


Recent Update : Endoscopic Treatment of EGC

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내용

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조기위암 내시경치료 최근 발표 자료 - 국내

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EMR for EGC: 국내 첫 임상연구

조기위암의 근저적 치료로서의 내시경적 점막절제술

서울대학교 의과대학 내과학교실, 건원연구소 및 병리학교실, 포서대병원 내과**

이준형 · 송정환 · 김병관 · 황진혁 · 정은오
최성아 · 이은혜 · 정복재 · 이태현** · 이영호**
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---Abstract---

Endoscopic Mucosal Resection(EMR) as a Curative Treatment of Early Gastric Cancer

Joo Hwang Lee, M.D., Jung-Hwan Yoon, M.D., Seung-Cheon Kim, M.D.,
Jin-Hyuk Hwang, M.D., Jun Oh Jeong, M.D., Young-Seok Lim, M.D.,
Dae-Han Lee, M.D., Won-Tae Jeong, M.D., Kook-Lae Lee, M.D.,**
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EMR for adenocarcinoma: 19 cases

operation(+): 7 cases operation(-): 12 cases

4 resection margin(+)
1 incomplete resection
2 F/U GFS, recur

surgical specimen		F/U gastroscopy	
cancer(+)	cancer(-)	cancer(+)	cancer(-)
5	2	4	8
depth of invasion	burning effect	poor surgical effect	disease free condition: for 3-13 mo
m: 3	sm: 2	LO, COPD, MM, lod age	burning effect: 2
(group A)	(group B)	(group C)	(group D)

이준형. 대한소화기내시경학회지 1996;16:928-934

ORIGINAL ARTICLE: Clinical Endoscopy

EMR for early gastric cancer in Korea: a multicenter retrospective study

Joo J. Kim, MD, Jun Haeng Lee, MD, Hwsoon-Yong Jung, MD, Gih Hyoung Lee, MD, Joo Yong Cho, MD, Chang Beom Ryu, MD, Hyeon Jai Chum, MD, Jong Jae Park, MD, Wan Sik Lee, MD, Hyun Soo Kim, MD, Moon Gi Chung, MD, Jeong Seop Moon, MD, Seok Ryoul Choi, MD, Geun An Song, MD, Hyun Yong Jeong, MD, Sun Byong Jee, MD, Sang Yong Seok, MD, Yong Bum Yoon, MD
Seoul, Gwangju, Wonju, Incheon, Busan, and Taeseon, Korea

Background: EMR has been accepted as a treatment modality for selected cases of early gastric cancer (EGC) in Japan. However, long-term outcomes after EMR for EGC have not been fully documented.

Objectives: We reviewed the experiences of EMR for EGC in Korea, with emphasis on the long-term outcome.

Design: Multicenter, retrospective study.

Methods: Data were collected retrospectively by use of the on-line database registry system. From January 2000 to December 2002, 514 EGCs in 506 patients were treated by EMR in 13 institutions in Korea. Median age of the patients was 60 years (range 45-83 years). The resection was registered as incomplete if histopathologic examination revealed a positive resection margin or submucosal invasion or positive lymphovascular invasion or undifferentiated histologic diagnosis.

Results: The most commonly used technique was circumferential precutting followed by snare resection (EMR; n = 269; 52.3%). Complete resection and incomplete resection after EMR were confirmed in 399 lesions (77.6% and 21.6%, respectively). For completely resected mucosal cancers (n = 399), the median duration of follow-up was 24.5 months (range 5-70 months). In this group, local recurrence was detected in 24 cases (6.0%) with a median interval between EMR and recurrence of 17.9 months (range 3.5-51.7 months). There were 9 cases with perforation and 71 cases with bleeding. No deaths were related to recurrence of gastric cancer during the overall median follow-up period of 39 months.

Limitations: Multicenter retrospective design, no controls.

Conclusions: EMR is an effective therapeutic modality for selected cases of EGC in Korea. (Gastrointest Endosc 2007;66:693-700.)

