan	EMR-L	11	11	11 (100)	11 (100)	0 (0)	0 (0)	0 (0)	17.4±4.4
			ESD	13	13	13 (100)	12 (92.3)	0 (0)	1 (7.7)	0 (0)	28.6±16.2
Onozato, et al.[16]	2010	Japan	Two-channel EMR	24	26	22 (84.6)	NR	0 (0)	4 (15.4)	-	9.3±2.2
			ESD	9	9	7 (77.8)	NR	0 (0)	2 (22.2)	-	25.6±8.8
Park, et al.[17]	2010	Korea	EMR	62	62	59 (95.2)	44 (71)	0 (0)	15 (24.2)	3 (4.8)	4.2±3.2
			ESD	31	31	31 (100)	28 (90.3)	0 (0)	2 (6.5)	1 (3.2)	11.4±3.7
Sung, et al.[18]	2012	Korea	EMR	14	14	10 (71.4)	NR	4 (28.6)	-	-	NR
			Two-channel EMR	58	58	43 (74.1)	NR	15 (25.9)	-	-	NR
			ESD	5	5	5 (100)	NR	0 (0)	-	-	NR
Zhao, et al.[19]	2012	China	EMR	10	10	8 (80)	NR	2 (20)	-	-	13.4±17.1
			EMR-C	10	10	10 (100)	NR	0 (0)	-	-	5.2±0.78
			ESD	10	10	10 (100)	NR	0 (0)	-	-	24.9±5.78
Zhou, et al.[20]	2010	China	EMR	23	23	20 (87)	12 (52.2)	0 (0)	8 (34.8)	3 (13.0)	12.3±15.4
			ESD	20	20	20 (100)	20 (100)	0 (0)	0 (0)	0 (0)	28.4±17.2

Study	Yr	Country	Treatment	Patients	No. of treated tumors	No. of bleedings	No. of perforations	No. of recurrence	Follow-up time (month)
Baek[7]	2010	Korea	EMR	9	9	0	0	0	28 (15–45)
			ESD	3	3	0	0	0	
Choi, et al.[8]	2013	Korea	EMR-B	29	29	0	0	NR	NR
			ESD	31	31	1	0	NR	
Dou, et al.[9]	2013	China	EMR	24	26	4	0	0	3–27
			ESD	19	20	0	1	0	
Kim, et al.[10]	2008	Korea	EMR-C	6	6	NR	NR	0	6.8±3.3
			ESD	2	2	NR	NR	0	5.0±2.8
Kim, et al.[11]	2012	Korea	EMR	55	55	0	0	NR	NR
			ESMR-L	45	45	2	0	NR	
Kim, et al.[12]	2013	Korea	EMR	31	31	0	0	0	13.1 (6–59)
			ESMR-L	40	40	0	1	0	
			ESD	44	44	0	0	0	

Table 2. Continued

Study	Yr	Country	Treatment	Patients	No. of treated tumors	No. of bleedings	No. of perforations	No. of recurrence	Follow-up time (month)
Lee, et al.[13]	2010	Korea	EMR	28	28	1	0	1	23 (3–63)
			ESD	46	46	2	1	0	
Lee, et al.[14]	2013	Korea	EMR-D	44	44	1	0	0	8 (1–58)
			ESD	26	26	2	0	0	
Niimi, et al.[15]	2012	Japan	EMR-L	11	11	1	0	1	24.0±32.5
			ESD	13	13	0	0	0	65.1±57.0
Onozato, et al.[16]	2010	Japan	Two-channel EMR	24	26	0	0	0	70.1±30.7
			ESD	9	9	0	0	0	
Park, et al.[17]	2010	Korea	EMR	62	62	4	1	0	33 (3–117)
			ESD	31	31	1	1	0	12.6 (6–24)
Sung, et al.[18]	2012	Korea	EMR	14	14	NR	NR	NR	18.5 (5–107)
			Two-channel EMR	58	58	NR	NR	NR	
			ESD	5	5	NR	NR	NR	
Zhao, et al.[19]	2012	China	EMR	10	10	0	0	0	18.43±9.76
			EMR-C	10	10	0	0	0	
			ESD	10	10	0	0	0	
Zhou, et al.[20]	2010	China	EMR	23	23	0	0	3	42.6±26.1
			ESD	20	20	0	1	0	18.7±10.6

