

Comparison of EMR vs ESD for Treatment of Rectal Neuroendocrine Tumors: A Systematic Review and Meta-Analysis

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Introduction

- Rectal neuroendocrine tumors (NETs) make up 12 to 27% of all neuroendocrine tumors.¹ Their incidence is increasing, and though often detected while small, rectal NET's have the capacity to metastasize.
- While tumors >20 mm are generally managed surgically, controversy remains about the optimal management of rectal NET's <20 mm in size.²
- Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are two treatment options of interest to therapeutic gastroenterologists.
- Recently the utilization of ESD, EMR (and its variations) in the management of rectal NET's has increased, yet studies comparing the techniques across diverse patient populations are lacking.
- The aim of this systematic review and meta-analysis is to analyze the findings of all studies which compare these two treatment modalities for efficacy in tumor resection and safety in the management of rectal NETs.

Methods

Search strategy:

- Studies were identified by searching key terms in PubMed, Google Scholar, and reviewing citations within previously published meta-analyses.
- Only articles in English included and 26 studies were eventually selected for final analysis

Statistical Analysis:

- The Newcastle-Ottawa Scale (NOS) was used to evaluate individual study quality.
- When comparing EMR to ESD, mean differences were estimated for procedure time, whereas risk ratios were calculated for histologic resection, perforation, and delayed bleeding rates (a continuity correction of 0.2 was used when any group had no adverse events).
- Pooled effects were estimated using random-effects meta-analysis, while between-study heterogeneity was calculated using the Paule-Mandel estimator with Hartung-Knapp adjusted standard errors.
- Funnel plots were used to assess publication bias.

Classification:

- Modified EMR (m-EMR):** Includes EMR with Cap (EMR-C), EMR with Loop Ligation Device (EMR-L), EMR with Ligation after Cap (EMR-LC), EMR with Band Ligation Device (EMR-B), EMR with Circumferential incision (EMR-CI), EMR with Dual Channel Endoscope (EMR-D).

Study	Duration	Country	Study Design	Treatment	# of Tumors	Mean Tumor Size (mm)	Mean Follow-Up Time (months)	Newcastle-Ottawa Score	Size Limit (mm)
Toriyama et al., 2021	5/2003 - 11/2019	Japan	Retrospective Cohort	ESD	24	5.5	31.3	6	10
				EMR	10	3.8	34.8		
				m-EMR	27	4	24.9		
Zheng et al., 2021	8/2010 - 10/2019	China	Retrospective Cohort	ESD	62	7.4	21.47	6	20
				m-EMR	36	4.36	35.36		
Kamiguchi et al., 2021	1/2001 - 12/2019	Japan	Retrospective Cohort	ESD	21	5.8	NR	4	10
				EMR	60	4.9	NR		
Wang et al., 2020	4/2007 - 1/2019	China	Retrospective Cohort	ESD	259	7.1	39	7	20
				m-EMR	79	5.8	39		
Lim et al., 2019	1/2011 - 12/2012	South Korea	Retrospective Cohort	ESD	16	7.08	41.9	6	10
				EMR-L	66	5.02	41.9		
Zhang et al., 2019	1/2016 - 12/2017	China	Retrospective Cohort	ESD	12	7.5	NR	5	10
				EMR-LC	22	7.23	NR		
Zheng et al., 2018	3/2012 - 6/2016	China	Retrospective Cohort	ESD	36	7.22	28	6	20
				EMR-CI	30	6.87	27		
Ebi et al., 2018	5/2003 - 6/2017	Japan	Retrospective Cohort	ESD	19	6	13.5	5	NR
				EMR	14	6.9	7.5		
Chen et al., 2016	1/2008 - 12/2013	China	Retrospective Cohort	ESD	28	8.21	NR	6	15
				CI-EMR	33	6.88	NR		
Kaneko et al., 2016	4/2001 - 8/2013	Japan	Retrospective Cohort	ESD	24	6	61.6	6	10
				EMR-L	22	6.3	61.6		
Yang et al., 2016	2009 - 2014	South Korea	Retrospective Cohort	ESD	32	9.1	19.9	6	15
				EMR	56	5	26.2		
				EMR-C	34	5.3	23.2		
Li et al., 2016	1/2010 - 11/2015	China	Retrospective Cohort	ESD	22	7.5	46	6	20
				EMR	20	5.7	45		
Park et al., 2015	7/2009 - 8/2014	South Korea	Retrospective Cohort	ESD	51	7.73	24	6	25
				EMR-C	65	4.62	24		
Wang et al., 2015	9/2007 - 8/2012	China	Retrospective Cohort	ESD	25	12.27	45.7	6	16
				EMR-C	30	10.35	50.1		
Jeon et al., 2014	2/2007 - 12/2011	South Korea	Retrospective Cohort	ESD	23	6.7	29.1	6	20
				EMR	29	6.1	20.4		
Lee et al., 2013	1/2005 - 9/2011	South Korea	Retrospective Cohort	ESD	26	6.2	8	6	16
				EMR-D	44	6.4	8		
Choi et al., 2013	11/2008 - 9/2011	South Korea	Retrospective Cohort	ESD	31	5.22	NR	6	10
				EMR-B	29	4.34	NR		
Kim et al., 2013	1/2005 - 6/2011	South Korea	Retrospective Cohort	ESD	44	4.27	13.1	6	10
				EMR	31	4.84	13.1		
Sung et al., 2012	1/2000 - 6/2010	South Korea	Prospective Cohort	ESD	5	7	27.2	6	15
				EMR	14	7	27.2		
Niimi et al., 2012	9/2003 - 4/2011	Japan	Retrospective Cohort	ESD	13	5.5	65.1	6	10
				EMR-L	11	4.4	24		
Zhao et al., 2012	1/2002 - 1/2008	China	Retrospective Cohort	ESD	10	NR	18.43	6	10
				EMR	10	NR	18.43		
Park et al., 2010	1/2000 - 1/2009	South Korea	Mixed Prospective case-series w/ retrospective control	ESD	31	5 to 13	12.6	6	16
				EMR	62	5 to 13	33		
Zhou et al., 2010	1/2004 - 12/2006	China	Retrospective Cohort	ESD	20	7.2	18.7	6	10
				EMR	23	6.7	42.6		
Lee et al., 2010	1/2003 - 6/2009	South Korea	Retrospective Cohort	ESD	46	6.2 +/- 3.1	23	6	15
				EMR	28	5.7 +/- 4.0	23		
Baek et al., 2010	4/2004 - 6/2009	South Korea	Retrospective Cohort	ESD	3	8.8	28	6	13
				EMR	9	8.8	28		
Onozato et al., 2010	1/1997 - 3/2008	Japan	Retrospective Cohort	ESD	9	7.7 +/- 1.0	76.8	6	10
				EMR-D	26	6.6 +/- 2.1	76.8		