Kim JJ. Gastrointest Endosc 2007;66:693-700

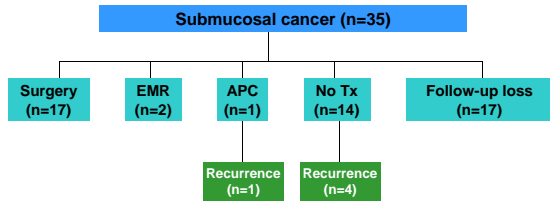
Follow-up results for mucosal cancer

Intramucosal cancer (n=479)

Complete resection (n=399, 82.2%)			Incomplete resection (n=68)			Not evaluable (n=12)		
f/u loss 25	Surgery 17	EMR 2	APC 14	PDT 1	No Tx 34	Surgery 34	EMR 1	No Tx 10
Recurrence 24	Metachronous 11	Recurrence 4	Recurrence 6	Metachronous 1	Recurrence 3	Metachronous 1		
Surgery 14	EMR 7	APC 1	CTI 1	No Tx 1	EMR 9	No Tx 2	Surgery 4	EMR 2
					Surgery 4	EMR 2	EMR 1	Surgery 3
								EMR 1

Kim JJ. Gastrointest Endosc 2007;66:693-700

Management for submucosal cancer



Kim JJ. Gastrointest Endosc 2007;66:693-700

ESD에 대한 용어의 정리

- ESD를 EMR에서 분리하여 새로운 시술로 봄

• ER = EMR + ESD

한시적 인정 비급여

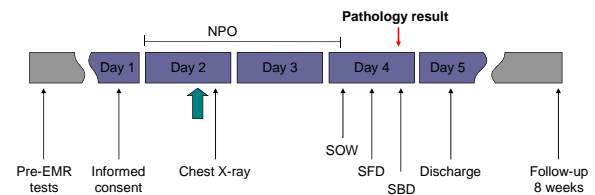


EMR-P vs ESD at SMC

- July 2003 – June 2006
- 346 EGCs in 346 patients at SMC
- 243 ESD and 103 EMR-P
- Median age: 62 years (range 26-84 years)
- Incomplete resection
 - positive resection margin
 - submucosal invasion (+)
 - lymphovascular invasion (+)
 - undifferentiated histology

Min. Dig Liver Dis. 2009 Mar;41(3):201-9

Critical pathway for ESD



- Pre-ESD tests: CBC, chemistry, PT/aPTT, chest PA, ECG, sono/CT
- H₂ receptor antagonist q 12 hours during admission → oral PPI for 4 weeks
- Soft diet for 2-3 days after discharge → regular diet
- Inform the patient about the risk of delayed bleeding
- H. pylori eradication at OPD (if indicated)

EMR-P vs ESD

- July 2003 to June 2006

Table 2
Clinical outcomes of EMR-P and ESD for all study subjects

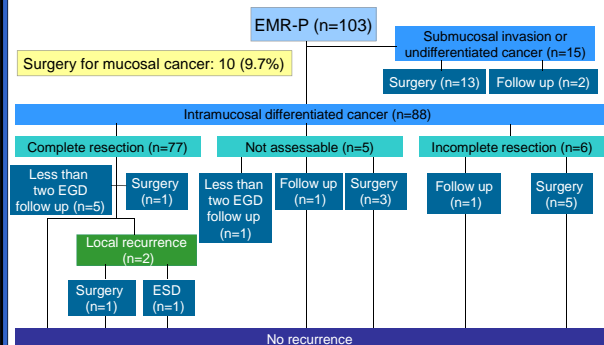
Characteristics	EMR-P (n = 103)	ESD (n = 243)	P-value
En bloc resection (%)	80 (77.7)	233 (95.9)	<0.001
R0 resection (%)	92 (89.3)	226 (93.0)	0.251
En bloc plus R0 resection (%)	78 (75.7)	216 (88.9)	0.002
Procedure time (min) ^a	24.3 ± 16.2	33.4 ± 16.6	<0.001
Bleeding (%)	4 (3.9)	13 (5.3)	0.564
Perforation (%)	2 (1.9)	11 (4.5)	0.359

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

^a The value was expressed as mean ± standard deviation.