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; EMR-B, EMR using a band-ligation device; EMR-C, EMR using a transparent cap; EMR-D, EMR using a dual-channel endoscope; EMR-L, EMR with a ligation device; ESMR-L, endoscopic submucosal resection with a ligation device; NR, not reported.

however, we failed to detect any difference between the ESD and m-EMR groups (OR=0.65, 95% CI: 0.18–2.34).

In addition, margin involvement was found in 84 cases in the EMR group (84/427), in 31 cases in the m-EMR group (31/224) and in 25 cases in the ESD group (25/260). The pooled data showed that the residual tumor positive rate in EMR group was higher than that in m-EMR or ESD group (EMR vs. ESD: OR=2.24, 95% CI: 1.38–3.63, EMR vs. m-EMR: OR=5.21, 95% CI: 1.17–23.18); whereas there was no obvious difference between the m-EMR group and ESD group (OR=0.89, 95% CI: 0.43–1.85).

Tumor size

Ten studies with available data reported endoscopic mean sizes of the tumor. There was no significant difference in all comparisons among the three groups (EMR vs. ESD: MD=-0.11, 95% CI: -0.51–0.30, m-EMR vs. ESD: MD=-0.23, 95% CI: -0.70–0.24, EMR vs. m-EMR: MD=0.42, 95% CI: -0.18–1.02). Five studies reported pathological mean sizes of the tumor, and similar results were found between EMR or m-EMR and ESD treatment (MD=0.24, 95% CI: -0.36–0.85; MD=-0.45, 95% CI: -1.18–0.29, respectively), however, significant difference was detected between EMR and m-EMR group (MD=0.80, 95% CI: 0.09–1.51).

Procedure time

Eleven studies reported the procedure time of various treatments. The procedure time of ESD was longer than that of EMR or m-EMR groups (MD=-11.29, 95% CI: -14.19–-8.38; MD=-10.90, 95% CI: -18.69 – -3.11, respectively), but the procedure time was not different between the EMR and m-EMR groups (MD=-1.36, 95% CI: -8.66–5.94) (Table 2, Fig. 2).

Complications

Eleven studies reported available data of complications (bleeding and perforation). Of those, bleeding occurred in 11 cases in the EMR group (11/349), 2 cases in the m-EMR group (2/160), and 6 cases in the ESD group (6/253), while perforation occurred in 2 cases in the EMR group (2/349), 1 case in the m-EMR group (1/160), and 4 cases in the ESD group (4/253). The pooled data showed no significant difference in all comparisons among the three groups (EMR vs. ESD: bleeding: OR=1.39, 95% CI: 0.54–3.57; perforation: OR=0.51, 95% CI: 0.14–1.92, m-EMR vs. ESD: bleeding: OR=0.64, 95% CI: 0.14–2.87; perforation: OR=3.38, 95%

