GastroZentrum Hirslanden
Klinik Hirslanden Zürich

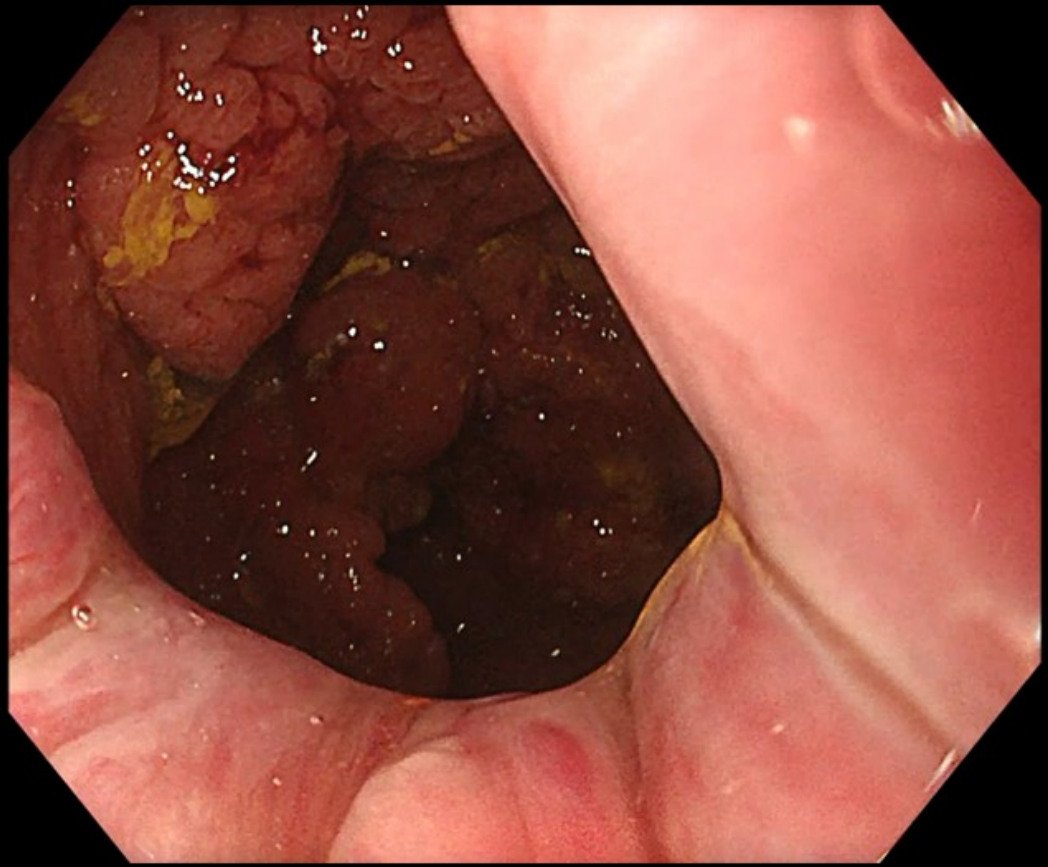