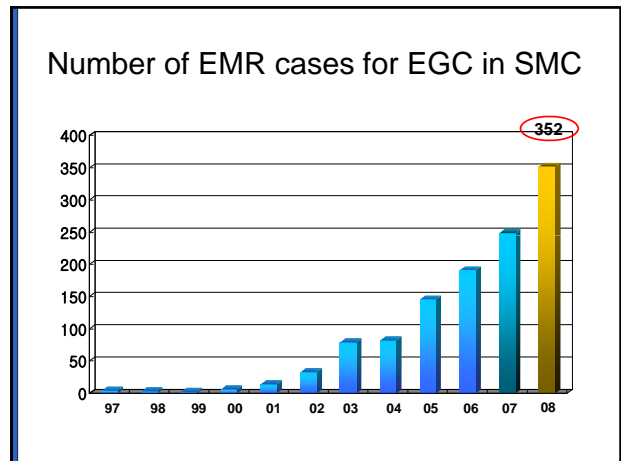
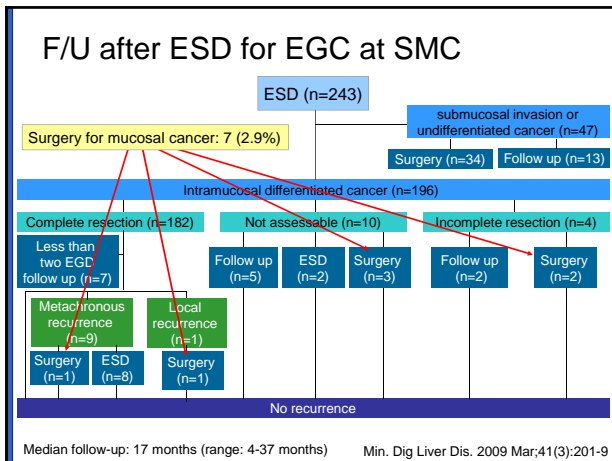
Min. Dig Liver Dis. 2009 Mar;41(3):201-9

F/U after EMR-P for EGC at SMC



Median follow-up: 29 months (range: 4-44 months)

Min. Dig Liver Dis. 2009 Mar;41(3):201-9



Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study

Il-Kwon Chung, MD, Jun Haeng Lee, MD, Suck-Ho Lee, MD, Sun-Joo Kim, MD, Joo Young Cho, MD, Won Young Cho, MD, Young Hwangbo, MD, Bo Ra Keum, MD, Jong Jae Park, MD, Hoon-Jai Chun, MD, Hoi Jin Kim, MD, Jae J. Kim, MD, Sam-Ryong Ji, MD, Sang Young Seol, MD
Cheonan, Seoul, Busan, Korea

Capsule Summary

What is already known on this topic

- Endoscopic submucosal dissection (ESD) facilitates en bloc resection of large early GI neoplasms but is technically difficult, is associated with a higher rate of complications, and requires advanced endoscopic skills and a long procedure time.

What this study adds to our knowledge

- In a retrospective multicenter study of ESD performed in 1000 early gastric neoplasms by 6 experienced endoscopists, an 87% rate of complete resection was achieved with a low rate of complications (bleeding 15.6%, perforation 1.2%).

Chung. Gastrointest Endosc. 2009 Feb 26. [Epub ahead of print]

Therapeutic outcome of 1,000 ESDs

Outcome of resection, no. (%)	
Piecemeal resection	41 (4.1)
En bloc resection	953 (95.3)
Free of margin	901 (90.1)
Horizontal (+)	26 (2.6)
Vertical (+)	18 (1.8)
Both (+)	9 (0.9)
Failure	6 (0.6)
ESD time (min), mean ± SD	47.8 ± 38.3
Invasion of tumor, no. (%)	
Submucosal invasion	74 (7.4)
Lymphovascular invasion	30 (3.0)
Complete resection, no. (%)	877 (87.7)