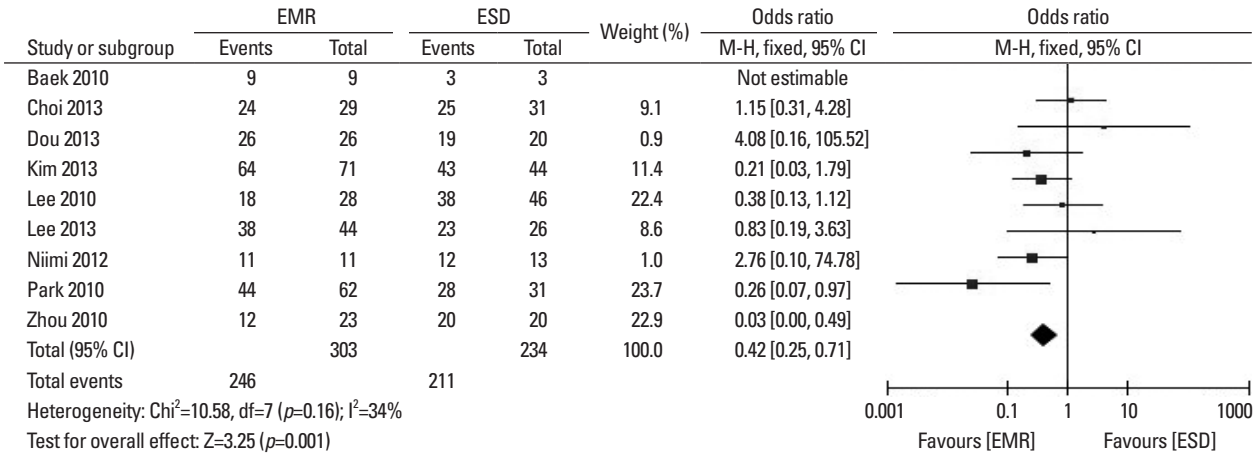


Fig. 1. Forest plots comparing treatment of rectal carcinoid tumors with ESD or EMR (or m-EMR) in terms of pathologically complete resection rate. (A) ESD vs. EMR. (B) ESD vs. m-EMR. (C) EMR vs. m-EMR. ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection; m-EMR, modified EMR; CI, confidence interval.

CI: 0.13–85.37, EMR vs. m-EMR: bleeding: OR=0.16, 95% CI: 0.01–3.35; perforation: OR=0.42, 95% CI: 0.02–10.62) (Table 2, Fig. 3A and B).

Recurrence

Eleven studies reported available data of recurrence during the follow-up time. Recurrence occurred in 5 cases in the EMR group (5/326), 1 case in the m-EMR group (1/137), and none in the ESD group (0/224), and the differences were not statistically significant (EMR vs. ESD: OR=5.39, 95% CI: 0.86–33.61, m-EMR vs. ESD: OR=3.86, 95% CI: 0.14–104.65) (Table 2, Fig. 3C). With regard to EMR vs. m-EMR, two studies listed the data and showed no recurrence in both EMR group and m-EMR group, and there was no significant difference between them (Table 2).

Sensitivity analysis and publication bias

The sensitivity analysis performed using sequential excluding of one study at a time did not alter the results. Then, Begg's funnel plot and Egger's test were performed to assess the potential publication bias in the available literature. The shape of the funnel plots did not reveal any evidence of asymmetry (data not shown). Egger's test also showed no statistical significance in evaluation of publication bias (endoscopic complete resection: p=0.276; pathological complete resection: p=0.895).

