

**Clinical features, outcomes and risk factors
for bleeding after endoscopic resection
of submucosal invasive colorectal neoplasms:
ENTER-K, a KASID multicenter cohort study**

Ji-Taek Hong

Ewha Womans University College of Medicine



BACKGROUND

- **Endoscopic resection (ER)** is an effective and safe procedure for the treatment of colorectal neoplasm
- One of the **major complications** associated with ER including endoscopic submucosal dissection and endoscopic mucosal resection is **bleeding (Intra-procedural, Delayed bleeding)**
- Investigations into the **risk factors** for bleeding following ER treatment for **submucosal** colorectal neoplasms are lacking.

OBJECTIVE

- The present study aimed
to investigate the **incidence** and **its clinical outcomes**
of intra-procedural and delayed bleeding
following ER
for submucosal invasive colorectal neoplasms
and its **risk factors**



DEFINITIONS

- Definitions of Intraprocedural bleeding and Delayed bleeding

Intraprocedural bleeding

Active bleeding that developed during the procedure that resulted in the use of endoscopic hemostatic clips

Delayed bleeding

- bleeding that resulted in overt hematochezia 6 h to 30 d after ER
- the observation of bleeding spots as confirmed by reintervention



DEFINITIONS

- Definitions of Major bleeding and Minor bleeding

Major bleeding

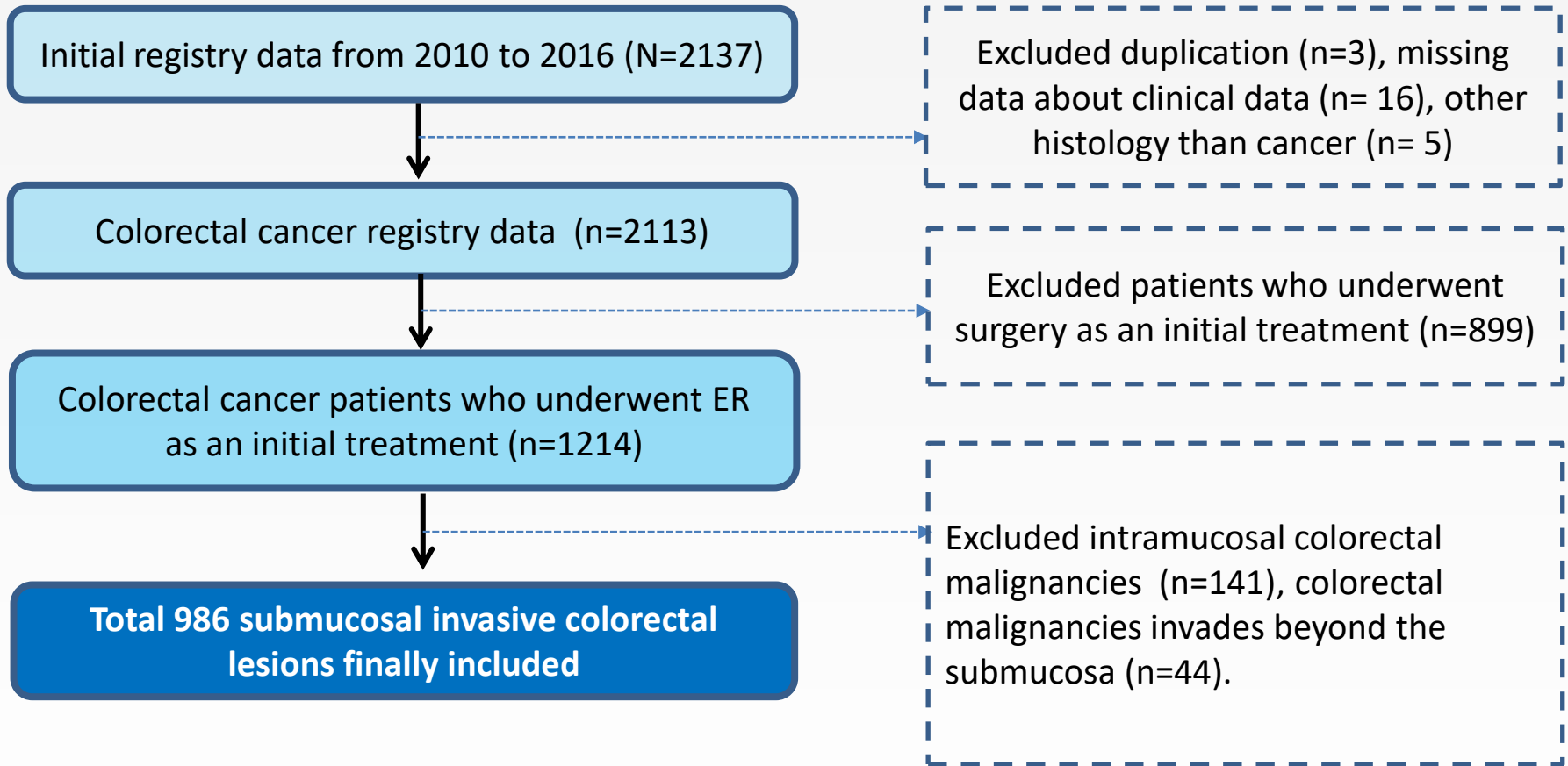
- Fall in the hemoglobin level by at least 2 g/dl, or hemodynamic instability
- Necessitation of hemostasis treatment (endoscopic, surgical or angiography)
- Any bleeding requiring hospitalization or blood transfusion