Rectal cancer in 2023

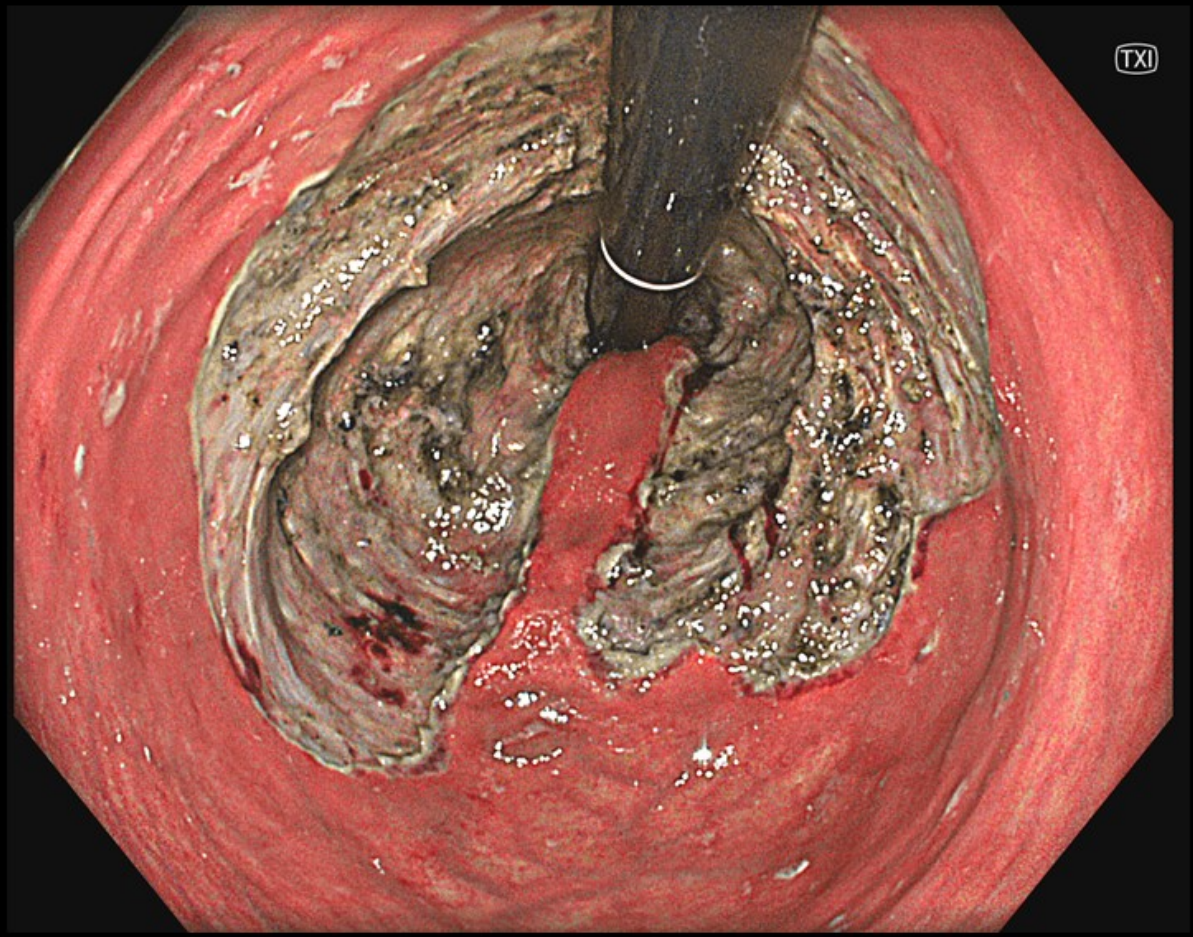
How far can we go with local resection?