Chung. Gastrointest Endosc. 2009 Feb 26. [Epub ahead of print]

Expanded indication of EMR for EGC

- Suggested by NCCH group (Japan)

Histology	Depth					
	M cancer				SM cancer	
	UL (-)		UL (+)		SM1	SM2, SM3
	≤ 20 mm	> 20 mm	≤ 30 mm	> 30 mm	≤ 30 mm	Any size
Differentiated	A	B	B	D	B	D
Undifferentiated	C	D	D	D	D	D

A: definite indication by guideline
 B: expanded indication
 C: surgery, but need for more consideration
 D: surgery

Hamanaka & Gotoda. Stomach Intest 2004;39:27-34

EMR for undifferentiated EGC

Therapeutic efficacies	No. of patients (%)			P value
	Total	Poorly differentiated	Signet ring cell	
En bloc resection	49 (84.5)	14 (82.4)	35 (85.4)	.773
Complete resection	39 (67.2)	10 (58.8)	29 (70.7)	.540
Incomplete resection	19 (32.8)	7 (41.2)	12 (29.3)	
Lateral cut end (+)	10 (52.6)	0 (0)	10 (83.3)	<.001
Vertical cut end (+)	9 (47.4)	7 (100)	2 (16.7)	
Recurrence, no. (%)	4 (6.9)	0 (0)	4 (9.8)	.310
In CR	2 (5.1)	0 (0)	2 (6.9)	
In incomplete resection	2 (10.5)	0 (0)	2 (16.7)	

ER, Endoscopic resection; CR, histologically complete resection.

Kim. Gastrointest Endosc 2009;69

성균관대학교 Unique Origin Unique Future

내시경치료 후 수술에 대하여

성균관대학교 의과대학 삼성서울병원 소화기내과
이준형

Surgery after ER for EGC: SMC experience

- 118 cases (6.8%) out of 1,743 EMR/ESD
- Presence of residual cancer: 24.6%
- A large-size cancer and a positive lateral margin was related with residual cancer.

이교원, 2009 대한위암학회 춘계 학술대회. p173

Is Gastrectomy Mandatory for All Residual or Recurrent Gastric Cancer Following Endoscopic Resection? A Large-Scale Korean Multi-Center Study

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Background and Objectives: To clarify optimal treatment guidelines for residual or local recurrence after endoscopic resection (ER).
Methods: Eighty-six patients underwent gastrectomy due to incomplete ER and local recurrence after ER. The pathological findings of ER and gastrectomy specimens were analyzed.
Results: The cause of gastrectomy was categorized into five groups; submucosal (sm) invasion without margin involvement, positive margin, margin not evaluable, high risk of lymph node metastasis and local recurrence after ER. According to the pathological findings of gastrectomy specimens, residual cancer and lymph node metastases were found in 56 (65.1%) and in 2 patients (2.3%), respectively. At 10 gastrectomy specimens which were sm invasion without margin involvement, the scattered residual cancer cells were found around the ulcer scar in 2 (20%) patients. In 11 of 44 margin involvement specimens, no residual cancer or lymph node metastasis was found. In patients with local recurrence, mean duration from ER to surgery was 14.8 months, and 19% of patients were found to have sm or deeper depth of invasion.
Conclusion: Gastrectomy with lymph node dissection should be performed in patients with sm invasion with or without margin involvement. However, minimal approach other than gastrectomy could further be applied to selected patients.
J. Surg. Oncol. 2008;98:6-10. © 2008 Wiley-Liss, Inc.

Song. J Surg Oncol 2008;98:6-10

Causes of surgery after EMR/ESD

Song. J Surg Oncol 2008;98:6-10

Patients with lymph node metastasis

TABLE II. Details of Five Patients With LN Metastasis

Case	One piece/ multipiece	Gross type	Histologic type	Depth	Lymphatic vs. invasion
1	One piece	I + IIc	Mod	m	Positive
2	Multipiece	IIb	Sig	sm	Positive
3	One piece	IIc	Sig	sm	Positive
4	Multipiece	IIc	Well	sm	Negative
5	Multipiece	IIa	Mod	sm	Negative

Mod, moderate differentiation; sig, signet ring cell histology; well, well differentiated; m, mucosa; sm, submucosa.

