

Advanced colonic polyps: polypectomy, EMR or surgery?

Roel Hompes MD, PhD, FASCRS(hon)

Colorectal Cancer Masterclass – Cairo, Egypt | 30th August 2022

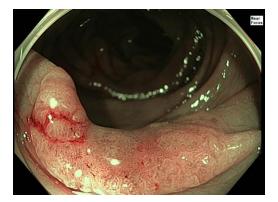


What is a "complex / advanced" CRC polyp?

- Higher risk of recurrence and/or incomplete resection
- Higher risk of (deep) submucosal invasive cancer
- Higher risk of complications



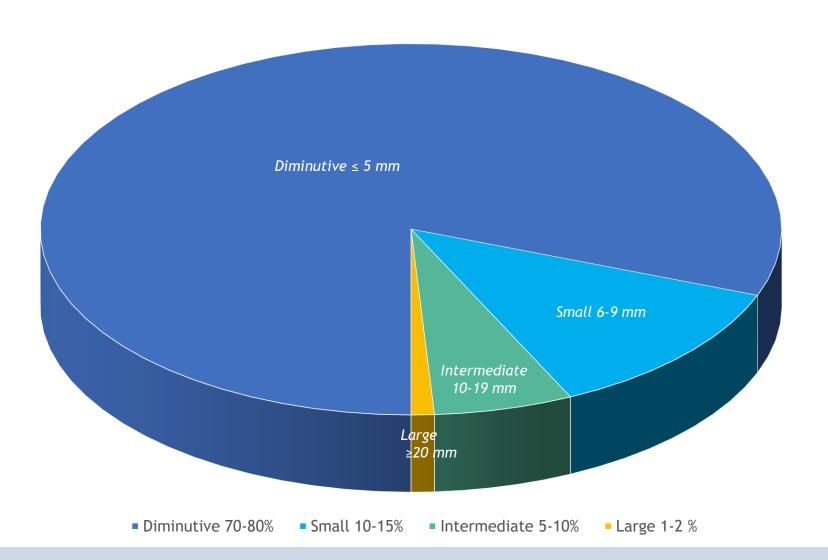


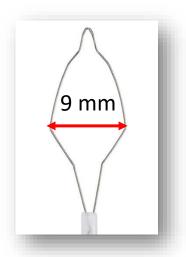






CRC polypsPrevalence by size

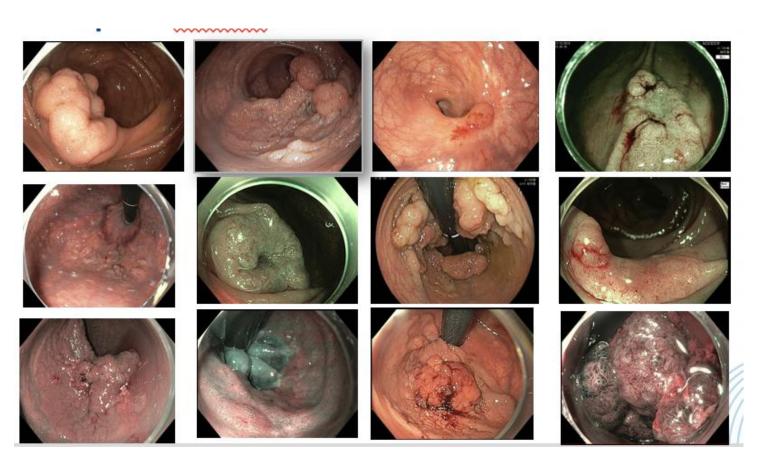


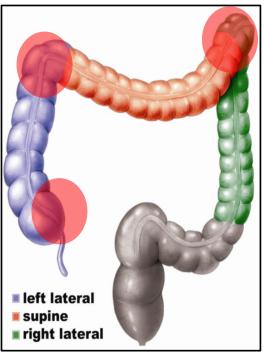






CRC polyps are diverse





IC valve

Appendix orifice

Dentate line

Inside flexures

Behind fold



Endoscopic techniques are diverse...

Cold / hot snare resection



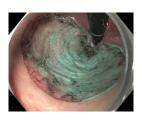
Pre-cut EMR



EMR



ESD



Underwater EMR



eFTR



Surgical techniques

Combined laparo-endoscopic wegde resection

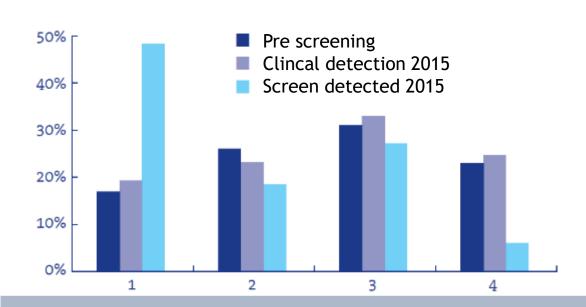
- Radical Oncologic resection
 - Completion
 - Primary





Bowel cancer screening programs





- Up tot 40% screen detected CRC is T1
- Overall risk LNM ~ 11% for T1
- Potential endoscopic/local therapy
- 75% T1 CRC located in colon 47% pedunculated
- Recognition is important!

Stage distribution CRC before & during screening program



Effective Mx CRC polyps: structured TX

1. Structured polyp assessment

- √ Size
- √ Shape/Morphology
- ✓ Location
- ✓Optical surface features

2. Planning

- ✓ Now or later? Appropriate consent?
- Refer to more exprienced/dedicated colleague
- ✓ Piecemeal (hot/cold) or en bloc?
- ✓ Refer to surgeon

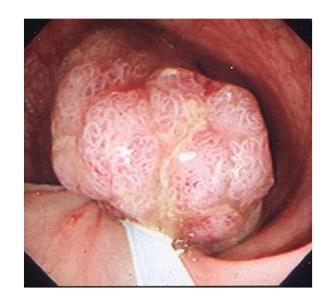
3. Post polypectomy management

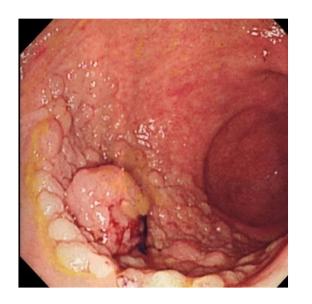
- ✓ Evaluation resection site
- ✓ Avoid complications & recurrence
- ✓ further Tx required?





Pedunculated vs Sessile (LNPCP)





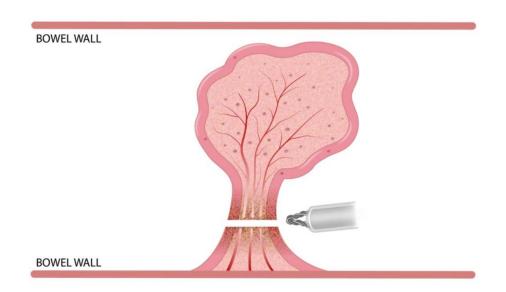


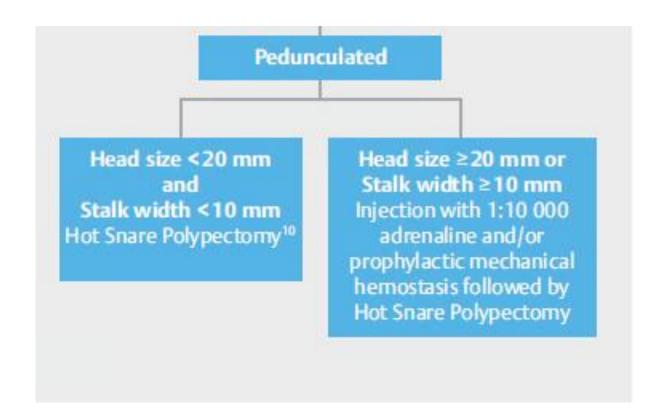




Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline

Always endoscopic removal!







Pedunculated morphology is associated with a lower risk of adverse outcome



Oncological Outcome	OR (95% CI)	P value
Adverse Outcome 222/1656 events (13.4%) T1 CRCs	0.49 (0.35-0.69)	<0.001
Metastasis 141/1656 events (8.5%) T1 CRCs	0.48 (0.32-0.72)	<0.001
Incomplete resection 108/1656 events (6.5%) T1 CRCs	0.54 (0.34-0.85)	0.008
Recurrence 90/1656 events (5.4%) T1 CRCs	0.61 (0.38-0.99)	0.05

14 Dutch units

N=1656 T1 CRC

43% PM

AE PM: 9.3%

AE NPM 16.6%

BUT.... Still high proportion referred for surgery: 46-76%



Pedunculated morphology: risk model



Histologic Model For Pedunculated T1 Colorectal Carcinomas



Hospitals: 13



Pedunculated T1 CRC: 708



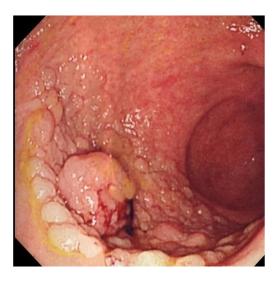
Metastasis: 5.2%

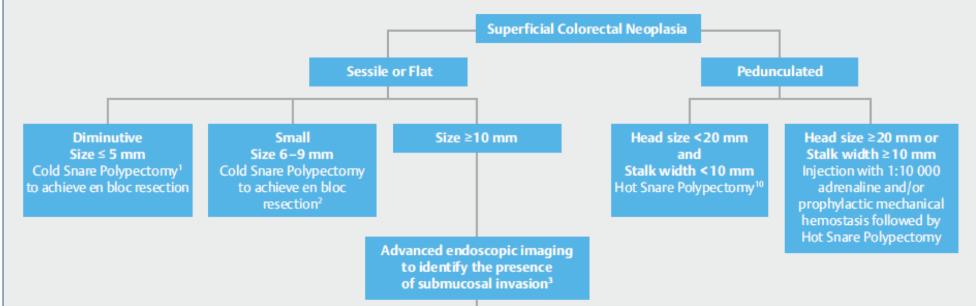
Car Durch			P	5
AKING CA	AUC	Low-risk T1 CRC	High-risk T1 CRC	Missed metastasis
Conventional model 1 (ASGE/ESGE)	0.67	43%	57%	1.3%
Conventional model 2 (JSCCR)	0.64	35%	65%	1.2%
Our new model	0.83	68%	32%	1.3%
			Gastro	oenterology





Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline







CRC polyps ≥ 10mm: LST

Endoscopic subtypes of colorectal laterally spreading tumors (LSTs) and the risk of submucosal invasion: a meta-analysis

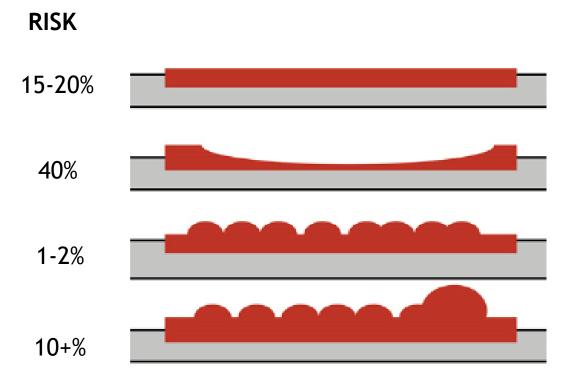
► Table 4 Risk of submucosal invasion in laterally spreading tumors, stratified by size.

	10-19mm	20-29mm	≥30 mm
Risk of containing submucosal invasion (95 %CI)	4.6 % (3.1 % – 6.0 %)	9.2% (6.6% – 11.8%)	16.5% (9.8%-23.3%)
Heterogeneity index, I ²	31.6%	14.1%	69.5%
References	[1,38,39,58,59,63,67,69]	[1,38,58,59,69]	[1,38,58,59,69]

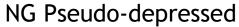


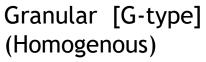
Laterally Spreading Tumours (LSTs)

> 10-20mm horizontal growth pattern



Non-granular [NG-type]





Granular [G-type] (Dominant nodule)







Location Laterally Spreading Tumours (LSTs)

> 10-20mm horizontal growth pattern

Risk of Covert Submucosal Cancer in Patients With Granular Mixed Laterally Spreading Tumors

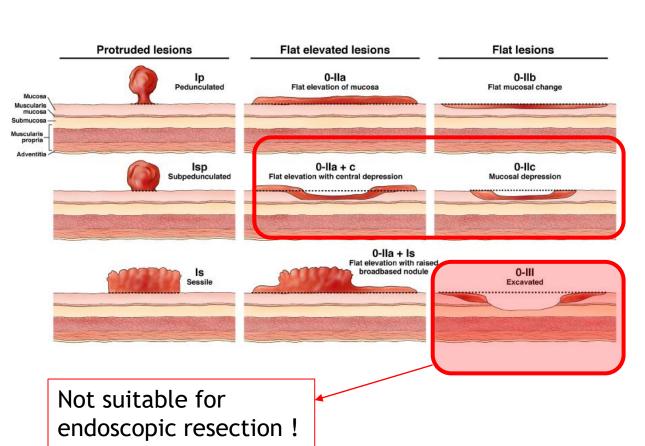
Ferdinando D'Amico,* Amaldo Amato,[‡] Andrea Iannone,[§] Cristina Trovato,[|]

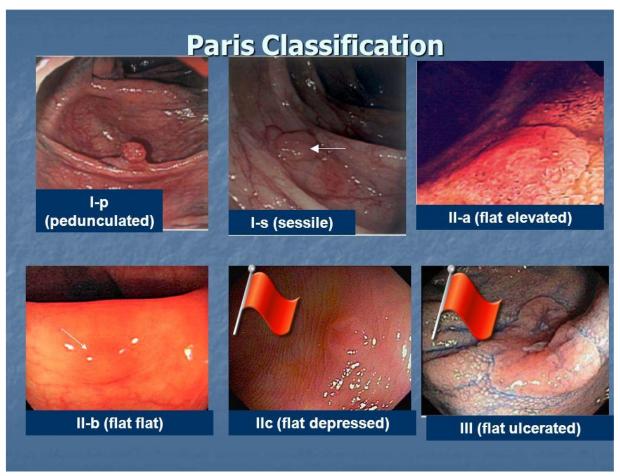


Table 3. Results of the Multivariate Analysis for Detection of Covert SMIC in GM-LSTs

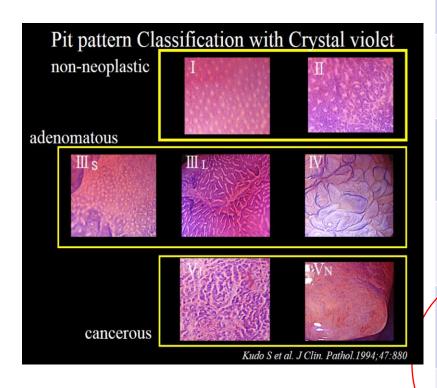
Variable	Adjusted Odds Ratio (95% CI) ^a	P Value
Sex		
Male ^b	1.00	.92
Female	0.98 (0.58-1.65)	
Age, years	0.99 (0.97-1.01)	.23
Lesion size, mm ^c	1.02 (1.01-1.03)	.003
Colonic location of the lesion ^c		
Right colon ^b	1.00	.004
Transverse colon	1.64 (0.51-5.21)	
Left colon	1.83 (0.67-4.99)	
Rectum	3.08 (1.62–5.83)	

Lesion morphology: Paris classification









Pit pattern	Adenoma(dysplasia)		Cai	ncer	Total
	Low grade	High grade	Tis	T 1	
IIIs	69 (58.9%)	16 (13.7%)	30 (25.6%)	2 (1.7%)	117
III _L	8,232 (83.4%)	1,126 (11.3%)	533 (5.3%)	0 (0.0%)	9,982
IV	1,456 (47.4%)	768 (25.0%)	738 (24.0%)	108 (3.5%)	3,070
V	90 (8.1%)	117 (10.5%)	504 (45.1%)	406 (36.3%)	1,117
V _N	0 (0.0%)	0 (0.0%)	16 (5.2%)	292 (94.8%)	308



Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team

EMR	ESD	Surgery
-----	-----	---------

	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	· Invisible • 1	• Regular caliber • Regular distribution (meshed/spiral pattern) • 2	Variable caliber Irregular distribution	· Loose vessel areas · Interruption of thick vessels
Surface pattern	Regular dark or white spots Similar to surrounding normal mucosa	• Regular (tubular/branched/papillary)	· Irregular or obscure	• Amorphous areas
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low grade intramucosal neoplasia	High grade intramucosal neoplasia/ Shallow submucosal invasive cancer *3	Deep submucosal invasive cancer
Endoscopic image				



Complex / advanced CRC polyp

Risk for recurrence/incomplete resection

- Lesion size ≥ 40 mm
- Prior failed resection
- Ileo-cecal valve or dentate line
- Size-morphology-site-access (SMSA) level 4

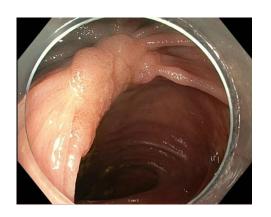




Table 3 Independent risk factors for failed endotherapy				
Feature	ture Statistical association (n=479)			
Previous intervention	OR: 3.75;)5% CI 1.77 to 7.94; p=0.001			
Ileocaecal valve involvement	OR=3.38; 95% CI 1.20 to 9.52; p=0.021			
Difficult position	OR-2 17: 95% CI 1.14 to 4.12; p=0.019			
Lesion size >40 mm	OR=4.37; 95% CI 2.43 to 7.88; p<0.001			
Previous APC use	OR=3.51; 95% CI 1.69 to 7.27; p=0.001			
APC, argon plasma coagulation.				