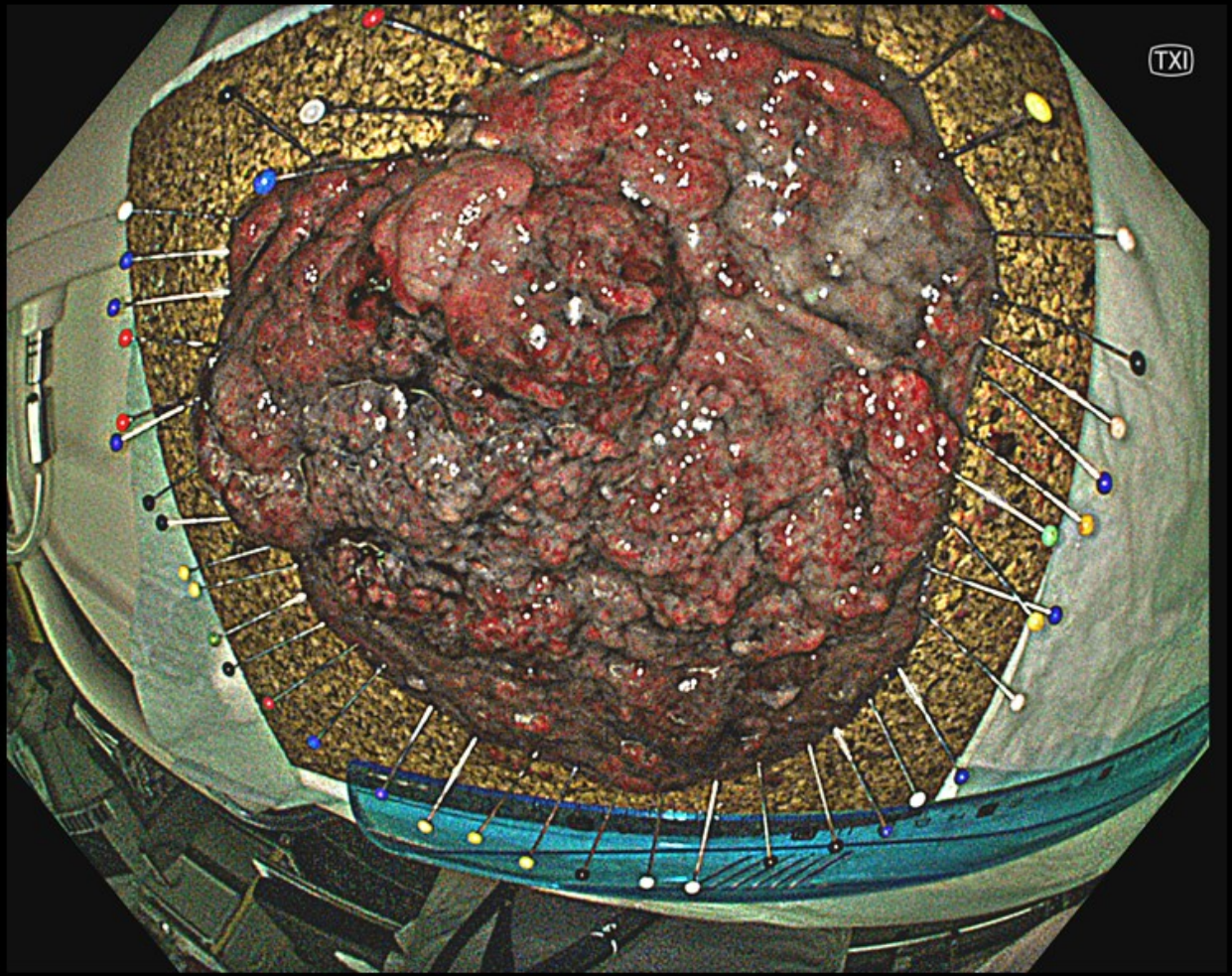
Stefan Seewald

42. Schweizerische Koloproktologie-Tagung

Bern, 14.Januar 2023



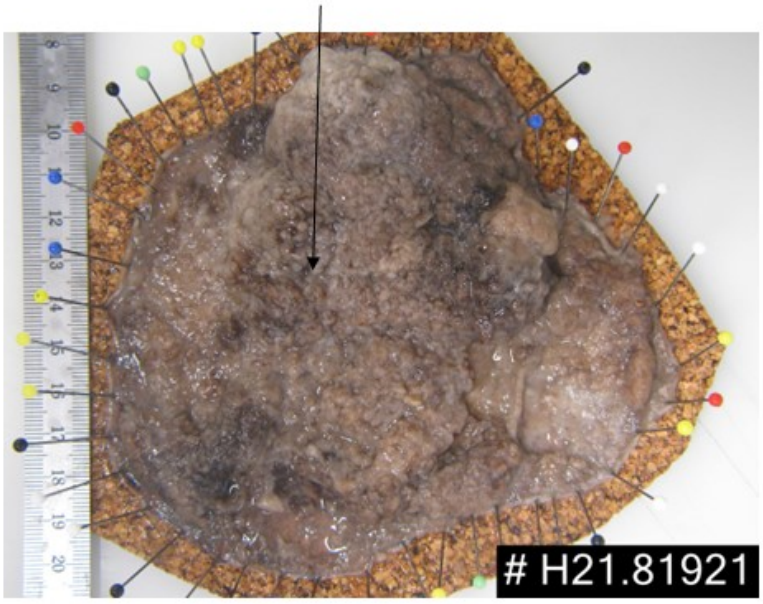

TXI

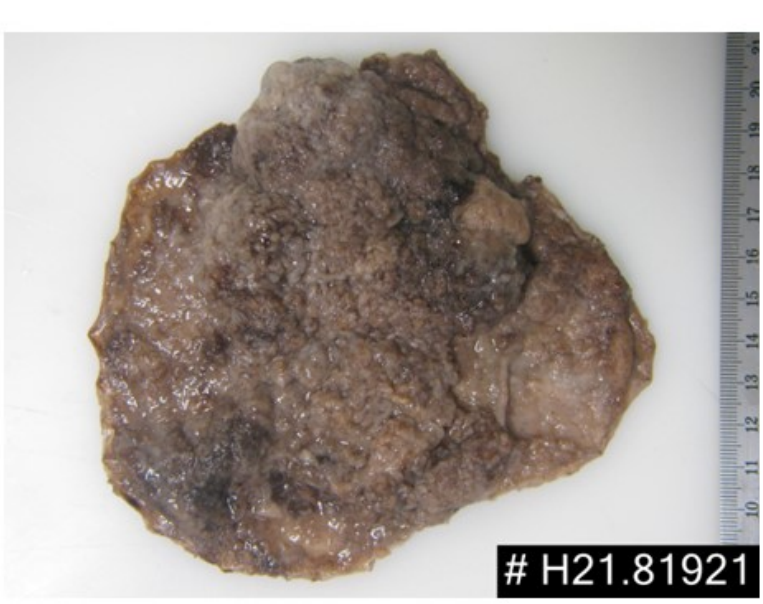