Song. J Surg Oncol 2008;98:6-10

Treatment strategy after non-curative endoscopic resection of early gastric cancer

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16.7% of 1,783 EGCs (495 EMR + 1,288 ESD), 1989-2003

Background: Endoscopic resection (ER) is indicated for patients with early gastric cancer who have a negligible risk of lymph node metastasis (LNM). Histological examination of the resected specimen may indicate a possible risk of LNM or a positive resection margin. These patients are considered to have undergone non-curative ER. The aim of this study was to determine the appropriate treatment strategy for such patients.
Methods: A total of 298 patients who had non-curative ER were classified into those with a positive lateral margin only (group 1; 72 patients) and those with a possible risk of LNM (group 2; 226 patients).
Results: Surgery was performed within 6 months of non-curative ER in 19 patients in group 1 and 144 in group 2. In group 1, nine patients were found to have local residual tumours, all limited to the mucosal layer without LNM. In Group 2, 13 patients had residual disease, including four local tumours without LNM, two local tumours with LNM and seven cases of LNM alone. The rate of LNM after surgery was 6.3 per cent in group 2.
Conclusion: Surgery remains the standard treatment after non-curative ER in patients with a possible risk of LNM.

Oda. Br J Surg 2008;95:1495-1500

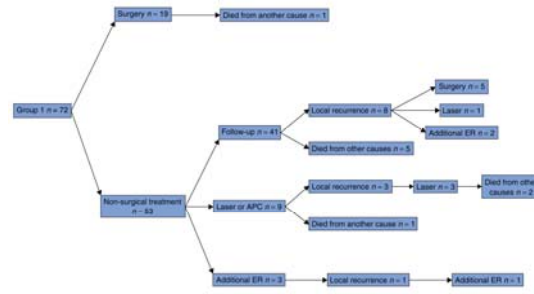
Surgical outcome

Outcome of endoscopic resection	No. of patients	Surgical outcome	
		Local residual tumour	LNM
Group 1 (positive lateral margin)	19 (11.7)	9 (47)	0 (0)
Group 2 (risk of LNM regardless of margin)	144 (88.3)	6 (4.2)	9 (6.3)
Total	163 (100)	15 (9.2)	9 (5.5)

Values in parentheses are percentages. LNM, lymph node metastasis.

Oda. Br J Surg 2008;95:1495-1500

Patients with lateral margin (+) only - no gastric cancer-related death



Oda. Br J Surg 2008;95:1495-1500

Reasons for risk of lymph node mets

	Surgical treatment	Non-surgical treatment
Predominantly undifferentiated type	33 (73)	12 (27)
Positive lymphatic and/or venous invasion	61 (73)	22 (27)
Submucosal deep invasion (sm2)	93 (77.5)	27 (22.5)
Intramucosal cancer > 30 mm in size with ulcer finding	13 (35)	24 (65)
Minute submucosal cancer (sm1) > 30 mm in size	8 (36)	14 (64)
Positive vertical margin	17 (68)	8 (32)

Values in parentheses are percentages. Some patients had more than one reason.