Complex / advanced CRC polyp

SMSA scoring system

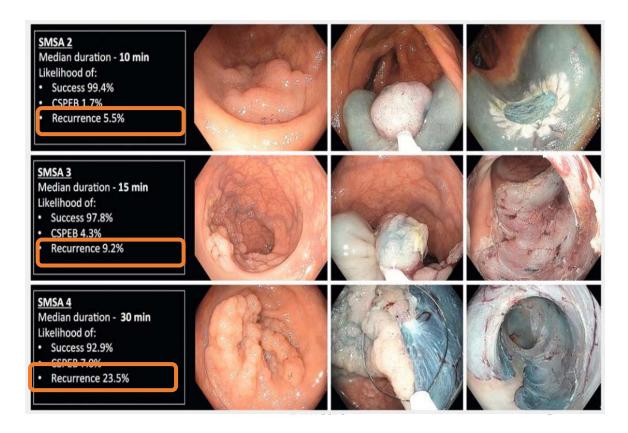


Table 3 Range of scores for each polyp level

Polyp level	Range of scores
Level I	4–5
Level II	6–8
Level III	9–12
Level IV	>12

Validation in 220 lesions >20 mm showed SMSA level 4

- Higher complication rate (8,6% vs 0%)
- Lower clearance rate (87% vs 97%)

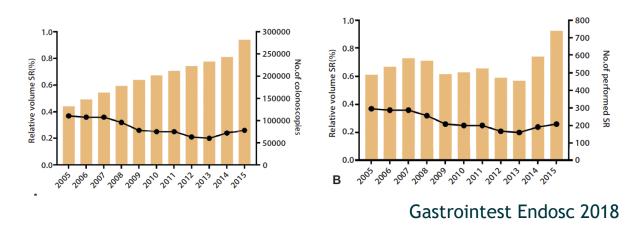


Surgery for benign polyps

Volume of surgery for benign colorectal polyps in the last 11 years

Maxime E. S. Bronzwaer, MD, ¹ Lianne Koens, MD, PhD, ² Willem A. Bemelman, MD, PhD, ³ Evelien Dekker, MD, PhD, ¹ Paul Fockens, MD, PhD¹; on behalf of the COPOS study group

- Absolute & relative volume <u>stable</u> 2005-2015:
- > 80% NO endoscopic resection
- 2,4% referral to expert center
- Mortality 1,4%
- Morbidity 35 %



The impact of the national bowel screening program in the Netherlands on detection and treatment of endoscopically unresectable benign polyps

C. C. M. Marres¹ · C. J. Buskens² · E. Schriever¹ · P. C. M. Verbeek¹ · M. W. Mundt³ · W. A. Bemelman² · A. W. H. van de Ven^{1,2}

Techniques in Coloproctology (2017) 21:887-891

After introduction of BCSP in 2014:

3X more radical resections for benign

CRC polyps

Table 3 Perioperative complications

Complications	N (%)
Perioperative death	2 (2.6)
Complication Clavien–Dindo > 3b	9 (11.8)
Complication Clavien–Dindo < 3b	16 (21.0)
Anastomotic leak	3 (3.9)
Conversion	3 (3.9)
Total	76 (100)





Polyp Advice

PANEL for complex polyps in NORTH-HOLLAND (NL)





Online tool for advice on Tx for complex CRC polyps and suspected T1 CRC cancers: www.poliepadvies.nl



Feedback within 5 working days from expert pannel (14 GI experts)

Non-pedunculated CRC polyps

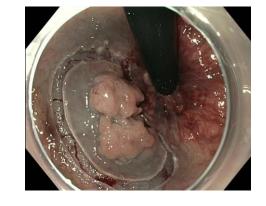


- Hot snare polypectomy
- En bloc EMR

RCT EMR vs HSP (10-25mm)

Improved R0 rates for EMR with lesion ≥ 14mm

- En bloc EMR
- Pre-cutting EMR
- Piece-meal EMR
- ESD ??



-> for lesions with high SMSA score: referral for expert endoscopist or surgeon



Colonic EMR - outcomes

- Safe
- Cheap
- Quick & easy
- Unlimited size
- Effective
 - Technical succes 90-92%
 - Avoiding surgical resection 83-92%
 - Secondary surgery indication
 - >60% submucosal invasion
 - <40% not succesfull
 - 1% complications



- Inadequate histology
 - -> problem for HGD / T1 CRC







- Recurrence 15-30% (max. 41% polyp > 4cm)
 - Endoscopic MX 93% surveillance
 - Invasive cancer at suveilance 0.3%

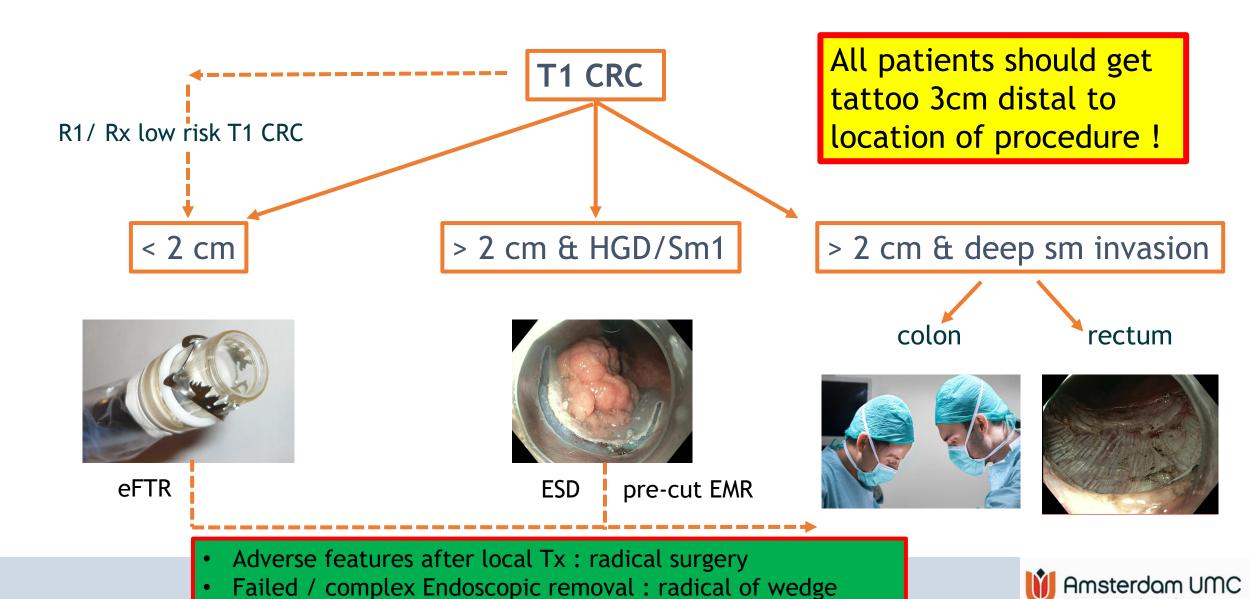




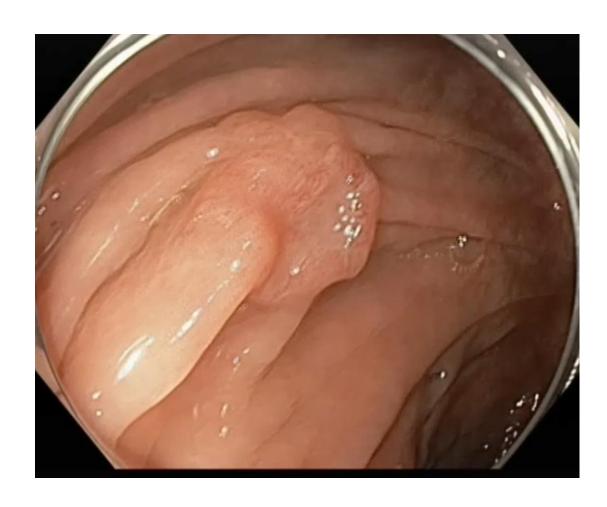
Delayed bleeding 6%

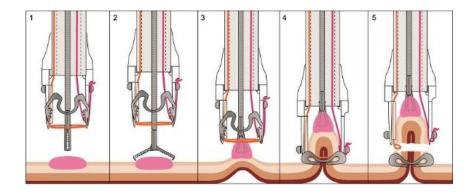


Non-pedunculated CRC polyps



eFTR for early colonic cancer











Dutch prospective eFTR registry

Prospective multicenter registry
Started august 2015
23 participating hospitals
39 certified endoscopists

700 eFTR registered procedures350 T1 CRC related

eFTR for T1 CRC is feasible and relative safe

- ✓ Technical succes: 87%
- ✓ R0 resectionm: 84% (80% for primary lesions)
- ✓ Severe adverse events : 2.2%

Delivers optimal histology/risk stratification in >98%

eFTR could change traditional TX paradigms and reduce the overuse of surgery:

- √ R0 resection in deep invasive cancers
- ✓ Completion treatment after previous Rx/R1 resection low risk T1 CRC



The right colorectal lesion for ESD

Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline

Siz

RECOMMENDATION

Update 2022

• Su

13 ESGE suggests that ESD should be considered for en bloc resection of colorectal (but particularly rectal) lesions with suspicion of limited submucosal invasion (demarcated depressed area with irregular surface pattern or a large protruding or bulky component, particularly if the lesions are larger than 20 mm), or for lesions that otherwise cannot be completely removed by snare-based techniques.

Ex

Weak recommendation, moderate quality evidence.

 $, \leq 1000$ um), based on

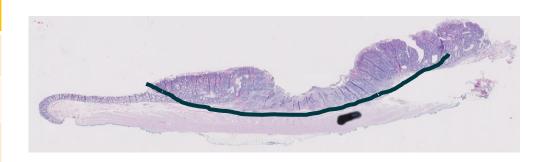
m invasion & relative safe)

Colonic ESD - outcomes

- Good histology en bloc specimen
- Larger tumours unlimited size
- T1 cancers without high risk features are cured
- Low recurrence

- Time / resource consuming
- Difficult : lack expertise outside Asia
- Higher complication rate (> 4-5cm)
- Costly
- No cure for deep Sm invasive cancer (R1)

	EMR	ESD	Pooled odds ratios (95% CI)
Duration	30 min	108 min	7.4 (6.4-8.3)
En-bloc resection	47%	92%	58.7 (36.2-79.9)
Bleeding	3.5%	2.0%	0.85 (0.45-1.6)
Perforation	1.4%	5.7%	5.0 (2.8-8.9)
Recurrence	12.2%	0.9%	0.08 (0.04-0.17)







LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF LARGE COLORECTAL TUMORS

Kinichi Hotta, Tsuneo Oyama, Tomoaki Shinohara, Yoshinori Miyata, Akiko Takahashi, Yoko Kitamura and Akihisa Tomori

Department of Gastroenterology, Saku Central Hospital, Saku, Nagano, Japan



Digestive Endoscopy (2010) 22, 302-306

80 must be carried out to acquire skill with ESD for large colorectal tumors

Lesion 2x2cm (4cm²)

48min in experienced hands!!

Lesion 3x3cm (9cm²)

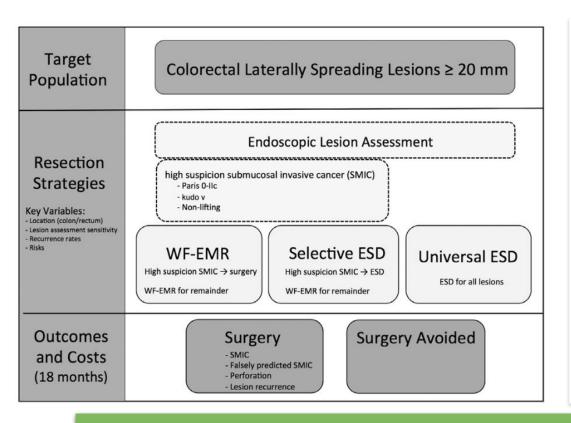
90 min in experienced hands!!

Lesion 5x5cm (4cm²)

250 min in experienced hands!!



EMR vs ESD: cost-effectiveness analysis

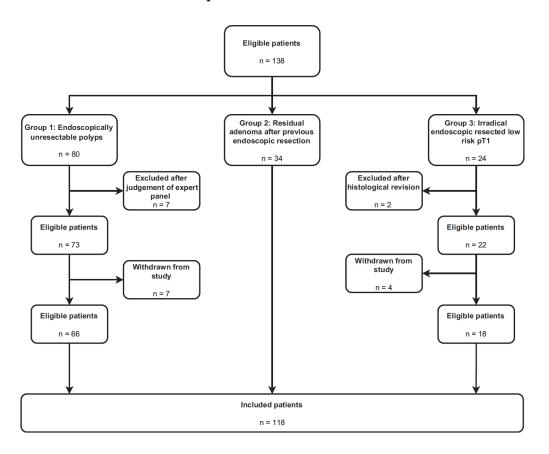


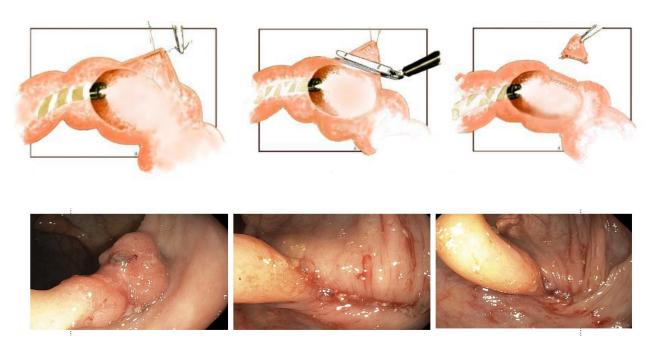
- ✓ Selective ESD prevents 19 additional surgeries per 1000 cases at slightly lower cost compared with WF-EMR.
- ✓ Universal ESD could prevent an additional 13 surgeries per 1000 cases compared with selective ESD, but at substantial increased cost.
- ✓ Expanding selective ESD criteria according to contemporary Japanese guidelines provides little additional benefit.