13.5 x 12 cm

Histology

Karzinom

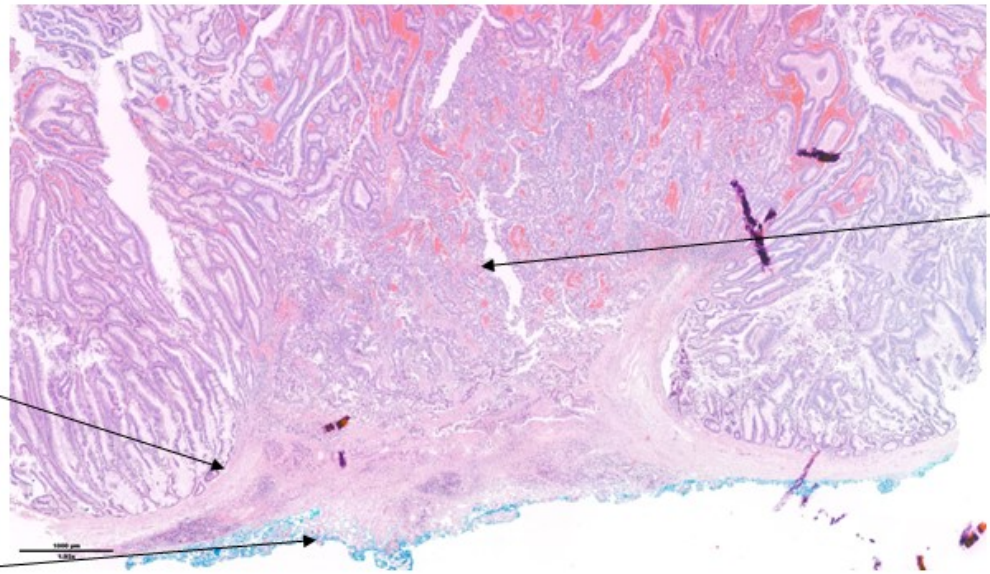




medica
MEDIZINISCHE LABORATORIEN Dr. F. KAEPPELI AG

PD Dr. Ewerton Maggio

Histology



pT1 (sm2) (1200 μm) G2 L0 V0 Pn0 R0 (vm-, hm-)