DISCUSSION

Carcinoid tumors of the rectum are rare, representing only

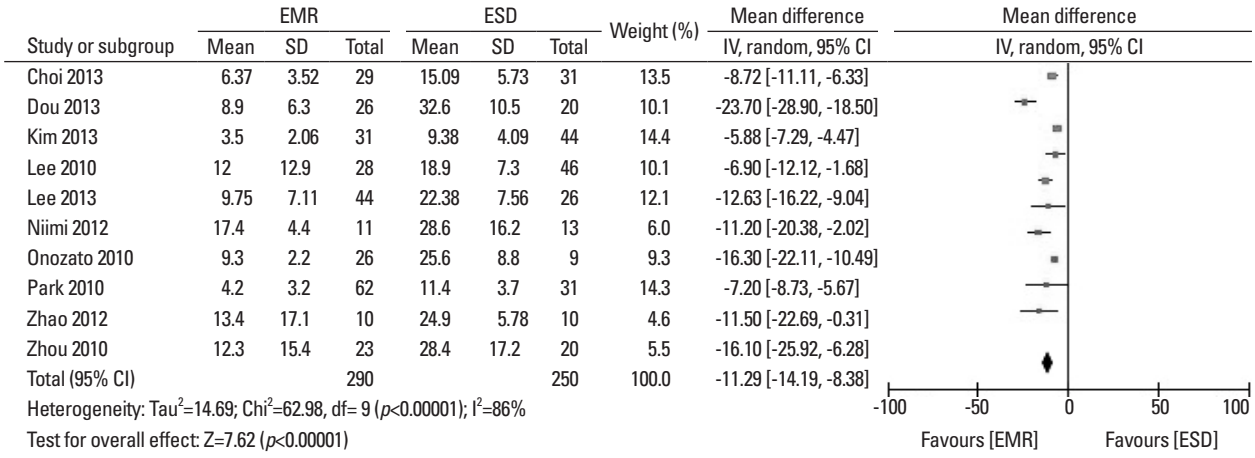
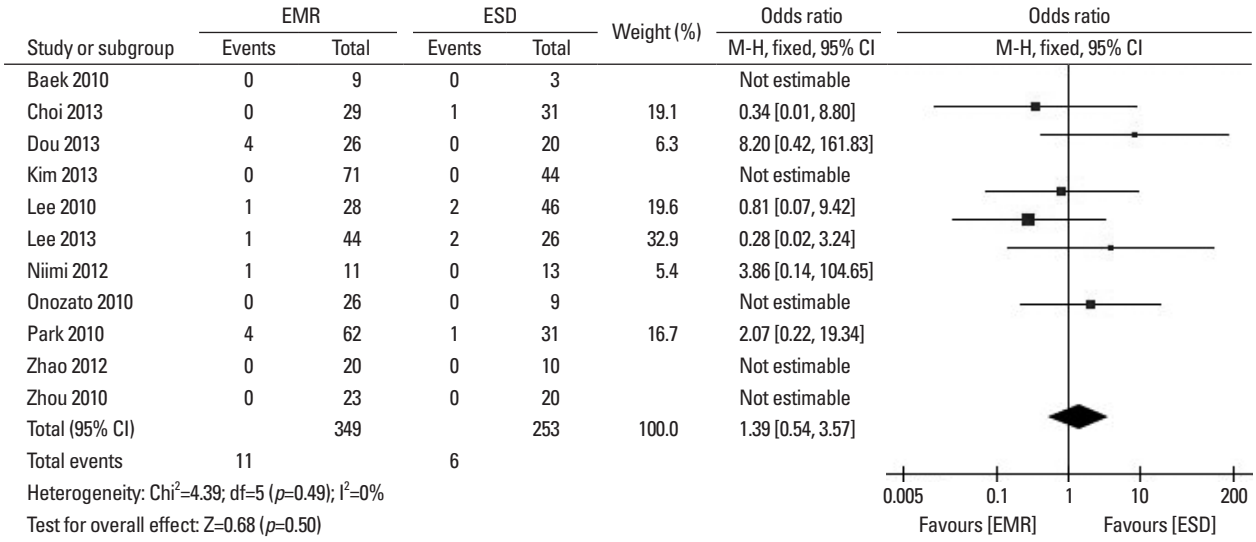


Fig. 2. Forest plots comparing treatment of rectal carcinoid tumors with ESD or EMR (or m-EMR) in terms of the procedure time. (A) ESD vs. EMR. (B) ESD vs. m-EMR. (C) EMR vs. m-EMR. ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection; m-EMR, modified EMR; CI, confidence interval.