Oda. Br J Surg 2008;95:1495-1500

Patients with risk of LN metastasis - 5 gastric cancer-related deaths



Oda. Br J Surg 2008;95:1495-1500

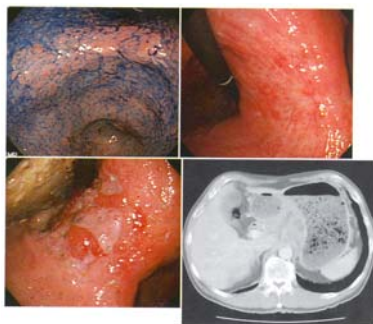
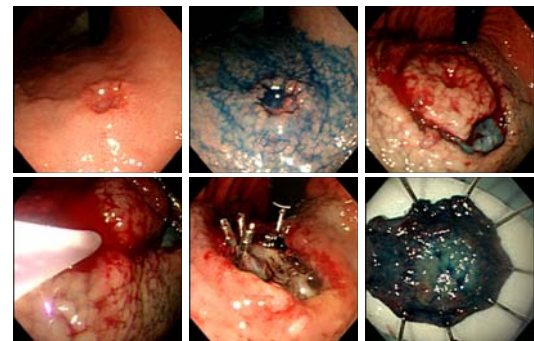
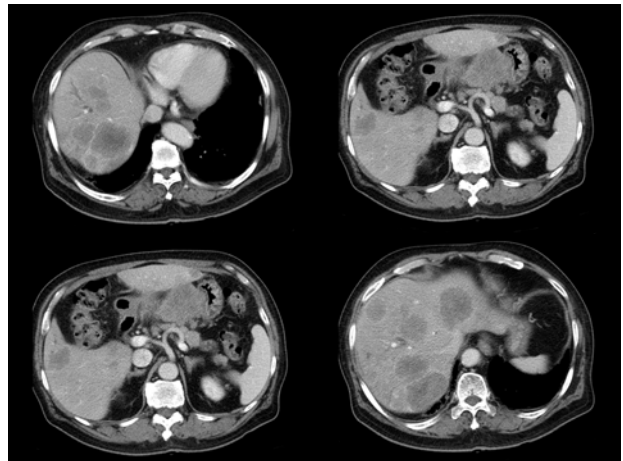
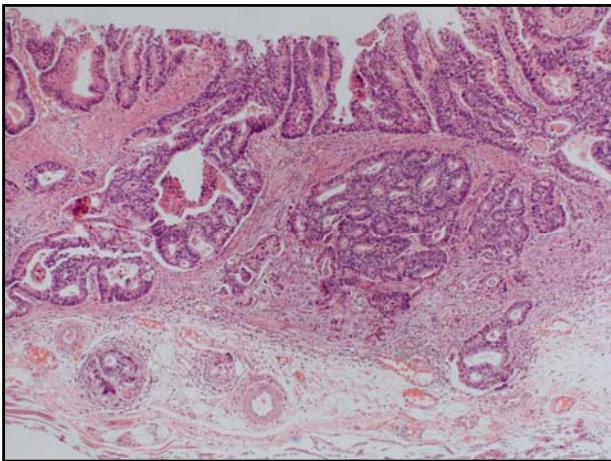


Fig. 2 A case with local recurrence and lymph node metastasis after piecemeal EMR. a. A large 90-Hz lesion 2.0 cm in size was detected on the gastric angle. Since the depth of tumor invasion was T1-M, EMR was regarded as having been a curative treatment. However, piecemeal resection was unfortunately carried out using IT table procedure, which was apparently not sufficiently effective in this case. b. No local recurrence was evident 2 years after piecemeal EMR. c. Local recurrence was found 3 years after the second EMR. d. Not only regional but also para-aortic lymph node metastasis was observed.

Hamanaka. Stomach Intest 2004;39:27-34

Hepatic metastasis after EMR for EGC - SM2 (+), lymphatic invasion (+), surgery refused





조기위암 EMR/ESD 후 암 사망에 분석

- 조기위암 내시경 치료의 적응증 초과
- 고령이나 전신질환으로 수술을 거부하고 내시경 치료를 선택
- 내시경 치료 후 병리에서 risk of lymph node metastasis (lateral margin positive only는 아님)로 수술을 추천하였으나 거부

EMR/ESD 후 사망예를 방지하기 위한 대책

- 보다 정확한 적응증 확립을 위한 지속적인 연구
- 보다 radical한 내시경치료를 위한 연구
- 내시경 시술 전 치료 후 최종 병리결과에 따라 수술이 필요하다고 나오는 경우 절대로 수술을 거부하지 않고 의사의 추천에 따라 반드시 수술을 받겠다는 환자 및 가족의 다짐을 받아두는 것이 내시경치료 후 사망예를 줄이는 지름길이다.