medica
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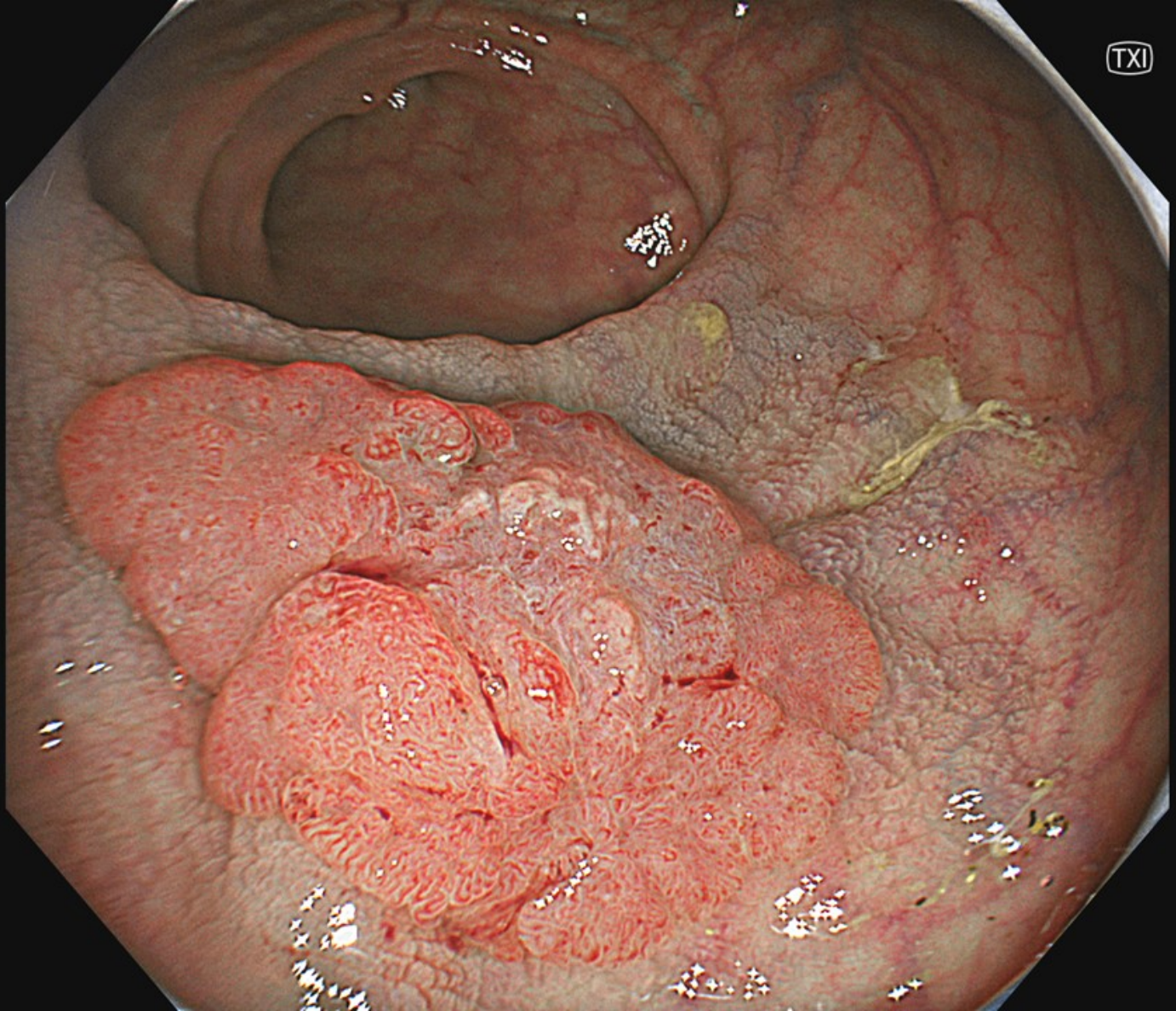
PD Dr. Ewerton Maggio

Rectal cancer in 2023

How far can we go with local resection?

- When do we have to suspect a cancer in a polyp?