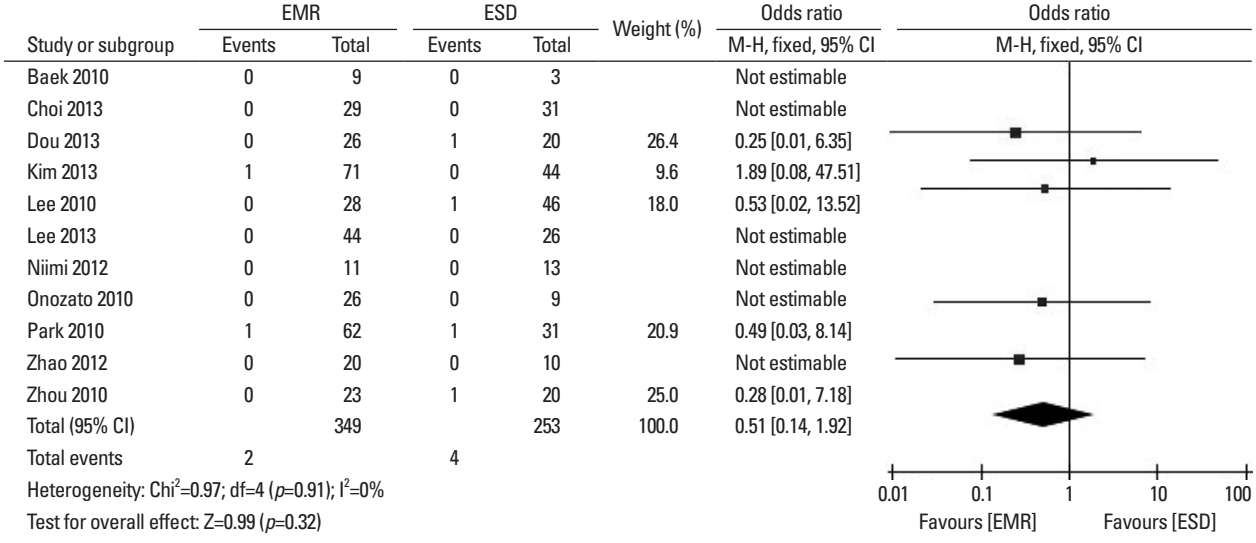
1.8% of anorectal neoplasms, and present a special therapeutic problem.[26] Most rectal carcinoid tumors are small, with 66% being less than 1 cm in diameter. As for the small tumor (<1 cm), the risk of metastatic disease is very low and local treatment is thus thought to be curative.[27,28] Up to now, various endoscopic resection procedures, such as an endoscopic polypectomy, EMR, ESD, and m-EMR (such as EMR-B, EMR-C, EMR-D, EMR-L, and ESMR-L) have all been described as effective treatments for rectal carcinoid tumors.[29-32] However, there are no specific recommendations for treatment choices in rectal carcinoid tumors.

The ESD technique was developed for en bloc resection of mucosal tumors of the gastrointestinal tract and has been applied specifically to early gastric cancer.[33] It has also been applied to resecting tumors extending to a portion of the submucosal layer because both the horizontal margin and the submucosal layer beneath the tumors can be visualized directly during the procedure. However, ESD is difficult for several reasons, including technical difficulty, lack of surgeon expertise, and the need for specific devices. Compared to ESD, EMR is simple, useful and safe for small and superficial neoplasms confined to the mucosa or superficial submucosa in the colorectum. However, its feasibility is still uncertain because of potential problem of incomplete excision. To improve resectability, various modified EMR have been utilized and could provide wider and deeper resection.