A universal ESD strategy in the colorectum is not justified

Colonoscopic-assisted Laparoscopic Wedge Resection for Colonic Lesions

A Prospective Multicenter Cohort Study (LIMERIC-Study)





- Multi center study (n=13): 2017-2019
- Short term safety & efficacy

Colonoscopic-assisted Laparoscopic Wedge Resection for Colonic Lesions

A Prospective Multicenter Cohort Study (LIMERIC-Study)

TABLE 2. Technical Success of Colonoscopic-Assisted Laparoscopic Wedge Resection in Patients Scheduled for CAL-WR

		I		
	Overall n = 118 (%)	Endoscopically- Unresectable Polyp n = 66 (%)	Residual Adenomatous Tissue $n = 34 (\%)$	Irradical Low Risk pT1 n = 18 (%)
Technical success	110 (93)	63 (95)	31 (91)	16 (89)
Location successful				
CAL-WR				
Caecum	50/52 (96)	35/36 (97)	14/15 (93)	1/1 (100)
Ascending colon and hepatic flexure	25/27 (93)	13/14 (93)	8/9 (89)	4/4 (100)
Transverse colon	10/11 (91)	7/7 (100)	3/4 (75)	_
Descending colon and splenic flexure	7/7 (100)	4/4 (100)	2/2 (100)	1/1 (100)
Sigmoid colon	18/21 (86)	4/5 (80)	4/4 (100)	10/12 (83)
CAL-WR not performed				
Reason:	8 (7)	3 (6)	3 (9)	2 (11)
Rectal lesion	3	1	_	2
Ingrowth in ileum*	1	_	1	_
Stenosis due to prior endoscopic resection	1	_	1	_
Suspicion of carcinoma	1	1	_	_
Lesion close to mesentery	1	_	1	_
No tension on suture possible	1	1	_	_
Converted into:				
TAMIS	2	1	_	1
eFTR	1	_	_	1
LEAWR with acceptance of irradicality	1	_	1	_
Right-sided hemicolectomy	4	2	2	_

^{*}CAL-WR was performed with acceptance of irradicality.

- Radical resection rate: 91%
- 12 patients completion radical colectomy
- Recurrence 5% (adenoma) 6 months endoscopy

TABLE 3. Clinical Outcome CAL-WR	
	$n = 110 \ (\%)$
Overall complications	7 (6)
Minor complications (CDG I-II)	7 (6)
Urinary retention	2
Urinary tract infection	1
Surgical site infection	1
Readmission due to pain	1
Opioid intoxication	1
Paralytic ileus	1
Major complications (CDG III-IV)	_
Median length of stay (range), d	2 (1-5)
Median operating time (range), min	58 (20-138)

CDG indicates Clavien Dindo Grade of complications.

- Benign pathology 69% (n=76)
- Invasive cancer: 20% (n=22)
 - pT1: n=13
 - pT2: n=7
 - pT3: n=3
- No residual cancer: 11% (n=12)

CAL-WR indicates colonoscopic-assisted laparoscopic wedge resection; eFTR, endoscopic full-thickness resection; TAMIS, transanal minimally invasive surgery.



Curative local Tx of T1 CRC depends on:

Radicality → en bloc R0 resection

- Absence of high risk features:
 - ✓ Deep submucosal invasion (i.e. ≥ 1000um, meaning Sm2-3 or Haggitt 4)
 - ✓ Lymphovascular invasion
 - ✓ Poor tumor-differentiation
 - ✓ Intense tumor budding (grade 2-3)

Let's RE-evaluate depth of invasion





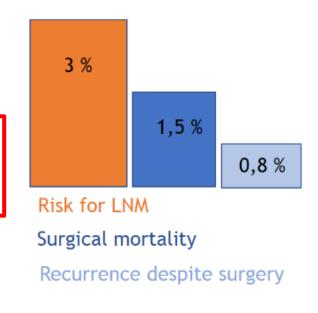
Sm invasion depth is a weak predictor for LNM

Risk of LNM if <u>only deep sm invasion</u> is present is <u>1 - 3 % ¹⁻⁵</u>

Study, year		N	Risk for LNM	
Suh	2012	118	2 (1,7 %)	
Nakadoi	2012	249	3 (1,2 %)	

Warning! Precise pathologic evaluation required !!!

Yasue	2019	258	4 (1,6 %)



⁴Oka et al, Dig Endoscopy 2013

¹ Suh et al, Endoscopy 2012

³ Nakadoi et al, J Gastroenterol Hepatol 2012

² Kim et al, Medicine 2016

Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis

Liselotte W. Zwager,^{1,2} Barbara A. J. Bastiaansen,^{1,2} Nahid S. M. Montazeri,³ Roel Hompes,⁴ Valeria Barresi,⁵ Katsuro Ichimasa,⁶ Hiroshi Kawachi,⁷ Isidro Machado,⁸ Tadahiko Masaki,⁹ Weiqi Sheng,¹⁰ Shinji Tanaka,¹¹ Kazutomo Togashi,¹² Chihiro Yasue,¹³ Paul Fockens,^{1,2} Leon M. G. Moons,¹⁴ and Evelien Dekker^{1,2}

Deep submucosal invasion is not an independent risk factor for lymph node metastasis in

T1 colorectal cancer: a meta-analysis

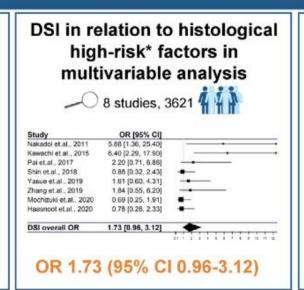
DSI in relation to LNM in univariable analysis 67 studies

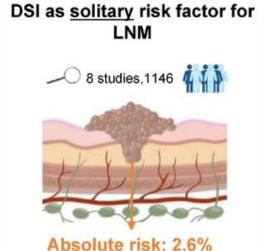
or studies

21,238 patients

Overall LNM-rate: 11.2%

OR 2.58 (95% CI 2.10-3.18)





DSI should be reconsidered as strong indicator for oncologic surgery

DSI (deep submucosal invasion); LNM (lymph node metastasis); OR (odds ratio). *poor differentiation grade, lymphovascular invasion and high-grade tumor budding Gastroenterology





Curative local Tx of T1 CRC depends on:

Radicality → en bloc R0 resection

- Absence of high risk features:
 - ✓ Deep submucosal invasion (i.e. ≥ 1000um, meaning Sm2-3 or Haggitt 4)
 - ✓ Lymphovascular invasion
 - ✓ Poor tumor-differentiation
 - ✓ Intense tumor budding (grade 2-3)

Conclusions

- Structural lesion assesment key for appropriate technique selection
 - Pedunculated vs NP CRC polyps
 - LST: plane of resection dependent on depth of invasion (EMR-ESD-eFTR-Surgery)
- Consider referral before considering surgery in complex benign lesions of T1 CRC
- Hybrid / Primary surgery: Endoscopic unresectable CRC polyps or deep sm invasion > 2cm
- Completion surgery in high risk T1 CRC (shared decision)







Thank you

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Conclusions

- Diminutive and small polyps: cold snare!
- Large stalked polyps (> 2 cm head, > 5mm stalk): hot snare after pretreatment of stalk, consider mechanically close defect when only adrenaline was used (1:10.000).
- Adequate lesion assessment for every LST: size, morphology, site, access
- Consider referral to experiencied center before considering surgery in complex benign lesions
- Routine clip closure post EMR is not recommended but can be considered in high risk cases
- Don't scope immediately in delayed bleeds that can be resuscitated, most bleedings settle spontaneously

11th IGILUC - Cairo, Egypt | July 2022

Recognize signs for imminent perforation ("target") and turn complication completely







Dilemma in T1 CRC...

Endoscopy

Vs

Surgery

- ✓ Locoregional recurrence
- ✓ Lymphatic spread
- ✓ Cancer related death



- ✓ Morbidity
- ✓ Mortality
- √ Functional loss

~ 90% overtreated with surgery!



THE OTHER WAY

THAT WAY



POLIEP

ADVIES

PANEL VOOR COMPLEXE POLIEPEN IN NOORD-HOLLAND





Online tool voor advies t.a.v. behandeling complexe poliepen vroegcarcinomen via www.poliepadvies.nl

Feedback binnen 5 werkdagen vanuit panel bestaande uit 14 L- artsen regio Noord-Holland & Flevoland

- Voor meer informatie:
- www.poliepadvies.nl

poliepadvies@amsterdamumc.nl



Dilemma in T1 CRC...

Endoscopy

Vs

Surgery

- ✓ Locoregional recurrence
- ✓ Lymphatic spread
- ✓ Cancer related death



- ✓ Morbidity
- ✓ Mortality
- √ Functional loss

~ 90% overtreated with surgery!





Key messages



Conclusions



Minimal invasive approach could be the first step

 Additional lymph node resection in selected cases (adjuvant therapy)

 Perhaps the focus should be on full thickness resection techniques (instead of submucosal dissection)



En bloc or not..? Rectum is different!

Colon



Rectum

- > 90% EMR
- Some ESD (superficial cancer only)...

A B C C

- Very low threshold ESD
 - Favourable risk-benefit
- Some EMR

Some eFTR (small T1 CRC etc)



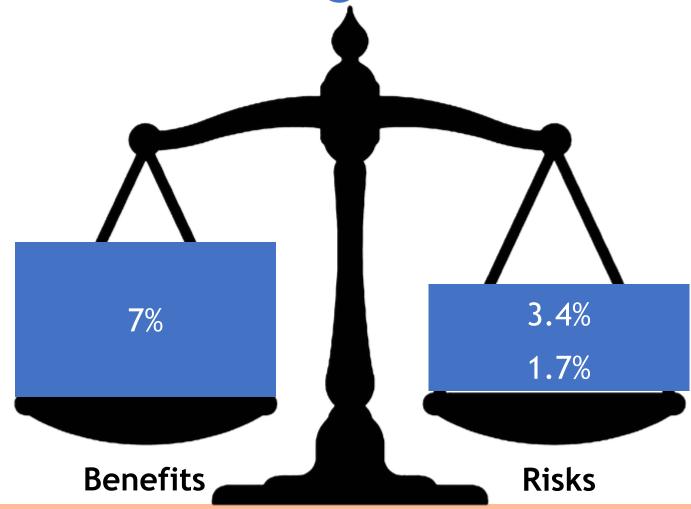












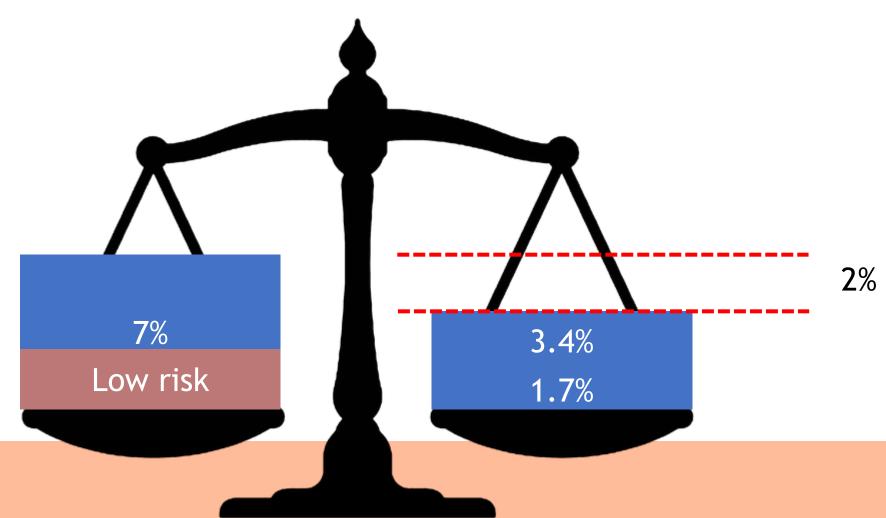
Surgery related mortality for TV CRCs is not lower than more advanced CRCs

Mortality of surgery T1 CRC was 1.7% in 5170 patiënts

Type of operation	Wo	men	Men		
Right colectomy*	6.1 (5.5-6.7)	10.0 (8.7-11.4)	8.7 (7.9-9.4)	16.7 (15.0-18.3)	
	N=6371	N=2075	N=5124	N=2093	
Left colectomy	8.8 (7.2-10.4)	15.9 (11.9-20.1)	11.5 (9.9-13.3)	18.8 (15.3-22.3)	
	N=1062	N=308	N=1345	N=484	
Sigmoid resection	5.0 (4.3-5.7)	11.7 (9.4-14.1)	8.3 (7.6-9.0)	13.9 (12.1-15.6)	
	N=3699	N=725	N=5387	N=1516	
LAR	6.3 (4.7-7.8)	9.5 (5.6-13.5)	15.0 (13.1-16.8)	22.7 (18.8-27.1)	
	N=891	N=201	N=1371	N=396	
APR	5.3 (2.0-8.7)	12.5 (2.9-24.4)	9.1 (6.3-12.5)	22.3 (14.9-30.0)	
	N=170	N=40	N=340	N=112	
	1 - 2	3 - 4	1 - 2	3 - 4	
	ASA				

What is the clinical benefit of adjuvant surgery







T1 Colorectaal carcinoom- vroege darmkanker

Randvoorwaarden:

- Lage kans op incomplete resectie
- Controle over de diepte van de resectie



Flowchart

T1 CRC



gesteeld

Always endoscopic resection

Histology

- Tumor budding poorly differentiated clusters
- Lymfangioinvasion
- Status of the m. Mucosae
- Haggitt-level 4

Niet-gesteeld

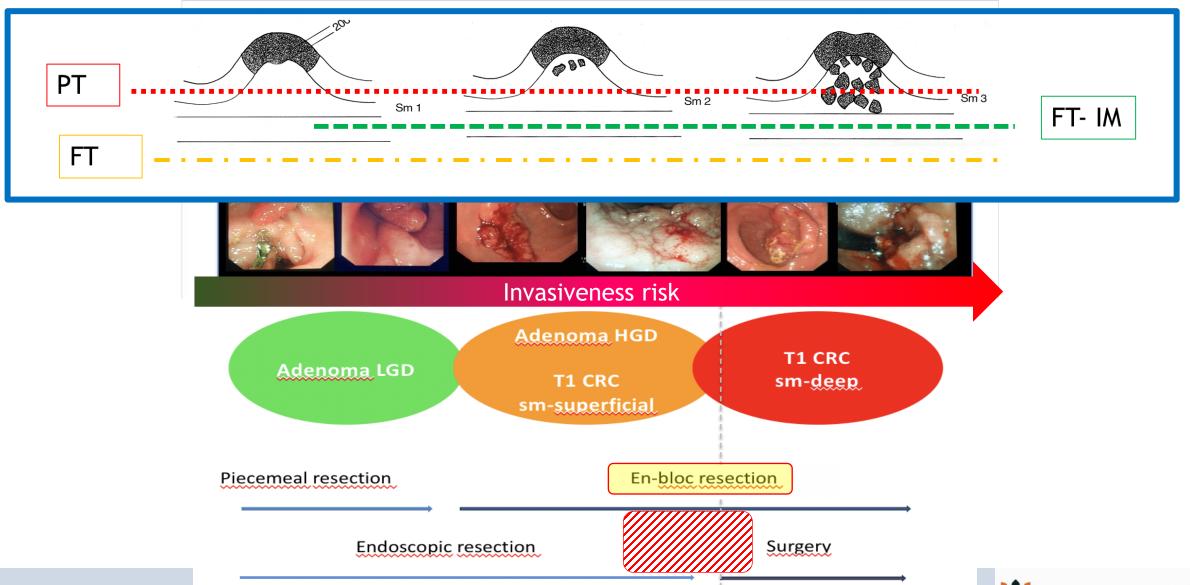
Minimaal invasive:

- Signs of superficial invasion
- Deep invasion but size < 15-20 mm

Histology

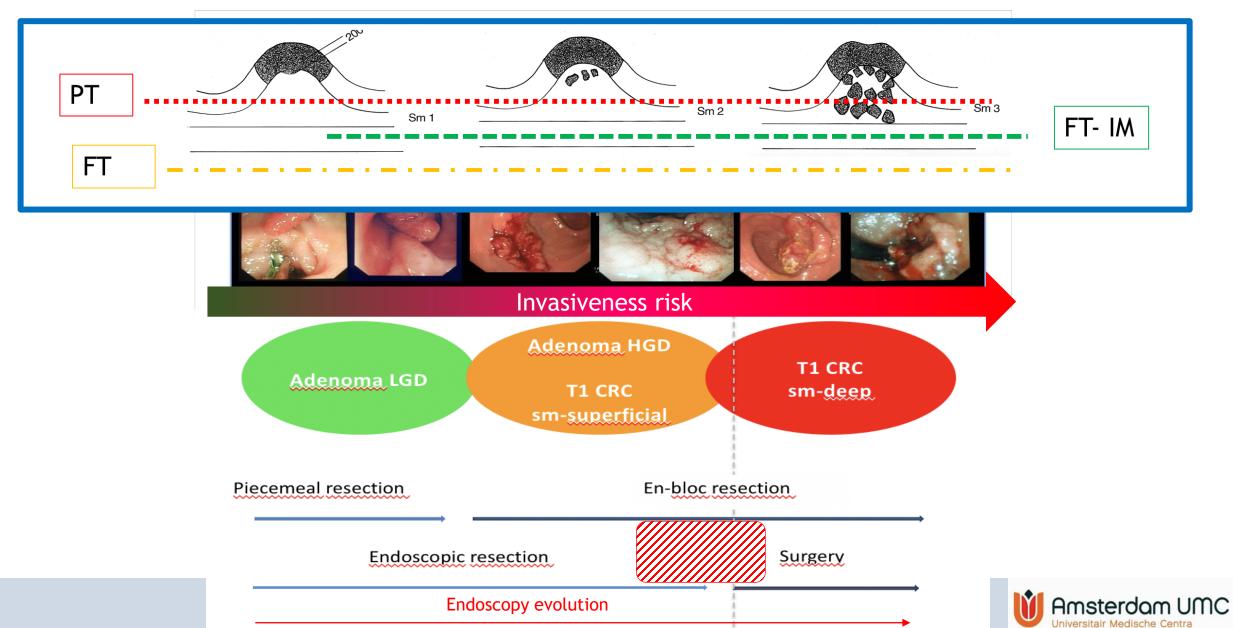
- Tumor budding/poorly differentiated clusters
- Lymfangioinvasion (MMP-7)
- Status of the m. propria
- ?? Molecular markers (immunoscore, CMS other)

Spectrum of interventions for very ERC

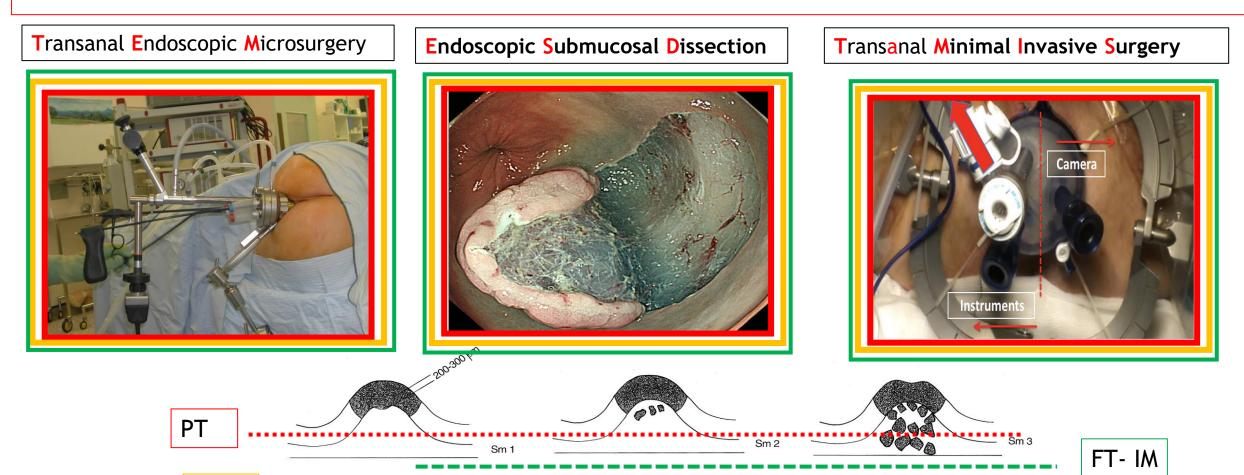




Spectrum of interventions for very ERC



Which Technique - Gl vs Surgeon





FT

Diagnostic accuracy of endoscopic evaluation

Conventional findings with chromoendoscopy

(0.2% indigo carmine)

→ Accuracy: 70-80%

Magnifying endoscopy with crystal violet staining

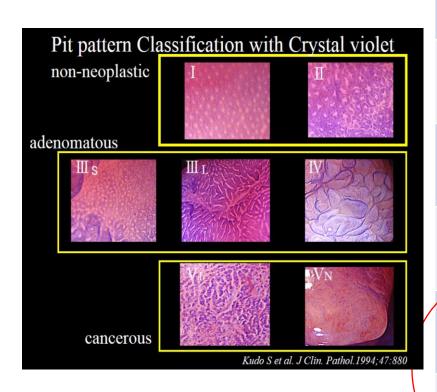
(0.05% crystal violet)

→ Accuracy: 83-94%

Narrow Band Imaging

→ Accuracy: 75-91%





Pit pattern	Adenoma((dysplasia)	Car	Cancer		
	Low grade	High grade	Tis	T 1		
IIIs	69 (58.9%)	16 (13.7%)	30 (25.6%)	2 (1.7%)	117	
III _L	8,232 (83.4%)	1,126 (11.3%)	533 (5.3%)	0 (0.0%)	9,982	
IV	1,456 (47.4%)	768 (25.0%)	738 (24.0%)	108 (3.5%)	3,070	
V	90 (8.1%)	117 (10.5%)	504 (45.1%)	406 (36.3%)	1,117	
V _N	0 (0.0%)	0 (0.0%)	16 (5.2%)	292 (94.8%)	308	

OPTICAL STUDY

LASSO-derived predicted probability of T1 CRC



				Proximal location			Distal location					
	WL		/L	Homogeneous granular	Granular with large nodule	Granular with non-granular erythematous area	Non-granular		Homogeneous granular	Granular with large nodule	Granular with non-granular erythematous area	Non- granular
		Bleeding	Depression -	3.4	4.5	5.5	6.9		4.4	5.8	7.0	8.7
	Even vessels	-	Depression +	3.6	4.7	5.7	7.1		4.6	6.0	7.2	9.0
	(NBI)	Bleeding	Depression -	6.5	8.5	10.2	12.6		8.3	10.7	12.8	15.7
		+	Depression +	6.7	8.7	10.5	12.9		8.6	11.0	13.2	16.2
		Bleeding	Depression -	10.7	13.7	16.2	19.7		13.4	17.0	20.1	24.2
NBI	Irregular vessels	-	Depression +	11.0	14.1	16.7	20.3		13.8	17.5	20.7	24.8
וטו	(NBI)	Bleeding	Depression -	18.9	23.6	27.5	32.5		23.2	28.6	32.9	38.4
		+	Depression +	19.4	24.2	28.2	33.2		23.8	29.3	33.7	39.2
		Bleeding	Depression -	26.9	32.8	37.4	43.1		32.3	38.8	43.7	49.6
	Absent	-	Depression +	27.6	33.6	38.2	44.0		33.1	39.6	44.5	50.5
	vessels (NBI)	Bleeding	Depression -	41.8	48.8	53.9	59.7		48.2	55.3	60.2	65.8
		+	Depression	42.7	49.7	54.7	60.5		49.1	56.1	61.1	66.6

Numbers indicate the LASSO derived predicted probability (%) of T1 CRC within a LNPCP Bleeding indicates spontaneous bleeding. – indicates absence; + indicates presence

Note: all regression coefficients, lasso-derived multivariate odds ratios, the intercept and 5-fold cross validation area under-the-curve of the score-chart can be found in the Supplementary Material.

The absolute risk for T1 CRC within a LNPCP was calculated using the formula $P = (1/[1 + exp(-1 * (\beta_0 + \beta_1 X_1 + \beta_2 X_2 + ... + \beta_k X_k))]) * 100$, in which β_0 is the intercept, and β_k is the regression coefficient for predictor X_k (the different endoscopic features that contributed to the differentiation of T1 CRCs from non-invasive polyps in LASSO regression-analysis). For example, the risk of T1 CRC in a non-granular LNPCP (regression coefficient: 0.24) located in the distal colon (regression coefficient: 0.26) without spontaneous bleeding or depression, and on NBI-assessment an even vessel pattern and distribution (regression coefficient: -1.21) is (1/[1 + exp(-1 * (-1.64 + (0.26 - 1.21 + 0.24)]) * 100 = 8.7%.

AUC: 0.85 - Validation set (100 LNPCP - AUC 0.81)

Sensitivity 78.7% - Specificity 94.2%

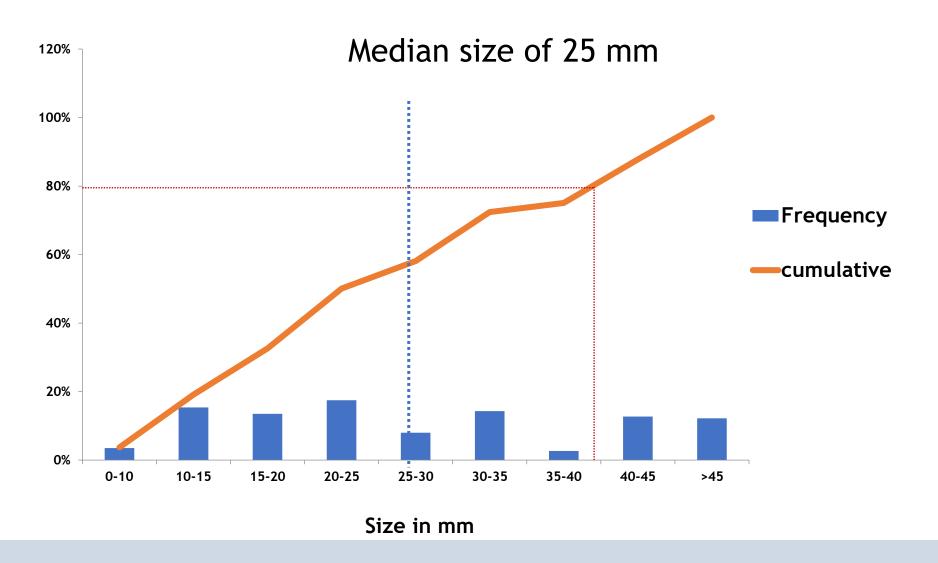


Some "important" T1 colonca cinoma Facts

- T1 CRCs are increasingly detected with the introduction of FIT based bowel cancer screening
- 75% of all T1 CRCs are located in the colon
- 47% of the colon T1 CRCs are pedunculated
- Median size of the T1 coloncarcinoma is 25 mm



Size of the T1 CRCs in the New erlands











Endoscopic recognition of T1 CRC in practi

Suboptimal endoscopic cancer recognition in colorectal lesions in a national bowel screening programme

Vleugels JLA, et al. Gut 2019



- 3622 screening colonoscopies, 274 CRC of which 91 T1 CRC
- 61% misdiagnosed as cancer
- > 30% piecemeal resections
- Leading to overuse of surgery: 41 % vs 11% (in correct recognized cancers)





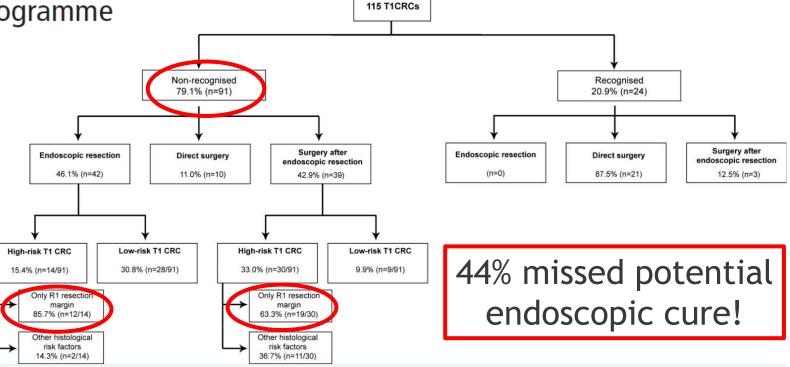






LETTER

Optical diagnosis of T1 CRCs and treatment consequences in the Dutch CRC screening programme Gut Month 2020 Vol 0 No 0



Lonne W T Meulen, Gut 2020











Shared decision...



Surgery related mortality for J1 CRCs is not lower than for more advanced CRCs

Mortality of surgery in T1 CRC patients was 1.7% in 5170 patients

Type of operation	Wo	men	Men		
Right colectomy*	6.1 (5.5-6.7)	10.0 (8.7-11.4)	8.7 (7.9-9.4)	16.7 (15.0-18.3)	
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Left colectomy	8.8 (7.2-10.4)	15.9 (11.9-20.1)	11.5 (9.9-13.3)	18.8 (15.3-22.3)	
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LAR	6.3 (4.7-7.8)	9.5 (5.6-13.5)	15.0 (13.1-16.8)	22.7 (18.8-27.1)	
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APR	5.3 (2.0-8.7)	12.5 (2.9-24.4)	9.1 (6.3-12.5)	22.3 (14.9-30.0)	
	N=170	N=40	N=340	N=112	
	1 - 2	3 - 4	1 - 2	3 - 4	
	ASA				

Colon surgery is associated with same mortality rate as for rectal cancer



	Colon (N=10184)	Rectum (N=4906)
Any Complication	2760(27%)	1775 (37%)
Severe complication	1863 (18%)	1218 (25%)
Post-operative mortality	347 (2.1%)	114 (1.7%)
Reintervention	1075 (11%)	687 (14%)
ICU-admission > 14 days	138 (1.4%)	53 (1.1%)

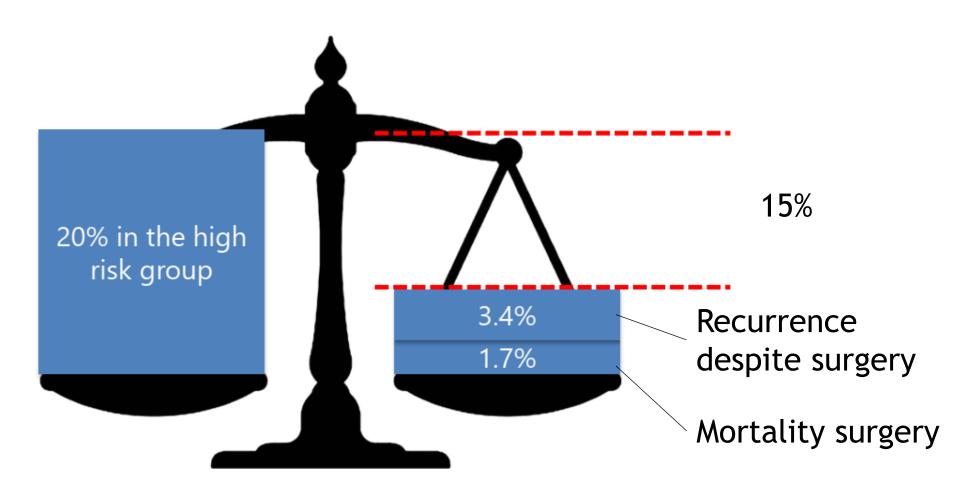


Pedunculated morphology is associated with a lower risk of adverse outcome



Oncological Outcome	OR (95% CI)	P value
Adverse Outcome 222/1656 events (13.4%) T1 CRCs	0.49 (0.35-0.69)	<0.001
Metastasis 141/1656 events (8.5%) T1 CRCs	0.48 (0.32-0.72)	<0.001
Incomplete resection 108/1656 events (6.5%) T1 CRCs	0.54 (0.34-0.85)	0.008
Recurrence 90/1656 events (5.4%) T1 CRCs	0.61 (0.38-0.99)	0.05