- How do we recognise endoscopically a sm cancer?
- How can we stage an early rectal cancer best?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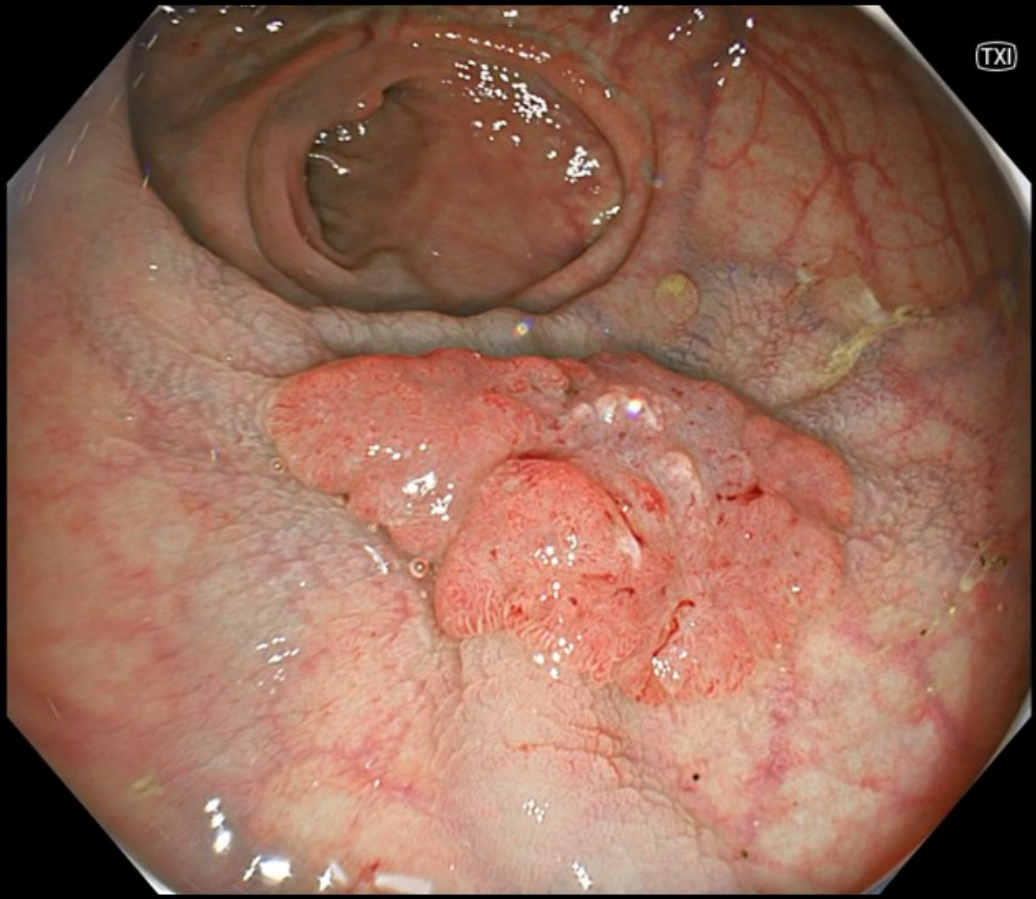
Can we go for a safe endoscopic local resection?