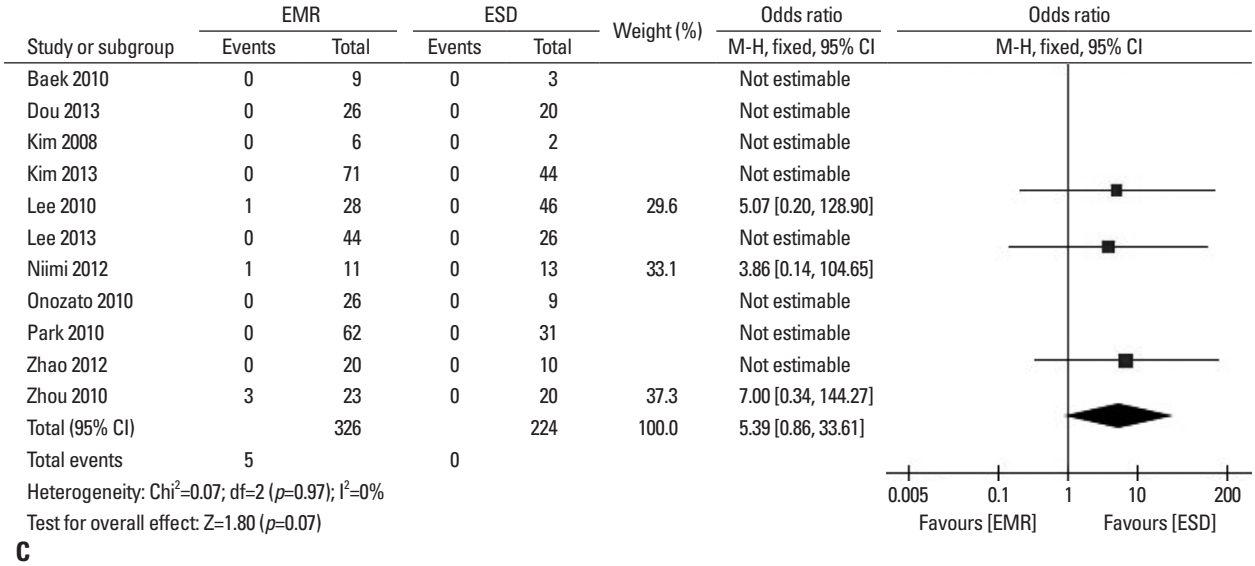
In this study, a total of fourteen studies involving 782 patients were included. Complete resection is crucial in guaranteeing a curative treatment for rectal carcinoid tumors. We



A



B



C

Fig. 3. Forest plots comparing treatment of rectal carcinoid tumors with ESD or EMR in terms of the complications or recurrence. (A) Bleeding. (B) Perforations. (C) Recurrence. ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection; CI, confidence interval.

found significantly higher rate of pathologically complete resection among patients treated with ESD or m-EMR than among those treated with EMR, while there was no significant difference between the m-EMR and ESD group; similarly, endoscopically complete resection rates were significantly higher in the ESD or m-EMR group compared with the EMR group, and we failed to detect any difference between ESD and m-EMR groups. We also observed that residual tumor positive rate in EMR group was higher than that in m-EMR or ESD group, and no obvious difference was detected between m-EMR and ESD groups. In addition, the mean tumor sizes (both pathological and endoscopic) before resection were not significantly different among these groups. In general, it has been demonstrated that ESD is a time consuming procedure. In this study, the procedure time in ESD group was longer than EMR or m-EMR groups, but there was no difference between EMR and m-EMR groups. The above results were in line with two previous meta-analyses.[34,35] However, in the current meta-analysis, we conducted a comprehensive literature search in different databases and included several additional studies,[7,9,10,14] which allowed for a larger number of subjects and more precise risk estimation.

Bleeding and perforation are main complications of endoscopic resection, especially for ESD. In this study, we found no significant differences among the treatment groups. These results can be explained as follows: first, most rectal carcinoid tumors are smaller than 1 cm in diameter, without invasion or metastasis at the time of diagnosis, therefore, the resection size is relatively small; second, rectal carcinoid tumors usually present as small solitary nodules in the lower rectum, where the wall is significantly thicker and supported by surrounding connective tissue. Third, an endoscope is easily manipulated in the rectum because the rectum is fixed to the retroperitoneum. Besides, recurrence is an another indicator to determine the therapeutic effect. Similarly, no significant differences among the treatment groups were detected in the follow-up time.