Minor bleeding

- Clinically overt bleeding that did not satisfy the criteria for major bleeding



DESIGN



A retrospective cohort study was conducted for 986 lesions resected via ER for submucosal invasive CRNs at ten hospitals in the Republic of Korea.



METHODS

- The risk factors for post-ER bleeding were assessed from data based on **patient-**, **treatment-**, and **lesion-**related variables.

The following factors using univariate and multivariate analyses:

- **patient-** age, gender, BMI, drinking, smoking, presence of comorbidities, use of antiplatelet and anticoagulant, family history, history of colon polyp
- **lesion-** pathology report before ER, biopsy before ER, endoscopic lesion size, location, morphology, histology, en-bloc resection rate, pathologic lesion size, lateral and vertical margin, lymphovascular invasion, endoscopic & pathologic complete resection rate
- **Treatment-** modality (EMR, ESD)



<u>Bleeding</u>	No (n=877, 88.9%)		Yes (n=109, 11.1%)			En-bloc resection rate	740	86.40	93	85.30	0.747	
						Endoscopic complete resection	806	94.3	100	91.7	0.296	
Characteristics	n	%	n	%	p value	Pathologic specimen size	13.0	(9.0-20.0)	15.0	(10.0-22.5)	0.020	
Age, year, mean (SD)	63.1	9.8	62.8	10.4	0.797	SM Depth	1030.0	(600.0-2000.0)	1500.0	(785.3-2000.0)	0.358	
Male sex	570	65.0	62	56.9%	0.096		SM Depth group					
BMI, Kg/m ² , mean (SD)	24.5	3.4	24.0	3.5	0.181	<1000	279	37.5	36	35.0	0.710	
Drinking	342	39.2	29	26.6%	0.011	<2000	197	26.5	29	28.2		
Smoking						<3000	138	18.5	23	22.3		
Non-smoker	589	67.5	80	73.4	0.021	>3000	130	17.5	15	14.6		
Ex-smoker	143	16.4	7	6.4		Lateral margin						
Current smoker	141	16.2	22	20.2		Negative	651	74.9	76	69.7	0.427	
Cardiovascular disease	99	11.40	15	13.80	0.459	Positive	94	10.8	15	13.8		
Hypertension	373	42.80	47	43.10	0.945	Indeterminate	85	9.8	10	9.2		
Diabetes mellitus	162	18.60	20	18.30	0.954	Adenoma	39	4.5	8	7.3	Vertical margin	
Hyperlipidemia	55	6.30	8	7.30	0.679	Negative	682	78.2	95	87.2	0.092	
Other malignancies	92	10.60	9	8.30	0.458	Positive	117	13.4	8	7.3		
Antiplaetet use	160	18.30	19	17.40	0.819	Indeterminate	73	8.4	6	5.5		
Antocoagulant use	13	1.50	4	3.70	0.110	Lymphovascular invasion						
Biopsy before ER	445	52.5%	63	58.3	0.251	No	735	84.7	92	85.2	0.969	
Treatment modality						Yes	105	12.1	13	12.0		
EMR	544	63.8	58	53.2	0.095	Indeterminate	28	3.2	3	2.8		
EPMR	63	7.4	10	9.2		Tumor_budding						
ESD	245	28.8	41	37.6		No	555	80.7%	43	74.1	0.343	
Treatment modality						Yes	131	19.0%	15	25.9		
EMR	607	71.2	68	62.4	0.057	Indeterminate	2	0.3%	0	0.0		
ESD	245	28.8	41	37.6		Pathologic complete resection						
Endoscopic size	15.0	(12.8-25.0)	20.0	(15.0-25.0)	0.022	No	256	29.3	31	28.4	0.339	
Location						Yes	541	62.0	65	59.6		
Right	231	26.90	25	22.90	0.599	Indeterminate	44	5.0	5	4.6		
Left	409	47.70	57	52.30		Adenoma	32	3.7	8	7.3		
Rectum	218	25.40	27	24.80								