An accurate endoscopic preassessment is mandatory before any resection!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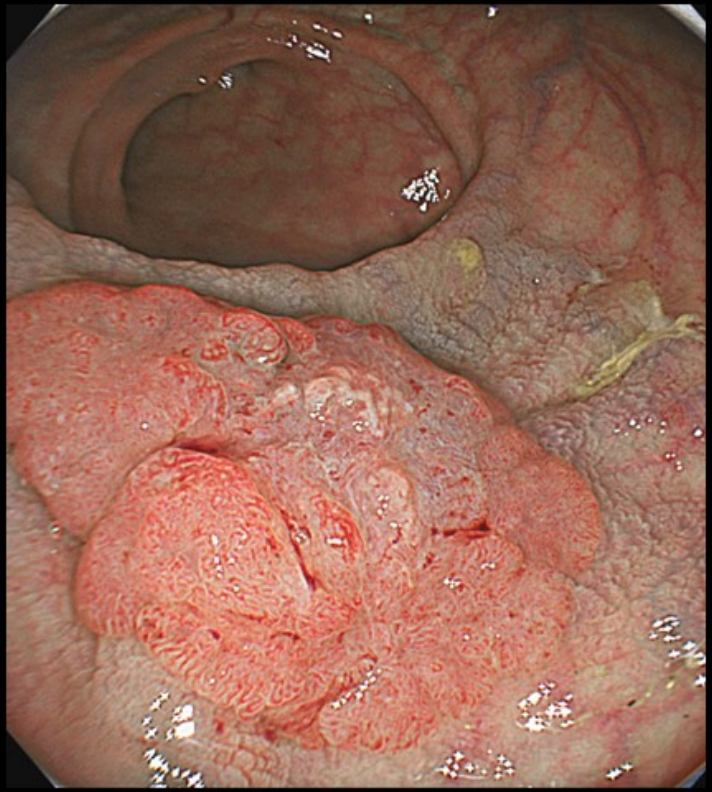
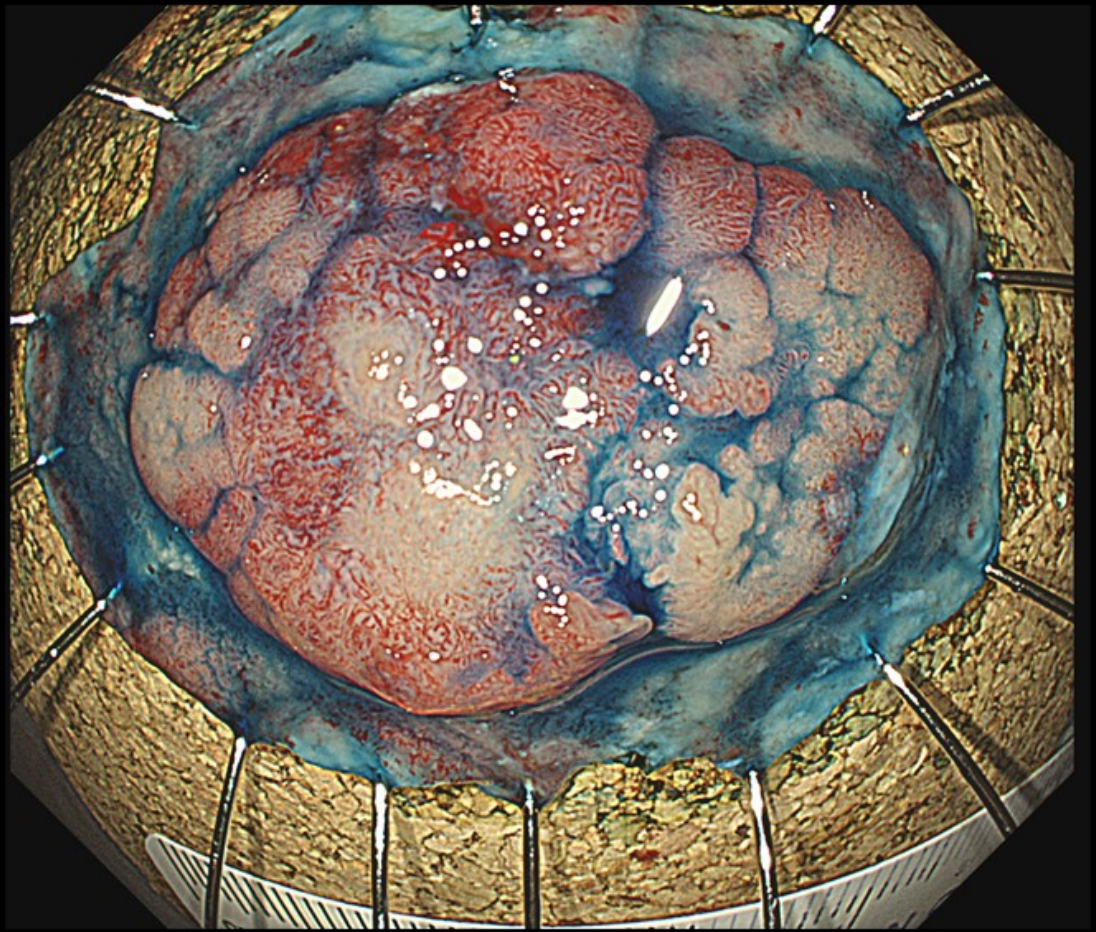
Endoscopic assessment