The sensitivity analysis using sequential exclusion of one trial at a time did not alter the results, thus indicating that our results were statistically robust. Nevertheless, some limitations of this meta-analysis should be addressed. First, All the articles included were retrospective studies, and the quality of the studies was relatively low, which might have influenced the results. Second, various types of modified EMR might have produced a small amount of bias. Third, there was conspicuous heterogeneity between studies included due to differences in procedure time, which may influence the results.

In conclusion, this meta-analysis showed that treatment of rectal carcinoid tumors with ESD or m-EMR is superior to EMR, and the efficacy of m-EMR is equivalent to ESD treatment. However, more well-designed trials are needed to confirm these findings.

REFERENCES

1. Godwin JD 2nd. Carcinoid tumors. An analysis of 2,837 cases. Cancer 1975;36:560-9.
2. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. Cancer 1997;79:813-29.
3. Modlin IM, Oberg K, Chung DC, Jensen RT, de Herder WW, Thakker RV, et al. Gastroenteropancreatic neuroendocrine tumours. Lancet Oncol 2008;9:61-72.
4. Scherübl H. Options for gastroenteropancreatic neuroendocrine tumours. Lancet Oncol 2008;9:203.
5. Modlin IM, Kidd M, Latich I, Zikusoka MN, Shapiro MD. Current status of gastrointestinal carcinoids. Gastroenterology 2005; 128:1717-51.
6. Caplin M, Sundin A, Nillson O, Baum RP, Klose KJ, Kelestimur F, et al. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms: colorectal neuroendocrine neoplasms. Neuroendocrinology 2012;95:88-97.
7. Baek IH. Endoscopic submucosal dissection or conventional endoscopic mucosal resection is an effective and safe treatment for rectal carcinoid tumors: a retrospective study. J Laparoendosc Adv Surg Tech A 2010;20:329-31.
8. Choi CW, Kang DH, Kim HW, Park SB, Jo WS, Song GA, et al. Comparison of endoscopic resection therapies for rectal carcinoid tumor: endoscopic submucosal dissection versus endoscopic mucosal resection using band ligation. J Clin Gastroenterol 2013;47: 432-6.
9. Dou LZ, Zhang YM, He S, Zou SM, Lu N, Zhao DB, et al. A control study of endoscopic mucosal resection and endoscopic submucosal dissection in treating rectal carcinoid tumors. Zhonghua Xiao Hua Nei Jing Za Zhi 2013;30:209-13.
10. Kim YJ, Lee SK, Cheon JH, Kim TI, Lee YC, Kim WH, et al. [Efficacy of endoscopic resection for small rectal carcinoid: a retrospective study]. Korean J Gastroenterol 2008;51:174-80.
11. Kim HH, Park SJ, Lee SH, Park HU, Song CS, Park MI, et al. Efficacy of endoscopic submucosal resection with a ligation device for removing small rectal carcinoid tumor compared with endoscopic mucosal resection: analysis of 100 cases. Dig Endosc 2012;24:159-63.
12. Kim KM, Eo SJ, Shim SG, Choi JH, Min BH, Lee JH, et al. Treatment outcomes according to endoscopic treatment modalities for rectal carcinoid tumors. Clin Res Hepatol Gastroenterol 2013;37:275-82.
13. Lee DS, Jeon SW, Park SY, Jung MK, Cho CM, Tak WY, et al. The feasibility of endoscopic submucosal dissection for rectal carcinoid tumors: comparison with endoscopic mucosal resection. Endoscopy 2010;42:647-51.
14. Lee WH, Kim SW, Lim CH, Kim JS, Cho YK, Lee IS, et al. Effi-