현재까지 EMR/ESD 관련 국내외 연구의 한계점

성균관대학교 의과대학 삼성서울병원 소화기내과 이준행

현재까지 국내연구의 한계점

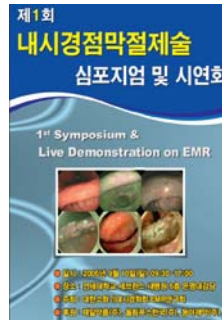
- Retrospective study (selection bias)
- 내과환자만 enroll 되어 big picture를 보기 어렵다
- 제한된 institutions
- 시술방법이 통일되지 못함
- 병리판독의 inter-observer variation
- 병리학적 완전절제에 대한 통일된 규정이 없음
- Follow-up 방법이 다양함
- 재발예에 대한 치료가 다양함

Publication bias

- 모든 EMR 증례에서 100% perfect한 결과가 나오는 것은 아니다.
- 다양한 경로(학회 초록, 구연 혹은 포스터 발표, 집담회, review, 전문가 코너, personal communication)로 발표되는 흥미로운 혹은 less-perfect한 증례들이 정식 research article에서는 포함되지 않는 경향이 있다.
- 논문에서는 임상에서의 경험들이 inclusion criteria, exclusion criteria라는 장치를 통하여 왜곡되기 쉽다.

▲ 상대적으로 경험이 적은 내시경 시술이나 직접 시술 하지 않는 관련 의료진의 잘못된 판단이 가능하다.

EMR symposium (2006. 9. 10.)



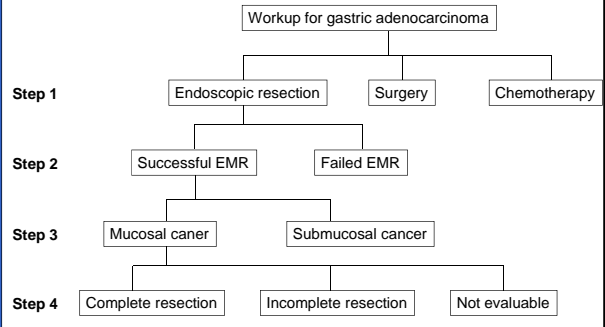
타지역에서 치료받는 환자가 많고 이는 follow-up rate를 낮추는 중요한 이유가 된다

구분	전체	취약	취약	취약	취약	취약	취약
서울	95.9	95.9	94.9	94.2	94.2	96.9	96.4
부산	10.3	10.3	9.3	12.0	9.2	14.1	4.6
대구	6.5	11.1	6.6	13.4	6.6	6.3	3.4
인천	30.7	31.9	24.8	35.1	23.2	33.1	30.5
광주	32.0	31.8	29.2	39.5	25.3	38.8	25.2
대전	26.3	23.3	22.6	32.9	22.1	35.2	14.7
울산	24.8	23.5	14.2	26.7	20.6	28.1	36.1
경기	51.2	51.5	45.9	53.1	45.6	57.4	46.7
강원	33.9	34.8	27.3	33.9	33.9	42.0	28.8
충북	48.6	52.1	43.0	50.3	41.4	53.3	48.4
충남	46.3	47.2	43.0	45.1	35.3	53.3	44.2
전북	33.2	36.7	28.4	46.3	22.1	36.7	25.8
전남	47.4	52.8	42.1	53.1	42.4	46.3	-
경북	25.6	27.6	21.1	29.8	24.6	30.5	18.8
경서	17.5	10.1	13.3	21.9	15.4	26.8	11.4
제주	68.2	77.6	60.4	66.2	66.2	68.6	70.0

전국적인 연구가 반드시 필요하다

http://www.fromdoctor.com/weekly/weekly_body.asp?num=5864&category=1

전향적 연구만이 big picture를 보여준다



Take home message

Endoscopic treatment is a *not-so-futuristic* approach to EGC.