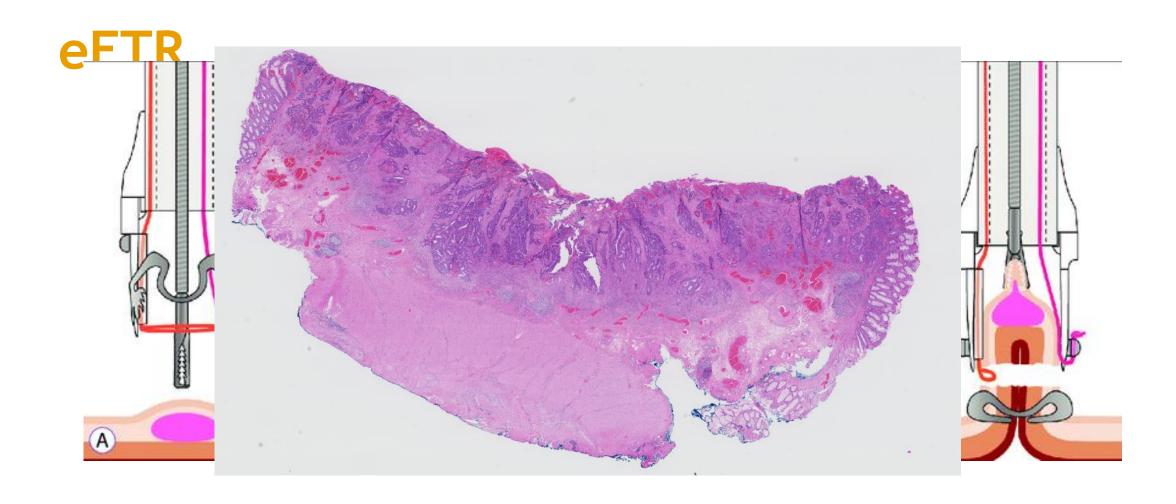
Risk-benefit in high risk tonpedunculated T1 CRCs



Potential techniques for Wocal excision

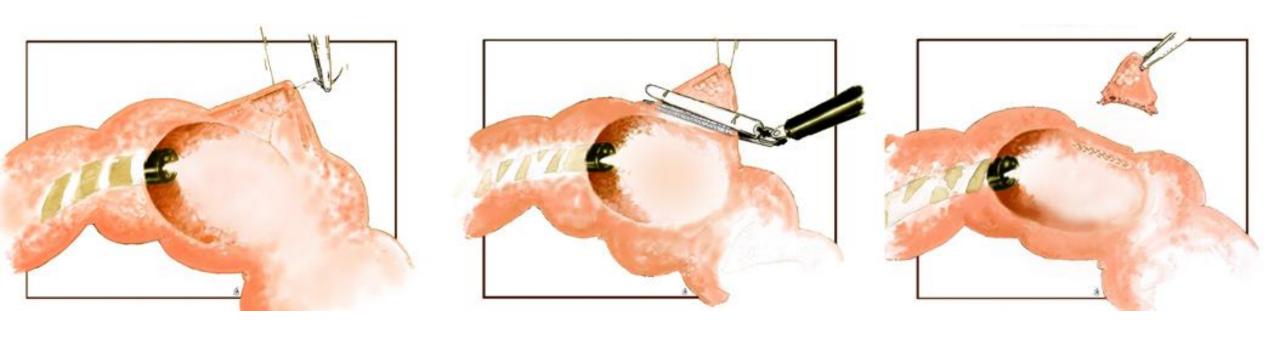
- Endoscopic submucosal Dissection
- Endoscopic Full Thickness Resection (eFTR)
- Endoscopy assisted laparoscopic wedge excision





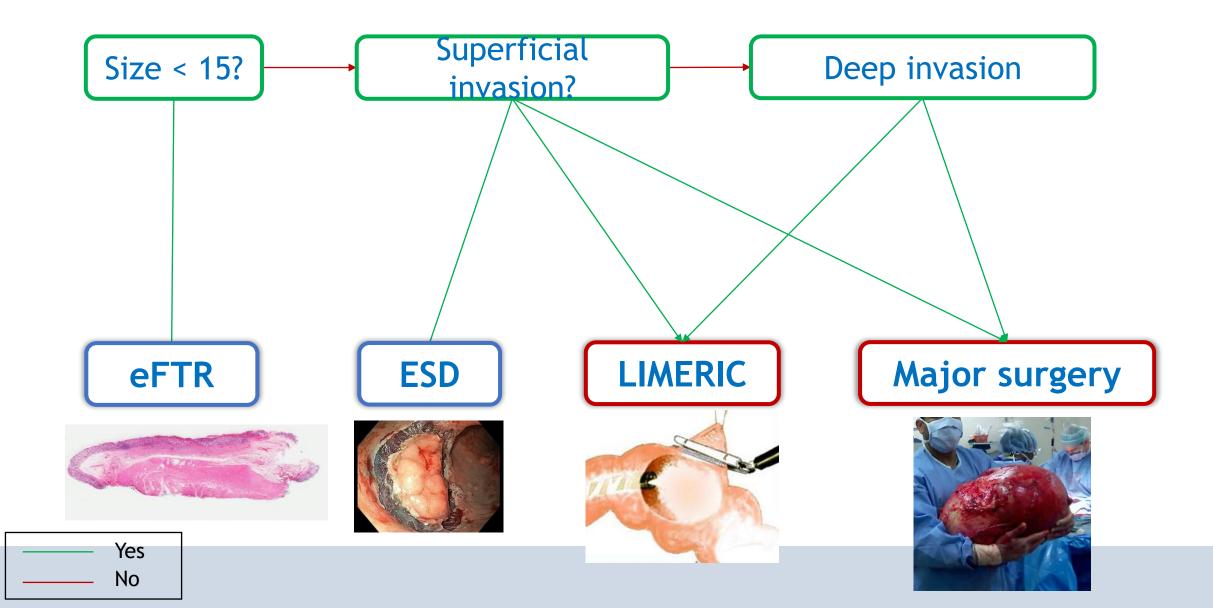


Limited laparoscopic wedge excision



Potential Algorithm





Significant colorectal neoplasia - ideal intervention-

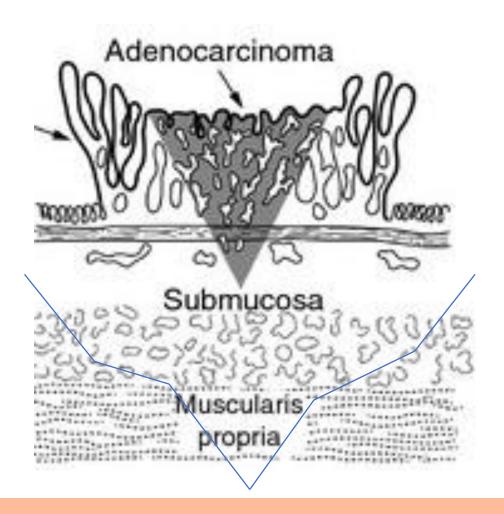


- Most effective
- Least invasive
- Lowest inconvenience
- Lowest risks
- Lowest costs and use of resources



Endoscopic Treatment of geep submucosal invasive carcinoma





H&E slide of the specimen



<u>Pathology</u>

- T1Sm3
- Lateral resection margin free
- Vertical resection margin free
- No tumor budding
- No lymphovascular invasion
- Moderate differentation

Conclusions



Minimal invasive approach could be the first step

 Additional lymph node resection in selected cases (adjuvant therapy)

 Perhaps the focus should be on full thickness resection techniques (instead of submucosal dissection)



Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team

EMR	ESD	Surgery
		5

	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	· Invisible • 1	• Regular caliber • Regular distribution (meshed/spiral pattern) • 2	Variable caliber Irregular distribution	· Loose vessel areas · Interruption of thick vessels
Surface pattern	Regular dark or white spots Similar to surrounding normal mucosa	• Regular (tubular/branched/papillary)	· Irregular or obscure	• Amorphous areas
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low grade intramucosal neoplasia	High grade intramucosal neoplasia/ Shallow submucosal invasive cancer *3	Deep submucosal invasive cancer
Endoscopic image				





Endoscopy



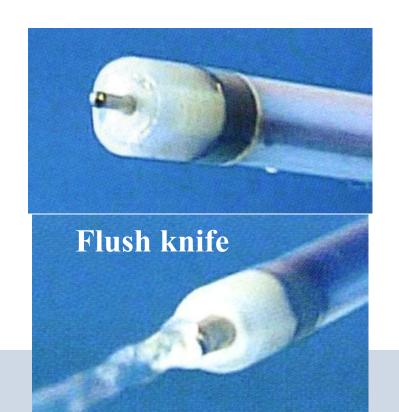






Endoscopic Submucosal Dissection (ESD)



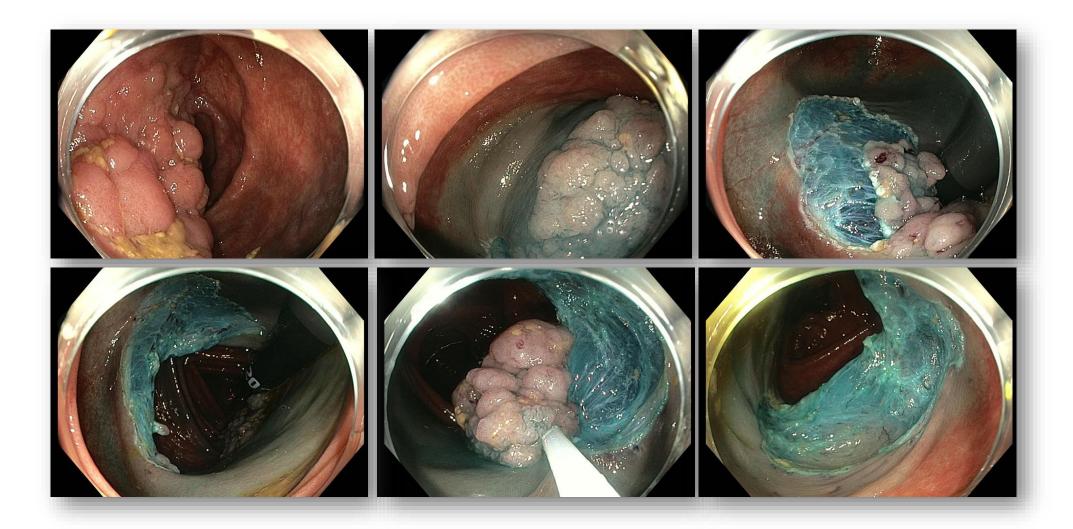






Needle knife

Colonic pEMR





Endoscopic recognition is important!



Optical diagnosis

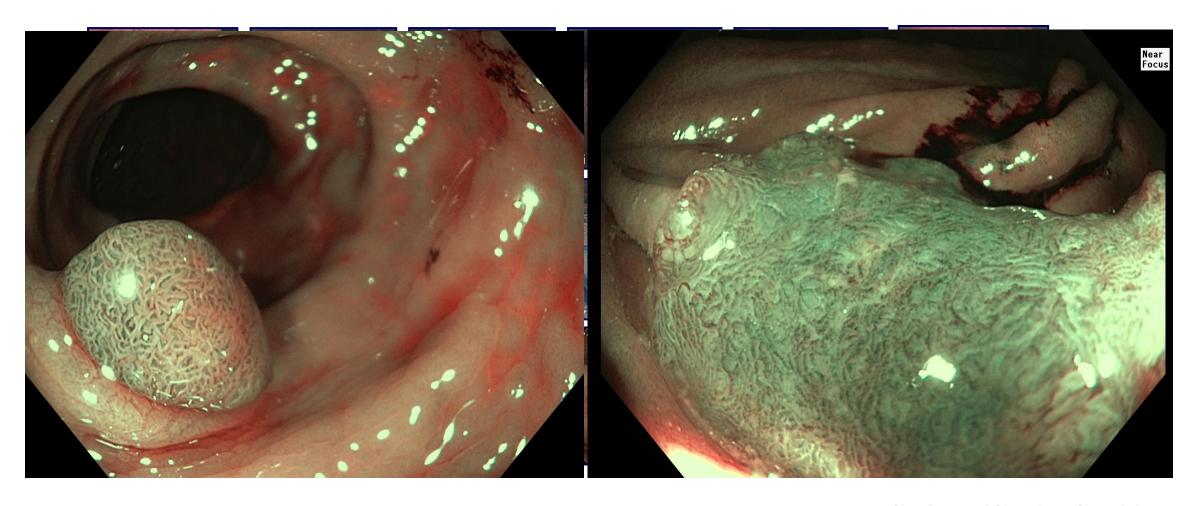
- Image enhancement:
 - Chromoendoscopy
 - "Virtual chromo": NBI/BLI/LCI/iScan

Near focus/magnification





Kudo pit pattern classification



Kudo S, J Clin Path 1994 Kudo S, Endoscopy 2001



NICE

NBI International Colorectal Endoscopic (NICE) Classification*

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels coursing across the lesion	Brown vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface Pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular or branched white structure surrounded by brown vessels**	Amorphous or absent surface pattern
Most likely pathology	Hyperplastic	Adenoma***	Deep submucosal invasive cancer
Examples			

^{*} Can be applied using colonoscopes with or without optical (zoom) magnification

^{**} These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.

^{***} Type 2 consists of Vienna classification types 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area).

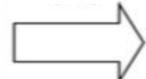


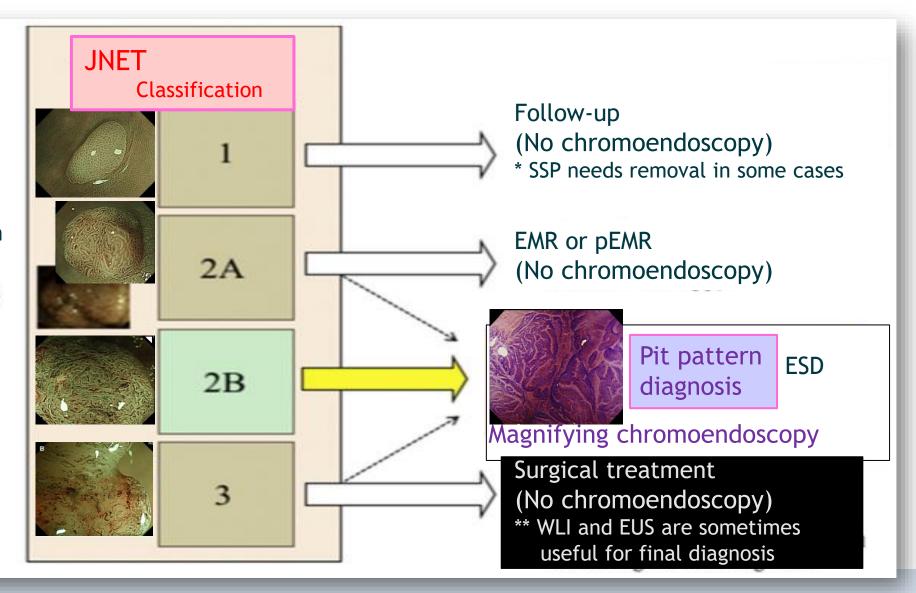
JNET

Detection



NBI magnification







Japanese NBI Expert Team (JNET)

Japanese NBI Expert Team (JNET) classification

NBI	Type 1	Type 2A	Type 2B	Type 3 *Loose vessel areas *Interruption of thick vessels	
Vessel pattern	· Invisible ^{#1}	•Regular caliber •Regular distribution #2 (meshed/spiral pattern)	Variable caliber Irregular distribution		
Surface pattern	•Regular dark or white spots •Similar to surrounding normal mucosa	•Regular (tubular/branched/papillary)	•Irregular or obscure	Amorphous areas	
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low-grade intramucosal neoplasia	High-grade intramucosal neoplasia/ Superficial 63 submucosal invasive cancer	Deep submucosal invasive cancer	
Examples					

- *1. If visible, the caliber in the lesion is similar to surrounding normal mucosa.
- *2. Microvessels are often distributed in a punctate pattern and well-ordered reticular or spiral vessels may not be observed in depressed lesions.
- *3. Deep submucosal invasive cancer may be included.
- *4. Low-grade intramucosal neoplasia: low-grade dysplasia.
- *5. High-grade intramucosal neoplasia: high-grade dysplasia.