cacy of endoscopic mucosal resection using a dual-channel endoscope compared with endoscopic submucosal dissection in the treatment of rectal neuroendocrine tumors. Surg Endosc 2013;27:4313-8.
15. Niimi K, Goto O, Fujishiro M, Kodashima S, Ono S, Mochizuki S, et al. Endoscopic mucosal resection with a ligation device or endoscopic submucosal dissection for rectal carcinoid tumors: an analysis of 24 consecutive cases. Dig Endosc 2012;24:443-7.
16. Onozato Y, Kakizaki S, Iizuka H, Sohara N, Mori M, Itoh H. Endoscopic treatment of rectal carcinoid tumors. Dis Colon Rectum 2010;53:169-76.
17. Park HW, Byeon JS, Park YS, Yang DH, Yoon SM, Kim KJ, et al. Endoscopic submucosal dissection for treatment of rectal carcinoid tumors. Gastrointest Endosc 2010;72:143-9.
18. Sung HY, Kim SW, Kang WK, Kim SY, Jung CK, Cho YK, et al. Long-term prognosis of an endoscopically treated rectal neuroendocrine tumor: 10-year experience in a single institution. Eur J Gastroenterol Hepatol 2012;24:978-83.
19. Zhao ZF, Zhang N, Ma SR, Yang Z, Han X, Zhao YF, et al. A comparative study on endoscopy treatment in rectal carcinoid tumors. Surg Laparosc Endosc Percutan Tech 2012;22:260-3.
20. Zhou PH, Yao LQ, Qin XY, Xu MD, Zhong YS, Chen WF, et al. Advantages of endoscopic submucosal dissection with needle-knife over endoscopic mucosal resection for small rectal carcinoid tumors: a retrospective study. Surg Endosc 2010;24:2607-12.
21. Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. Ann Intern Med 1997;127:820-6.
22. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177-88.
23. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719-48.
24. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088-101.
25. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34.
26. Kwaan MR, Goldberg JE, Bleday R. Rectal carcinoid tumors: review of results after endoscopic and surgical therapy. Arch Surg 2008;143:471-5.
27. Al Natour RH, Saund MS, Sanchez VM, Whang EE, Sharma AM, Huang Q, et al. Tumor size and depth predict rate of lymph node metastasis in colon carcinoids and can be used to select patients for endoscopic resection. J Gastrointest Surg 2012;16:595-602.
28. Soga J. Early-stage carcinoids of the gastrointestinal tract: an analysis of 1914 reported cases. Cancer 2005;103:1587-95.
29. Ono A, Fujii T, Saito Y, Matsuda T, Lee DT, Gotoda T, et al. Endoscopic submucosal resection of rectal carcinoid tumors with a ligation device. Gastrointest Endosc 2003;57:583-7.
30. Mashimo Y, Matsuda T, Uraoka T, Saito Y, Sano Y, Fu K, et al. Endoscopic submucosal resection with a ligation device is an effective and safe treatment for carcinoid tumors in the lower rectum. J Gastroenterol Hepatol 2008;23:218-21.
31. Kim HR, Lee WY, Jung KU, Chung HJ, Kim CJ, Yun HR, et al. Transanal endoscopic microsurgery for the treatment of well-differentiated rectal neuroendocrine tumors. J Korean Soc Coloproctol 2012;28:201-4.
32. Choi HH, Kim JS, Cheung DY, Cho YS. Which endoscopic treatment is the best for small rectal carcinoid tumors? World J Gastrointest Endosc 2013;5:487-94.
33. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, et al. Endoscopic mucosal resection for treatment of early gastric cancer. Gut 2001;48:225-9.
34. Zhong DD, Shao LM, Cai JT. Endoscopic mucosal resection vs endoscopic submucosal dissection for rectal carcinoid tumours: a systematic review and meta-analysis. Colorectal Dis 2013;15:283-91.
35. Zhou X, Xie H, Xie L, Li J, Cao W, Fu W. Endoscopic resection therapies for rectal neuroendocrine tumors: a systematic review and meta-analysis. J Gastroenterol Hepatol 2014;29:259-68.