Bleeding Incidence and Clinical outcomes

- **Procedure-related bleeding** occurred in 109 lesions (109/986, 11.1%)
- The overall rates of **Intra-procedural, delayed, and major bleeding** were 8.2% (81/986), 2.6% (26/986), and 3.2% (30/929), respectively.
- All **major bleeding** could be successfully managed with endoscopy or conservative observation **without surgery**.
- All cases of recognized bleeding were successfully managed by endoscopy (95.1%), conservative observation (3.9%), and angiography (1.0%).
- In the present large consecutive study with a median follow-up period of more than 4 years, **no ER related death due to bleeding was observed**.



Bleeding

Bleeding	Univariate				Multivariate (Stepwise selection)			
	OR	lower 95% CI	upper 95% CI	p value	OR	lower 95% CI	upper 95% CI	p value
Characteristics								
Age, year, mean (SD)	0.997	0.977	1.018	0.797	0.992	0.972	1.012	0.423
Male sex	0.710	0.475	1.064	0.097	0.848	0.527	1.364	0.496
BMI, Kg/m ² , mean (SD)	0.959	0.901	1.020	0.181				
Drinking	0.563	0.360	0.879	0.012	0.548	0.310	0.967	0.038
Smoking								
Non-smoker	1.000							
Ex-smoker	0.360	0.163	0.797	0.012	0.582	0.242	1.399	0.227
Current smoker	1.149	0.692	1.906	0.591	1.917	1.020	3.604	0.043
Anticoagulant use, n (%)	2.520	0.807	7.871	0.112				
Pathology report before endoscopic resection								
Adenoma	1.455	0.791	2.677	0.228				
Hyperplastic polyp	1.327	0.159	11.103	0.794				
Adenoma+hyperplastic polyp	0.885	0.286	2.738	0.831				
Adenocarcinoma	2.167	1.208	3.887	0.009				
None	1.000							
Treatment modality								
EMR (EMR +EPMR)	1.000							
ESD	1.494	0.986	2.262	0.058				
Endoscopic size	1.013	0.997	1.030	0.100				
Pathologic specimen size	1.024	1.006	1.042	0.009	1.026	1.008	1.045	0.006
Vertical margin								
Negative	1.000							
Positive	0.491	0.232	1.037	0.062	0.410	0.190	0.884	0.023
Indeterminate	0.590	0.250	1.394	0.229	0.550	0.231	1.310	0.177



Intra-procedural Bleeding

Intra-procedural Bleeding	Univariate				Multivariate (Stepwise selection)			
	OR	lower 95% CI	upper 95% CI	p value	OR	lower 95% CI	upper 95% CI	p value
Characteristics								
Age, year, mean (SD)	0.994	0.972	1.017	0.602	0.989	0.967	1.012	0.364
Male sex	0.673	0.427	1.059	0.087	0.819	0.479	1.398	0.464
BMI, Kg/m ² , mean (SD)	0.963	0.898	1.033	0.291				
Drinking	0.531	0.318	0.887	0.016	0.521	0.271	1.000	0.050
Smoking								
Non-smoker	1.000							
Ex-smoker	0.273	0.098	0.763	0.013	0.473	0.156	1.434	0.186
Current smoker	1.237	0.710	2.158	0.453	2.136	1.059	4.308	0.034
Anticoagulant use	0.673	0.088	5.139	0.703				
Pathology report before endoscopic resection								
Adenoma	1.902	0.898	4.030	0.093				
Hyperplastic polyp	2.333	0.269	20.257	0.442				
Adenoma+hyperplastic polyp	1.145	0.305	4.305	0.841				
Adenocarcinoma	3.249	1.590	6.639	0.001				
None	1.000							
Treatment modality								
EMR (EMR +EPMR)	1.000							
ESD	1.375	0.859	2.202	0.185				
Endoscopic size	1.012	0.994	1.031	0.176				
Pathologic specimen size	1.024	1.004	1.044	0.018	1.024	1.003	1.044	0.022
Vertical margin, n (%)								
Negative	1.000							
Positive	0.599	0.269	1.335	0.21				
Indeterminate	0.83	0.349	1.977	0.674				