TABLE 3. Performance characteristics of each type of the JNET classification®

JNET classification	Sensitivity	Specificity	PPV	NPV	Accuracy
Type 1	87.5 (81.9-93.1)	99.9 (99.8-100.0)	97.5 (94.8-100.3)	99.4 (99.1-99.7)	99.3 (99.0-99.6)
Type 2A	74.3 (72.6-76.0)	92.7 (90.2-95.1)	98.3 (97.7-98.9)	38.7 (35.7-41.6)	77.1 (75.5-78.6)
Type 2B	61.9 (58.1-65.6)	82.8 (81.2-84.3)	50.9 (47.5-54.4)	88.2 (86.9-89.6)	78.1 (76.6-79.6)
Type 3	55.4 (48.7-62.1)	99.8 (99.6-100.0)	95.2 (91.4-98.9)	96.6 (95.9-97.3)	96.6 (95.9-97.2)

[&]quot;Values are percents with 95% confidence interval in parentheses.

Positive predictive value type 2A (LGD) 98% But in type IIB (HGD/Sm1) only 51%

Risk of Occult Submucosal Invasive Cancer (SMIC) According to Gross Morphology and Location n = 1712



A tipical proximally located 0-fla Granular Lesion. Overall risk of SMIC 0.7%

SMIC risk by Paris Type Alone 2.1% SMIC risk by Surface Morphology Alone 3.5%

0-IIa G

SMIC Risk 0.8%

Proximal 0.7% Very Low Risk

Distal 1.2% Low Risk



SMIC risk by Paris Type Alone 2.1% SMIC risk by Surface Morphology Alone 8.1%

SMIC Risk 4.2%

Proximal 3.8%

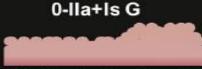
Distal 6.4%



A proximal 0-la Non-Granular Lesion. Overall risk of SMIC 3.8%



A rectal (distal) 0-lla+ls Granular Leson Overallrisk of SMIC 10.1%

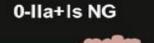


SMIC risk by Paris Type Alone 8.4% SMIC risk by Surface Morphology Alone 3.5%

SMIC Risk 7.1%

Proximal 4.2%

Distal 10.1%



SMIC risk by Paris Type Alone 8.4% SMIC risk by Surface Morphology Alone 8.1%

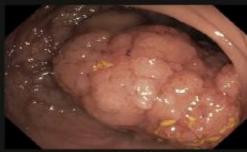
SMIC Risk 14.1%

Proximal 12.7%

Distal 15.9%



A transpersection (proximal) 0-lla-lls Non-Granular Lesion Overall risk of SMIC 12.7%



A sigmoid colon (distal) 0-is Granular Lesion Overall risk of SMIC 5.7%



SMIC risk by Paris Type Alone 6.0% SMIC risk by Surface Morphology Alone 3.5%

SMIC Risk 3.1%

Proximal 2.3% Low Risk

Distal 5.7%

0-Is NG

SMIC risk by Paris Type Alone 6.0% SMIC risk by Surface Morphology Alone 8.1%

SMIC Risk 15.3%

Proximal 12.3% High Risk

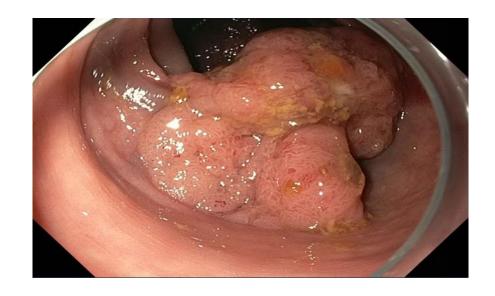
Distal 21.4%

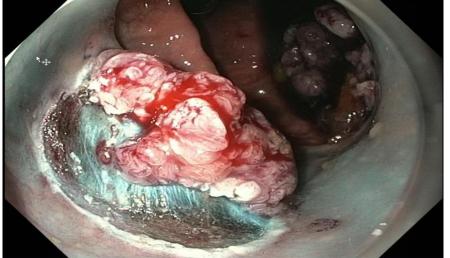


An ascending solon (proximal) 0-is Non-Granular Lesion. Overall risk of SMIC 12.3%

Unexpected cancers in LSTs

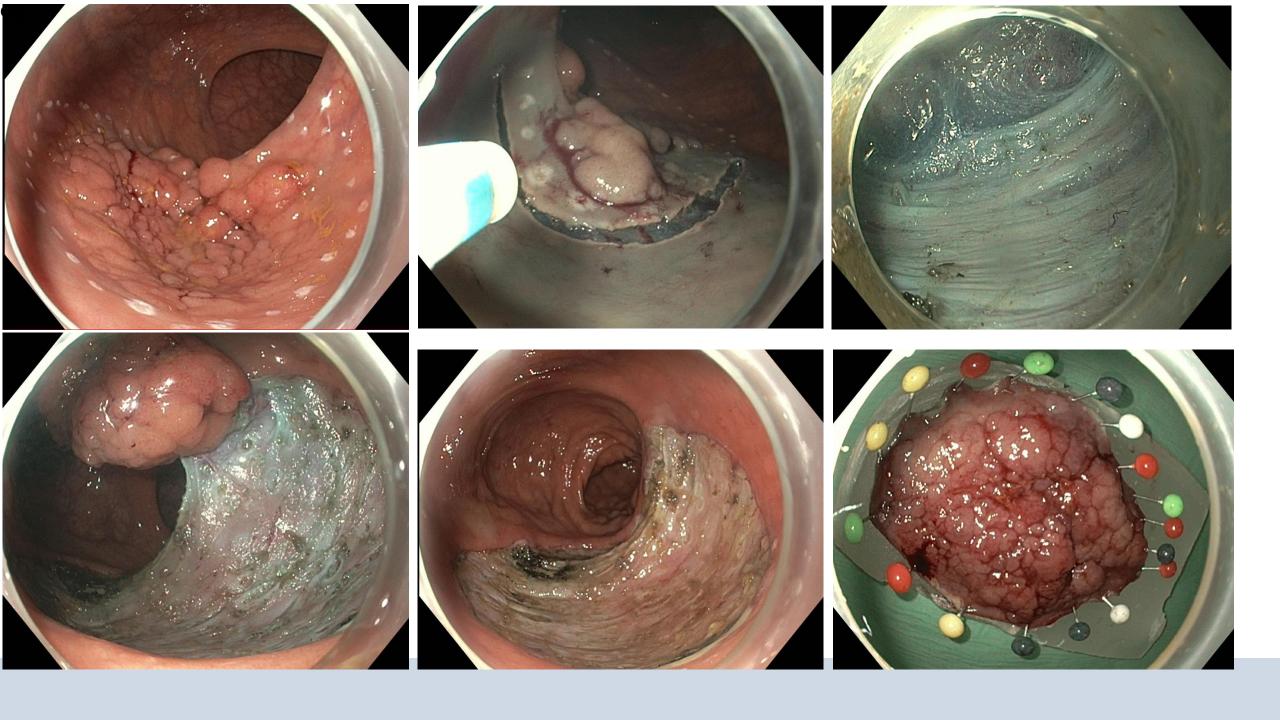
In total 13% (27/204) of rectal LSTs incorrectly diagnosed as benign but turned out to be cancer...





Colonic ESD







ESD in expert hands already in 2010...

- 1111 tumors: 356 tubular adenomas, 519 intramucosal cancers (HGD), 112 superficial submucosal (SM) cancers, 101 SM deep cancers, 18 carcinoids, 1 MALT lymphoma, 4 serrated lesions
- En-bloc and curative resection rates: 88% and 89%
- Mean procedural time 116 ±88 min mean size of 35 ±18 mm
- Perforations in 54 cases (4.9%) & postoperative bleeding in 17 (1.5%)



	First study period (10/2004–07/2013) Resections 1–125	Second study period (07/2013-03/2016) Resections 126-250	P value
Diameter, median (range), mm	40 (18 – 120)	45 (20 – 115)	0.086
En bloc resection, n (%)	94 (75.2%)	114 (91.2%)	0.001
R0 or R1 resection			< 0.001
R0	69 (55.2%)	106 (84.8%)	
R1	56 (44.8%)	19 (15.2%)	
Recurrence, n (%)	8 (6.4%)	4 (3.2%)	0.375
	(95%CI 3.2% – 12.1%)	(95%CI 1.3%-7.9%)	
After en bloc ESD	1/94 (1.1%)	0/114	
After piecemeal resection	7/31 (22.6%)	4/11 (36.4%)	
Complications, n (%)			
Bleeding	10 (8 %)	3 (2.4%)	0.087
Transmural perforation	1 (0.8%)	1 (0.8%)	1.0

Probst Endoscopy 2017



Indications ESD

- 1) Optical diagnosis is carcinoma with <1000 µm submucosal invasion
 - Diagnosis not very accurate based on optical diagnosis and morphology
 - -> what is acceptable risk to perform ESD?? 5%? 10%?
 - -> or all rectal lesions and all other lesions with "suspicion T1"?
- 1) Recurrence/fibrosis etc: technical reasons



(Relative) contra-indications for ESD

- 1) Suspicion of deep invasive cancer
- 2) Very large lesions??



Size of lesion

- >5cm: more complications (OR 2.1; 95% CI 1.1-3.4; *P* .0198)¹
- Severe submucosal fibrosis is significant risk factor for non-curative resection and long procedural time. Tumor size and morphology might help to predict the severity of fibrosis.



LEARNING CURVE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF LARGE COLORECTAL TUMORS

Digestive Endoscopy (2010) 22, 302-306

Kinichi Hotta, Tsuneo Oyama, Tomoaki Shinohara, Yoshinori Miyata, Akiko Takahashi, Yoko Kitamura and Akihisa Tomori

Department of Gastroenterology, Saku Central Hospital, Saku, Nagano, Japan

Background and Aim: No studies have previously described the learning curve for colonic endoscopic submucosal dissection (ESD). The aim of the present study was to describe the learning curve for ESD of large colorectal tumors based on a single colonoscopist's experience.

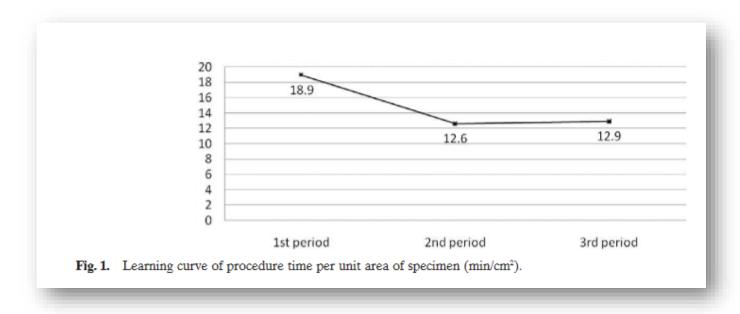
Methods: ESD was carried out for 120 colorectal tumors in 115 patients (68 males, median age 70 years). All procedures were carried out by a single experienced colonoscopist. The cases were grouped chronologically into three periods: (1st): cases 1–40; (2nd): cases 41–80; and (3rd): cases 81–120.

Results: The learning curve was the changes in proficiency over time. Proficiency was expressed as procedure time per unit area of specimen. In the 1st, 2nd and 3rd periods, the proficiencies were 18.9, 12.6 and 12.9 (min/cm²), respectively. The proficiencies in the 2nd and 3rd periods were significantly shorter than in the 1st period (t-test, P < 0.05). The en-bloc resection rates of the 1st, 2nd and 3rd periods were 92.5% (37/40), 90% (36/40) and 97.5% (39/40), respectively. The en-bloc and R0 resection rates of the 1st, 2nd and 3rd periods were 85% (34/40), 77.5% (31/40) and 92.5% (37/40), respectively. The perforation rates of the 1st, 2nd and 3rd periods were 12.5% (5/40), 5% (2/40) and 5% (2/40), respectively.

Conclusion: Based on our analysis of the learning curve, approximately 80 procedures must be carried out to acquire skill with ESD for large colorectal tumors. However, approximately 40 procedures were sufficient to acquire skill in avoiding perforations during the ESD procedure.



How much time??



12 mins per cm²



Stepwise training in rectal and colonic endoscopic submucosal dissection with differentiated learning curves Background: Endoscopic submucosal dissection neoplasms, but adoption in Western countries is s

Gastrointestinal Endoscopy

ges 1188-1196

Federico Iacopini, MD,¹ Antonino Bella, MSTAT,² Guido Costamagna, MD, F Yutaka Saito, MD,⁵ Walter Elisei, MD,¹ Cristina Grossi, MD,¹ Patrizia Rigato, Agostino Scozzarro, MD, PhD¹

Rome, Italy; Tokyo, Japan

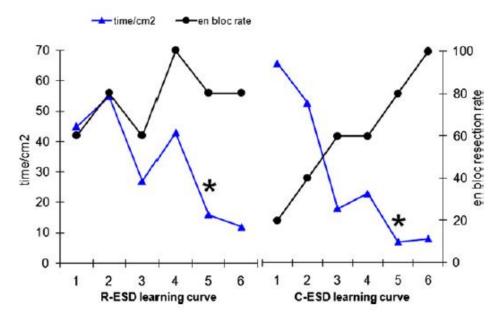


Figure 1. Learning curves of rectal (r-ESD) and colonic ESD (c-ESD). *Significant difference compared with results in block 1.

Background: Endoscopic submucosal dissection (ESD) has revolutionized the resection of GI superficial neoplasms, but adoption in Western countries is significantly delayed.

Objective: To evaluate a stepwise colorectal endoscopic submucosal dissection (ESD) learning and operative training protocol.

Design: Prospective study in the Western setting.

Setting: This study took place in a nonacademic hospital with one endoscopist expert in therapeutic endoscopy but novice in ESD.

Patients: Indications for ESD were superficial neoplasms 20 mm and larger without ulcerations or fibrosis.

Intervention: Training consisted of 5 unsupervised ESDs on isolated stomach, an observation period at an ESD expert Japanese center, 1 supervised ESD on isolated stomach, and retraining on 1 rectal ESD under supervision. The operative training on patients was performed without supervision moving from the rectum to the colon according to the competence achieved

Main Outcome Measurements: Competence was defined as an 80% en bloc resection rate plus a statistically significant reduction in operating time per square centimeter. Learning curves were calculated based on consecutive blocks of 5 procedures.