Figure 1. Overall Study Characteristics

Data in red indicates values presented in the study as median. Values in blue represent the mean of all groups. 26 total studies (South Korea: 11, China: 9, Japan: 6). Date range of procedures 1/1997 to 12/2019. Total Tumors treated: 1,890

Results

	Conventional EMR	Modified EMR	ESD
Mean Procedure Time	7.3 mins	9.3 mins	24.3 mins
Mean Overall Complication Rate	2.9%	1.9%	4.6%
Mean Histologic Resection Rate	74.1%	85.0%	90.3%
Mean En Bloc Resection Rate	92.2%	96.4%	99.6%

Figure 2. Aggregate Data

Overall complication rate includes the combined delayed bleeding and perforation rates. Histologic resection defined by pathologically clear tumor margins.

Results

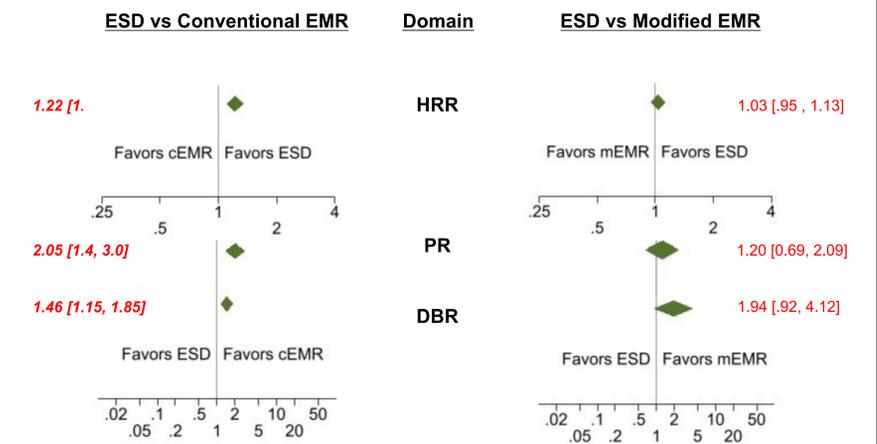


Figure 3. Meta-Regression Forest Plots of Primary and Secondary Outcomes. Numerical risk ratio and 95 % confidence interval appears in red beside each corresponding diamond. Statistically significant values bolded and italicized. HRR = Histologic resection rate. PR= Perforation Rate. DBR = Delayed Bleeding Rate.

Conclusions

- EMR and ESD are increasingly prevalent treatment options for superficial rectal neoplasms.
- Complete histologic resection was more likely with ESD compared to conventional EMR, but no statistically significant difference shown between ESD and modified EMR.
- Our data indicates that conventional EMR is superior to ESD for decreasing procedure time and minimizing perforation and bleeding rates. However, modified EMR techniques did not show statistically significant improvement in perforation and bleeding rates over ESD.
- Given the poor methodologic quality of current studies, additional randomized, prospective, multicenter trials should be performed to better understand the efficacy and safety outcomes of ESD and EMR techniques for treatment of rectal NETs.

References

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