Delayed Bleeding

Delayed Bleeding	Univariate				Multivariate (Stepwise selection)			
	OR	lower 95% CI	upper 95% CI	p value	OR	lower 95% CI	upper 95% CI	p value
Characteristics								
Age, year, mean (SD)	1.012	0.973	1.051	0.562	1.005	0.967	1.046	0.789
Male sex	1.008	0.460	2.209	0.983	0.962	0.436	2.123	0.923
BMI, Kg/m ² , mean (SD)	0.966	0.862	1.083	0.553				
Drinking	0.651	0.284	1.494	0.311				
Smoking								
Non-smoker	1.000							
Ex-smoker	0.630	0.185	2.139	0.459				
Current smoker	0.776	0.263	2.293	0.647				
Anticoagulant use	8.057	2.177	29.822	0.002	7.833	2.061	29.769	0.003
Pathology report before endoscopic resection								
Adenoma	0.901	0.330	2.456	0.838				
Hyperplastic polyp	NA							
Adenoma+hyperplastic polyp	0.534	0.064	4.428	0.561				
Adenocarcinoma	0.712	0.246	2.061	0.531				
None	1.000							
Treatment modality								
EMR (EMR +EPMR)	1.000							
ESD	1.804	0.842	3.863	0.129				
Endoscopic size	1.012	0.983	1.042	0.423				
Pathologic specimen size	1.017	0.984	1.050	0.324				
Vertical margin								
Negative	1.000							
Positive	0.224	0.030	1.663	0.144				
Indeterminate	NA							



Major Bleeding

Major Bleeding	Univariate				Multivariate (Stepwise selection)			
	OR	lower 95% CI	upper 95% CI	p value	OR	lower 95% CI	upper 95% CI	p value
Characteristics								
Age, year, mean (SD)	1.000	0.964	1.038	0.998	0.997	0.960	1.035	0.872
Male sex	1.075	0.497	2.326	0.854	1.068	0.491	2.323	0.869
BMI, Kg/m ² , mean (SD)	0.949	0.848	1.062	0.364				
Drinking	0.669	0.303	1.478	0.321				
Smoking								
Non-smoker	1.000							
Ex-smoker	0.838	0.282	2.488	0.750				
Current smoker	1.231	0.486	3.119	0.662				
Anticoagulant use	4.490	0.974	20.706	0.054				
Pathology report before endoscopic resection								
Adenoma	2.609	0.847	8.042	0.095				
Hyperplastic polyp	0.000	0.000		0.999				
Adenoma +hyperplastic polyp	2.943	0.639	13.553	0.166				
Adenocarcinoma	1.721	0.523	5.664	0.372				
None	1.000							
Treatment modality								
EMR (EMR +EPMR)	1.000							
ESD	3.241	1.551	6.771	0.002	3.244	1.552	6.780	0.002
Endoscopic size	1.032	1.010	1.054	0.005				
Pathologic specimen size	1.022	0.992	1.053	0.146				
Vertical margin								
Negative	1.000							
Positive	0.435	0.102	1.854	0.260				
Indeterminate	0.345	0.046	2.576	0.300				



CONCLUSION

- An adequate safety profile about bleedings after endoscopic resection of submucosal invasive colorectal neoplasms
- An increased risks of intra-procedural, delayed, and major bleeding were associated with pathologic lesion size, the use of anticoagulant medicines, and ESD treatment method, respectively
- Careful and additional management is recommended for patients with these risk factors