Results: From February 2009 to February 2012, 30 rectal and 30 colonic ESDs were performed. The rectal ESD learning curve showed that the en bloc resection rate was 80% after 5 procedures (P = not significant); the operating time per square centimeter significantly decreased after 20 procedures (P = .0079); perforation occurred in 1 patient. The colonic ESD learning curve showed that the en bloc resection rate was 80% after 20 procedures (P = not significant); the operating time per square centimeter significantly decreased after 20 procedures (P = .031); perforations occurred in 2 patients.

Limitations: Single-center design.

Conclusions: A minimal intensive training seems sufficient for endoscopists expert in therapeutic procedures to take up ESD in a not overly arduous incremental method with separate and sequential learning curves for the rectum and colon. (Gastrointest Endosc 2012;76:1188-96.)

Expens . 10 IIIIII:



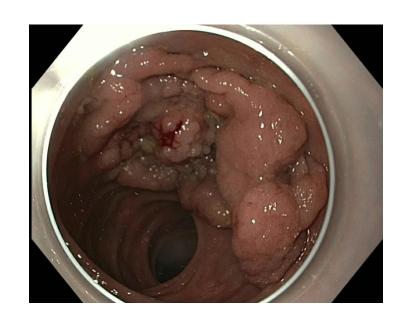
-> 3x3 cm lesion: 9x10 mins in expert hands =1,5 hours

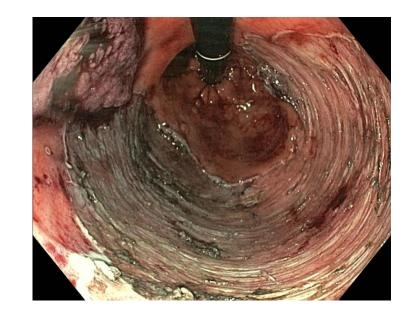






-> 5x5 cm lesion: 25x10 mins in expert hands: 250 min = 4 hours

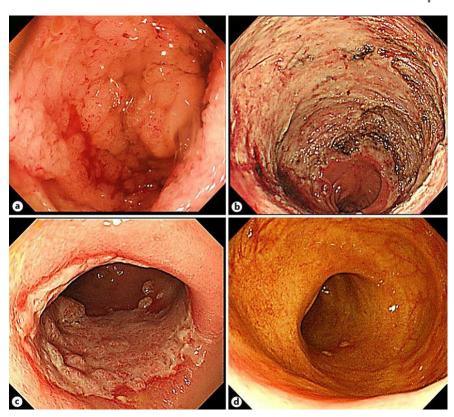






10x10cm: 1000 min = 16,6 hrs \approx 1000 min...

Case Rep Gastroenterol 2015;9:126-131

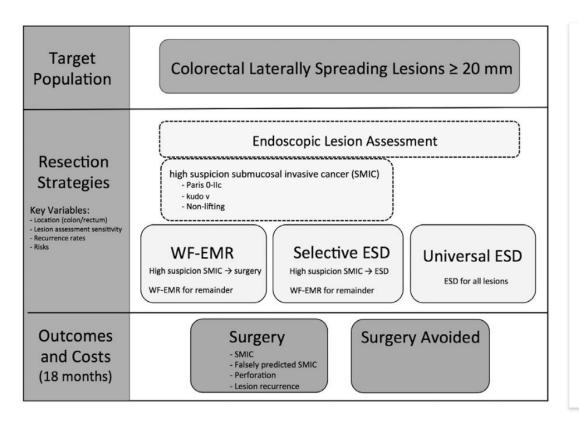


Abstract

An 81-year-old female consulted a local physician due to diarrhea. Since general fatigue and body weight loss were observed, she was admitted for detailed examination and treatment. Colonoscopy revealed a circumferential giant tumor with a maximum diameter of 10 cm in the rectum, and biopsy findings indicated villous adenoma. The tumor secreted a large amount of mucus, and a diagnosis of electrolyte depletion syndrome causing electrolyte disorders was made. We performed endoscopic submucosal dissection (ESD) as a less invasive procedure. The tumor was so big that the procedure had to be completed in two separate steps and it took 1,381 min in total. The tumor was histologically diagnosed as well-differentiated adenocarcinoma in high-grade adenoma located in the lower to upper rectum, invading into the mucosa without lymphatic or venous invasion. The stump of the resected specimen was negative for adenocarcinoma, however the horizontal stump was positive for adenoma. We administered steroid suppositories to prevent stenosis. After ESD, general fatigue and diarrhea disappeared and electrolyte disorders resolved. The patient had good clinical outcome without recurrence or stenosis.



EMR vs ESD: cost-effectiveness analysis



- ✓ <u>Selective ESD</u> prevents 19 additional surgeries per 1000 cases at slightly lower cost compared with WF-EMR.
- ✓ <u>Universal ESD</u> could prevent an additional 13 surgeries per 1000 cases compared with selective ESD, but at substantial increased cost.
- ✓ Expanding selective ESD criteria according to contemporary Japanese guidelines provides little additional benefit.

A universal ESD strategy in the colorectum is not justified



Gut. 2018 Aug;67(8):1464-1474. doi: 10.1136/gutjnl-2017-315103. Epub 2017 Dec 5.

Why attempt en bloc resection of non-pedunculated colorectal adenomas? A systematic review of the prevalence of superficial submucosal invasive cancer after endoscopic submucosal dissection.

Fuccio L^{#1}, Repici A^{#2}, Hassan C^{#3}, Ponchon T⁴, Bhandari P⁵, Jover R⁶, Triantafyllou K⁷, Mandolesi D¹, Frazzoni L¹, Bellisario C⁸, Bazzoli F¹, Sharma P^{9,10}, Rösch T¹¹, Rex DK^{#12}.

- 51 studies (2006-2016)
 - ✓ 41 Asia
 - ✓ 10 Europe
- 11260 colorectal ESD's
 - √ 67% above rectum
 - ✓ Average size 33.2 mm (range 19-60 mm)
- Primary outcome
 - ✓ Prevalence of superficially invasive cancer (SMIC SM1)
- Secondary outcome
 - ✓ Prevalence of deep invasive cancer (SMIC SM2)
 - √ R0 resection, curative Tx, complications





Gut. 2018 Aug;67(8):1464-1474. doi: 10.1136/gutjnl-2017-315103. Epub 2017 Dec 5.

Why attempt en bloc resection of non-pedunculated colorectal adenomas? A systematic review of the prevalence of superficial submucosal invasive cancer after endoscopic submucosal dissection.

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Outcome	Studies (n)	Lesions (n)	Overall (%) (95% CI)	Asia (%) (95% CI)	Europe (%) (95% CI)
SM-1 rate	51	11 260	8.0 (6.1 to 10.3)	8.1 (6.0 to 10.8)	7.4 (3.8 to 13.8)
SM-2 rate	51	11 260	7.7 (6.6 to 9.0)	8.0 (6.7 to 9.4)	6.6 (4.6 to 9.4)
Adenomas	51	11 260	82.2 (75.8 to 89.3)	81.9 (77.9 to 85.3)	83.6 (75.8 to 89.3)
Low-grade dysplasia	37	9153	26.8 (21.2 to 33.1)	23.8 (18.5 to 30.1)	40.8 (26.3 to 57.2)
High-grade dysplasia	37	9153	55.4 (49.4 to 61.1)	58.9 (52.9 to 64.5)	39.9 (27.4 to 53.9)
Laterally spreading tumour	37	9342	80.3 (75.3to 84.4)	81.9 (77.1 to 85.9)	65.1 (54.0 to 74.7)
Granular type	36	9109	46.4 (41.9 to 51.0)	49.1 (44.7 to 53.5)	31.6 (25.9 to 37.8)
Non-granular type	36	9109	34.1 (31.0 to 37.4)	33.8 (30.9 to 36.7)	36.4 (21.4 to 54.6)
Recurrence rate after R0 resection (any follow-up)	30	4961	1.3 (1.0 to 1.8)	1.0 (0.7 to 1.4)	4.4 (2.3 to 8.1)
Bleeding rate	50	11140	2.2 (1.7 to 2.7)	2.1 (CI 1.6 to 2.7)	2.8 (1.6 to 5.0)
Perforation rate	51	11 260	5.1 (4.3 to 6.1)	4.8 (4.0 to 5.7)	8.2 (4.8 to 13.8)
Surgery rate for complications	49	9127	1.0 (0.7 to 1.4)	0.8 (0.6 to 1.1)	2.9 (1.6 to 5.4)





To ESD or not to ESD..?

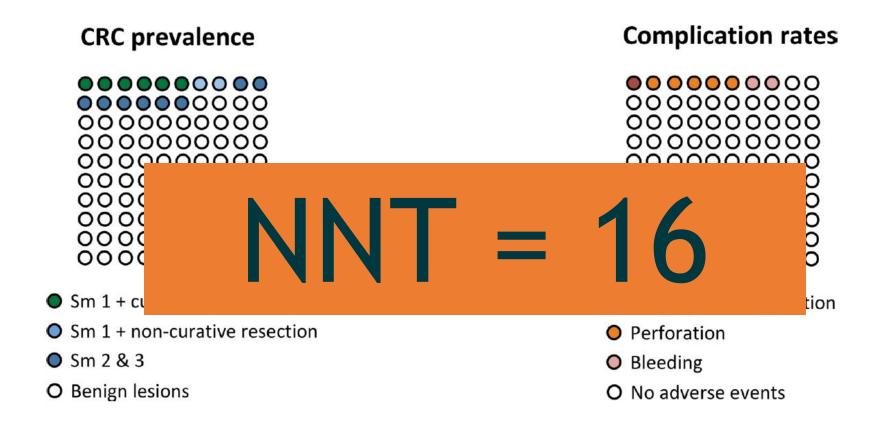


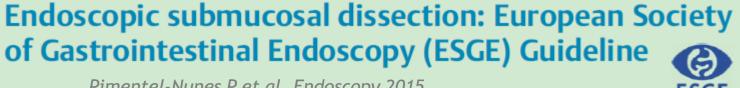
Figure 1 Prevalence of colorectal cancer (CRC) among 100 non-pedunculated colorectal lesions and complications related to resection by endoscopic submucosal dissection.





The right colorectal lesion for ESD

- Size >20 mm, or in which en bloc EMR difficult
- Suspicion of limited submucosal invasion (Sm1, ≤ 1000um), based on
 - ✓ Depressed morphology (Paris 0-IIc)
 - ✓ Irregular surface pattern (Kudo Vi)
 - ✓ Non granular surface pattern
- Extended indications in rectum (higher risk of Sm invasion & relative safe)
 - ✓ granular, non granular or mixed type lesions > 20 mm







The right institution for ESD

- High volume/referral center (> 25 cases/year)
- Dedicated team and equipment
- Management of complications

 acces to emergency surgery
- Acces to expert GI pathology
- Multidisciplinary team discussion
- Prospective recording of all procedures and quality parameters
 - ✓ En bloc resection > 90%
 - ✓ R0 resection > 80%
 - √ < 3% perforations, < 1% emergency surgery
 </p>







Clinical outcomes after endoscopic submucosal dissection for colorectal neoplasia: a systematic review and meta-analysis

Lorenzo Fuccio, MD,¹ Cesare Hassan, MD, PhD,² Thierry Ponchon, MD,³ Daniele Mandolesi, MD,¹ Andrea Farioli, MD, PhD,¹ Alessandro Cucchetti, MD,¹ Leonardo Frazzoni, MD,¹ Pradeep Bhandari, MD, Cristina Bellisario, PhD,⁵ Franco Bazzoli, MD,¹ Alessandro Repici, MD⁶

SUPPLEMENTARY TABLE 5. R0 resection rates stratified according to the number of lesions resected per year and per countries

Mean number of ESDs/year Overall		Overall	Non-Asian countries	Asian countries	
Low volume (≤24 ESDs/year)	79.6%	(95% CI, 75.4%-83.3%)	71.6% (95% CI, 64.2%-78.0%)	82.3% (95% CI, 77.9%-85.9%)	
High volume (>24 ESDs/year)	85.5%	(95% CI, 82.9%-87.7%)	72.0% (95% CI, 59.5%-81.8%)	87.4% (95% CI, 85.2%-89.4%)	

ESD, Endoscopic submucosal dissection.

RECOMMENDATION

In order to maintain proficiency in ESD, ESGE recommends a minimum case load of 25 ESD procedures per year. Level of agreement 100 %.





The right person for ESD



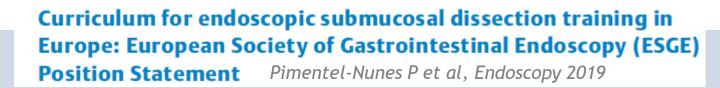
- Time
- Patience
- Dedication

RECOMMENDATION

Advanced endoscopy diagnostic practice is advised before initiating ESD training.
Level of agreement 95%.

RECOMMENDATION

Training in ESD should be considered only by fully trained endoscopists. Proficiency in EMR and adverse event management is recommended before starting ESD training. Level of agreement 100%.







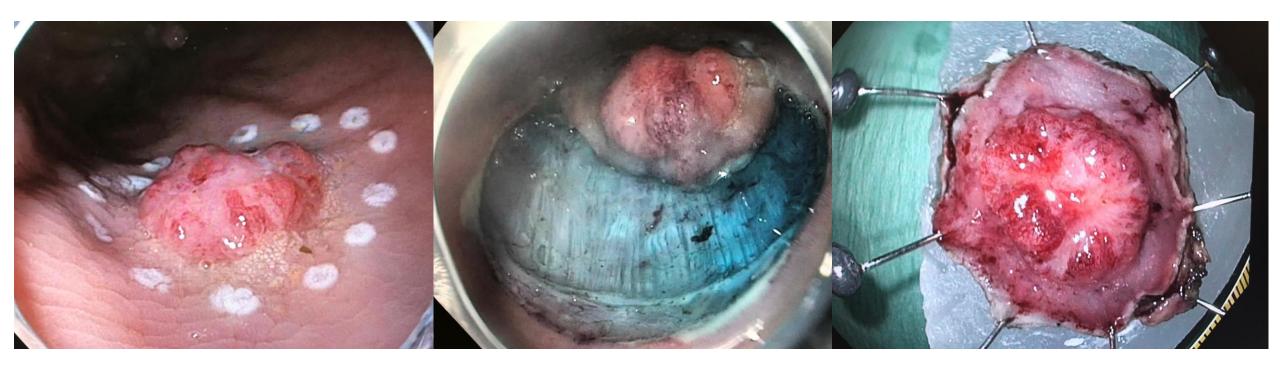
ESD



- Fantastic technique
- But let's keep it practical..!

-> Good patient-selection and procedures by experienced endoscopists

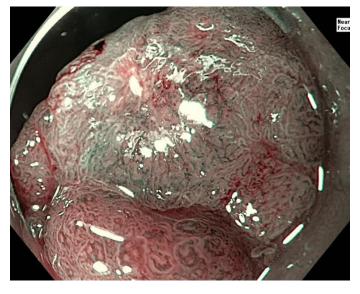
Endoscopic Technique (ESD-IM)





Endoscopic Intermuscular Dissection (EID)

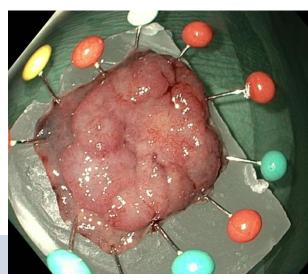










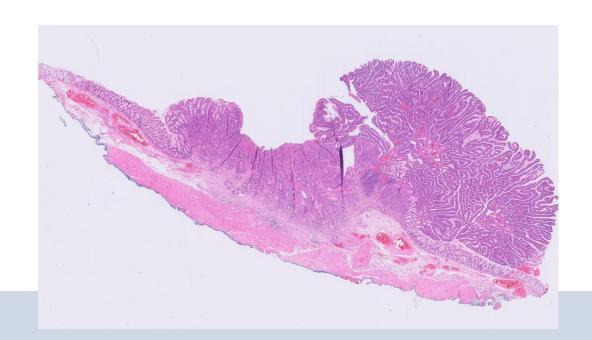




EID for suspect deep Sm invasive rectal cancer



EID histology





Parameter	Number %
Technical succes	
Overall	64/67 (96%)
pT1	44/45 (98%)
R0 resection	
Overall	54/67 (81%)
Technical succesfull cases	54/64 (84%)
pT1	41/45 (91%)
Curative resection	
Overall	30/67 (45%)
Technical succesfull cases	30/64 (47%)
pT1	22/45 (49%)
pT2	14 (21%)
pT1sm2-3	40 (59%)

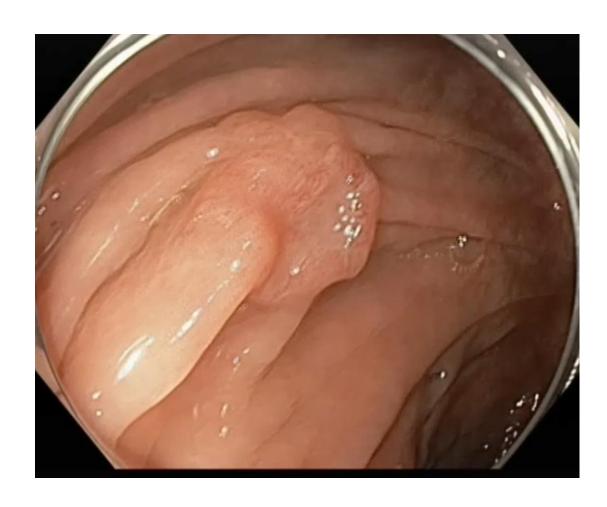


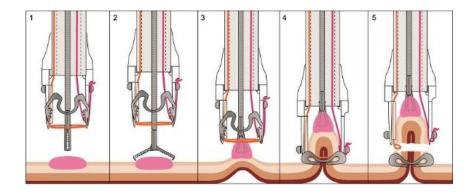


eFTR for early colonic cancer



eFTR for early colonic cancer

















Case- 55 yo male patient

- 2005: T3N0 sigmoid carcinoma →
- (open) sigmoid resection with anastomosis at 15 cm
- 2015: p-EMR adenoma HGD descending colon,
- no follow up...
- 2018: Surveillance colonoscopy
 - ➤ Polyp 15 mm descending colon, partial non lifting
 - ➤ Piecemeal resection attempt in referring center
 - ➤ Distal marking tattoo
 - Histology: "at least"HGD, strong suspicion submucosal cancer







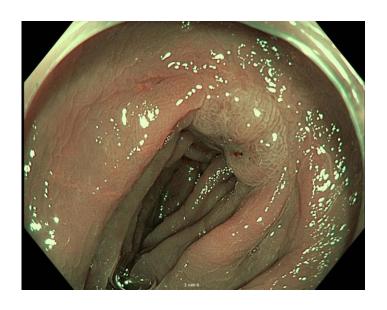








Case- 55 yo male patient







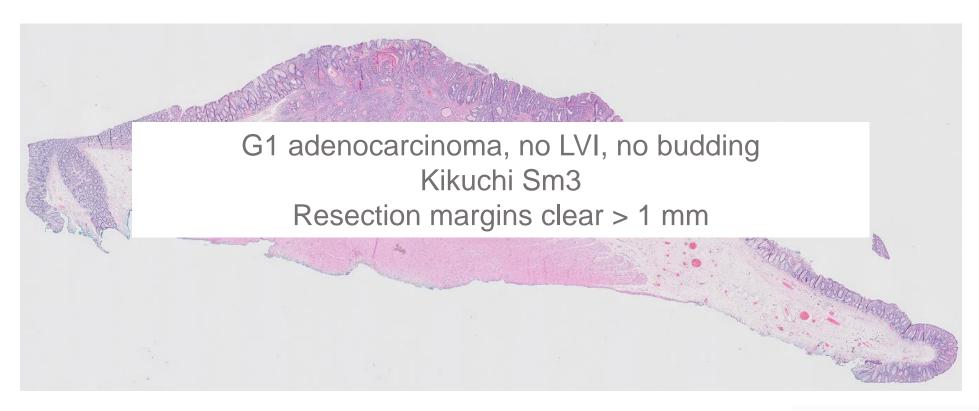








Case- 55 yo male patient





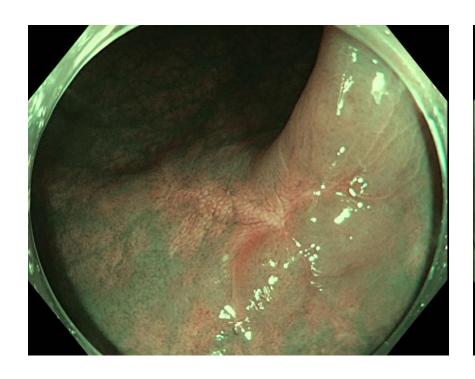


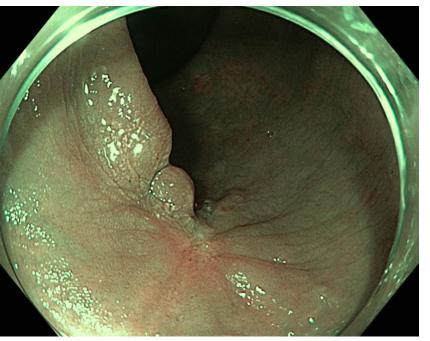






Completion eFTR after previous incomplete resection T1







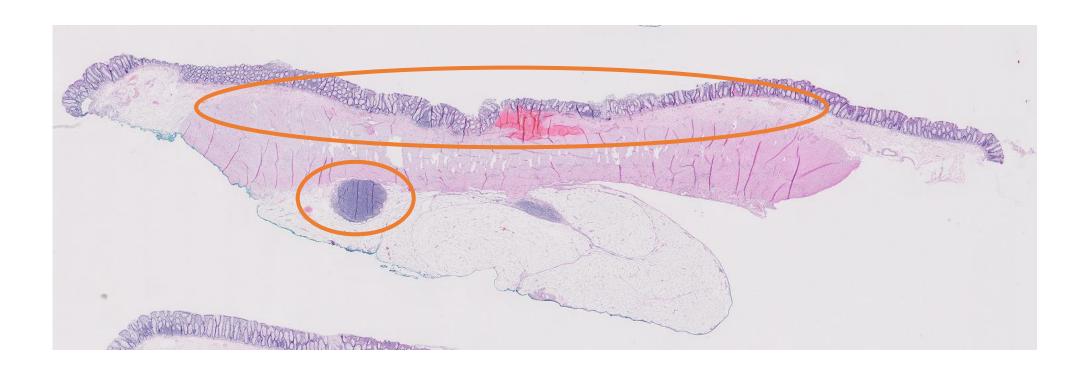








Completion eFTR after previous incomplete resection T1













eFTR for T1 CRC

Endoscopic full-thickness resection for early colorectal cancer

Armin Kuellmer, MD, ^{1,*} Julius Mueller, ^{1,*} Karel Caca, MD, ² Patrick Aepli, MD, ³ David Albers, MD, ⁴ Brigitte Schumacher, MD, ⁴ Anne Glitsch, MD, ⁵ Claus Schäfer, ⁶ Ingo Wallstabe, MD, ⁷ Christopher Hofmann, MD, ⁸ Andreas Erhardt, ⁹ Benjamin Meier, MD, ² Dominik Bettinger, MD, ¹ Robert Thimme, MD, ¹ Arthur Schmidt, MD¹, the FTRD study group



Freiburg, Germany

- Retrospective multicenter trial (96 hospitals)
- 1234 screened patients \rightarrow n = 156
- ❖group 1: re-resections after previous Rx/R1, n = 64
- ❖group 2: primary non lifting, n = 92
- Endpoints: i.a. technical succes ନ Relimentates la le risk str

Webinar | Resection techniques in endoluminal regery









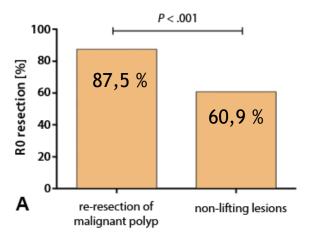
Endoscopic full-thickness resection for early colorectal cancer

Armin Kuellmer, MD, ^{1,*} Julius Mueller, ^{1,*} Karel Caca, MD, ² Patrick Aepli, MD, ³ David Albers, MD, ⁴ Brigitte Schumacher, MD, ⁴ Anne Glitsch, MD, ⁵ Claus Schäfer, ⁶ Ingo Wallstabe, MD, ⁷ Christopher Hofmann, MD, ⁸ Andreas Erhardt, ⁹ Benjamin Meier, MD, ² Dominik Bettinger, MD, ¹ Robert Thimme, MD, ¹ Arthur Schmidt, MD¹, the FTRD study group

Freiburg, Germany



Overall R0 rate 71.8% (112 of 156)



• Exact histologic risk stratification ring 99 93% FIE jan 2019



Colonic ESD



Colonic ESD



Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum: a new endoscopic approach



Leon M. G. Moons[‡], Barbara A. J. Bastiaansen[‡], Milan C. Richir, Wouter L. Hazen, Jurriaan Tuynman, Sjoerd G. Elias, Ruud W M. Schrauwen, Frank P. Vleggaar, Evelien Dekker , Philip Bos, Arantza Fariña Sarasqueta, Miangela Lacle, Roel Hompes, Paul Didden



- Optical diagnosis deep sm invasion
- 2018-2020 : consecutive patients
- Outcome
 - Technical success
 - R0 resection
 - Curative resection

Final pathology: Tis n=8	pT1 n=45 pT2 n=14
Technical success	96% 98% (44/45) 98% (39/40)
R0 rate • Overall • pT1 • pT1 (sm2-3)	81% 91% (41/45) 90% (36/40)
Curative resection	45% (30/67) 49% (22/45) 45% (18/40)

Conclusions

- Structural lesion assesment important prior to any procedure
- Plane of resection dependent on depth of invasion & Location
- For superificial sm invasion (rectum): treatment according to local expertise
- IM plane: new frontier to resect early neoplastic rectal lesions with suspected deep sm invasion







Thank you

roelhompes@gmail.com r.hompes@amc.uva.nl



Early rectal lesions?

Surgeons





Endoscopists



Rules of engagement

Every significant rectal lesion should be discussed at MDT
Strategic planning should be performed
Every suspect lesion should be staged by MRI, EUS before treatment
Patient counselling on alternatives





Curative local Tx of T1 CRC depends on:

Radicality → en bloc R0 resection

- Absence of high risk features:
 - ✓ Deep submucosal invasion (i.e. ≥ 1000um, meaning Sm2-3 or Haggitt 4)
 - ✓ Lymphovascular invasion
 - ✓ Poor tumor-differentiation
 - ✓ Intense tumor budding (grade 2-3)



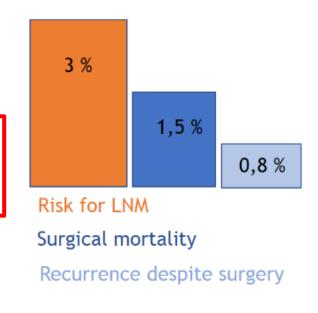
Sm invasion depth is a weak predictor for LNM

Risk of LNM if <u>only deep sm invasion</u> is present is <u>1 - 3 % ¹⁻⁵</u>

Study,	year	N	Risk for LNM	
Suh	2012	118	2 (1,7 %)	
Nakadoi	2012	249	3 (1,2 %)	

Warning! Precise pathologic evaluation required !!!

Yasue	2019	258	4 (1,6 %)



⁴Oka et al, Dig Endoscopy 2013

¹ Suh et al, Endoscopy 2012

³ Nakadoi et al, J Gastroenterol Hepatol 2012

² Kim et al, Medicine 2016

Pathological risk factors and predictive endoscopic factors for lymph node metastasis of T1 colorectal cancer: a single-center study of 846 lesions

Chihiro Yasue¹ · Akiko Chino¹ · Manabu Takamatsu² · Ken Namikawa¹ · Daisuke Ide¹ · Shoichi Saito¹ · Masahiro Igarashi¹ · Junko Fujisaki¹

Single Center - retrospective review

T1 - N=846 (2005-2016) - Surg/Endosc (excluding pedunculated/lynch/FAP)

Review all pathological RF for LNM

Table 4 Relationship between the number of risk factors and lymph node metastasis

Risk factor	LNM (-) group	LNM (+) group	Total	Incidence of LNM (%)		
(1) Depth of invasion ≥ 1000 μm	254	4	258	1.6		
(2) Lymphovascular invasion	17	3	20	15.0		
(3) Tumor budding grade 2/3	1	0	1	0		
(4) por/sig/muc histological differentiation	3	In conclus	ion whe	en DI was the only nathological risk		
(1) + (2)	165	In conclusion, when DI was the only pathological risk factor in T1 colorectal cancer, the rate of lymph node metastasis was extremely low. In addition, rectal tumor				
(1) + (3)	37					
(1) + (4)	15					
(2) + (3)	1					
(2) + (4)	1	location, dep	ression,	protuberance within the depression,		
(3) + (4)	1	expansiveness, and loss of mucosal patterns could be pre-				
(1) + (2) + (3)	67	•	•			
(1) + (2) + (4)	12	dictive factors for HRC.				
(1) + (3) + (4)	8					
(2) + (3) + (4)	2	0	2	0		
(1) + (2) + (3) + (4)	29	15	44	34.1		

LNM lymph node metastasis, por poorly differentiated adenocarcinoma, sig signet-ring cell carcinoma, muc mucinous carcinoma



Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis

Liselotte W. Zwager,^{1,2} Barbara A. J. Bastiaansen,^{1,2} Nahid S. M. Montazeri,³ Roel Hompes,⁴ Valeria Barresi,⁵ Katsuro Ichimasa,⁶ Hiroshi Kawachi,⁷ Isidro Machado,⁸ Tadahiko Masaki,⁹ Weiqi Sheng,¹⁰ Shinji Tanaka,¹¹ Kazutomo Togashi,¹² Chihiro Yasue,¹³ Paul Fockens,^{1,2} Leon M. G. Moons,¹⁴ and Evelien Dekker^{1,2}

Deep submucosal invasion is not an independent risk factor for lymph node metastasis in

T1 colorectal cancer: a meta-analysis

DSI in relation to LNM in univariable analysis

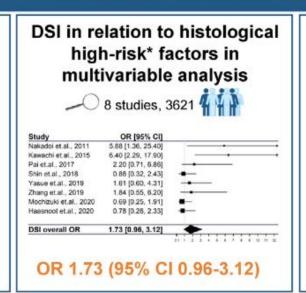
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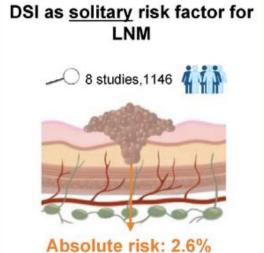
67 studies

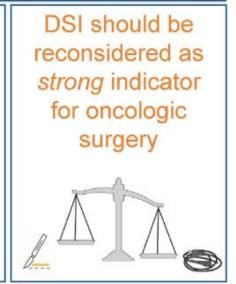
21,238 patients

Overall LNM-rate: 11.2%

OR 2.58 (95% CI 2.10-3.18)







DSI (deep submucosal invasion); LNM (lymph node metastasis); OR (odds ratio). *poor differentiation grade, lymphovascular invasion and high-grade tumor budding Gastroenterology





Future Criteria (?) for a curative endoscopic/surgical resection of a T1 CRC

- Moderate to well differentiation
- Grade 1 tumor budding
- No (lympho)vascular invasion
- Negative resection margin (assessable and > 0.1mm)