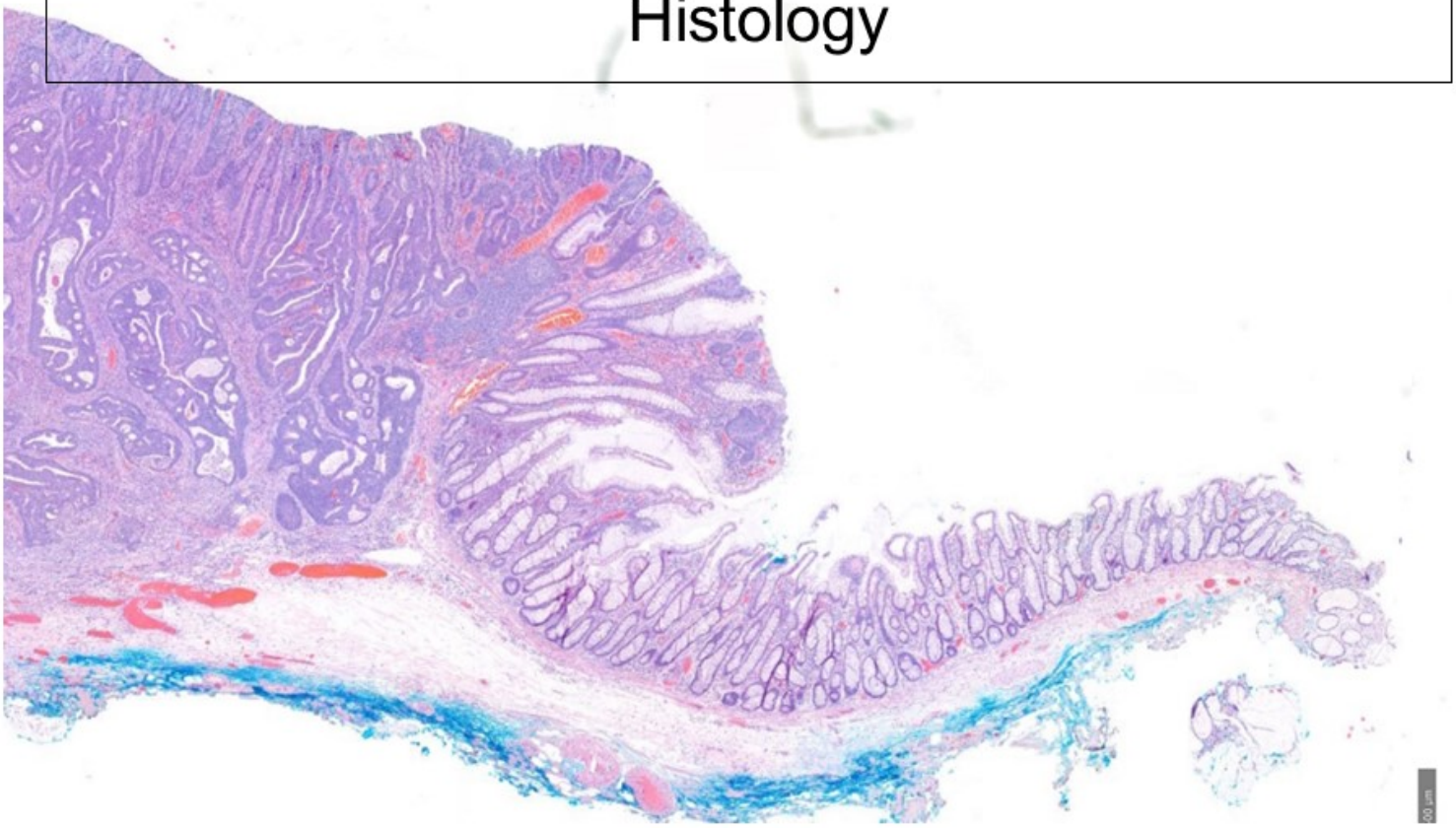


- LST-NG pseudodepressed
- 0-IIa+c
- JNET Typ 2B-3
- Pit Pattern: Typ V_I-V_N
- Estimated: sm deep
- Soft issue of the lesion
- Lifting sign: positive

In histologically proven or suspected
early rectal cancer
endoscopic „en bloc“ resection
is the best staging procedure



Histology



HE Tumor + horizontaler Rand

medica
MEDIZINISCHE LABORATORIEN Dr. F. KAEPPELI AG

pT1 (sm2) (1400 μm) G1 L0 V0 Pn0 R0 (VM0,HM0)

PD Dr. Ewerton Maggio

Resection techniques

- EMR
- FTRD
- ESD
- Hybrid ESD (EMR + ESD)
- EID Endoscopic intermuscular dissection
- TAMIS Transanal minimally invasive surgery
- TEM Trananal endoscopic microsurgery
- TEO Transanal endoscopic operation

Resection techniques

- EMR
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R0 resection

Resection techniques

- EMR
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R0 resection

A potential TME should not be complicated

Resection techniques

- EMR
- FTRD
- ESD
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Schmidt A et al; ***Endoscopy 2015***; 47: 719
Sorlani P et al; ***Endoscopy International Open 2017;*** 05:E1081
Aepli P et al; ***United European Gastroenterol J 2018*** Apr;6(3):463
Kuellmer A et al; ***Gatsrointest Endosc 2019***; 89 (6): 1180

ORIGINAL ARTICLE

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,[5] 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, MD[1], the FTRD study group

Freiburg, Germany

Background and Aims: Current international guidelines recommend endoscopic resection for T1 colorectal cancer (CRC) with low-risk histology features and oncologic resection for those at high risk of lymphatic metastasis. Exact risk stratification is therefore crucial to avoid under-treatment as well as over-treatment. Endoscopic full-thickness resection (EFTR) has shown to be effective for treatment of non-lifting benign lesions. In this multicenter, retrospective study we aimed to evaluate efficacy, safety, and clinical value of EFTR for early CRC.

Methods: Records of 1234 patients undergoing EFTR for various indications at 96 centers were screened for eligibility. A total of 156 patients with histologic evidence of adenocarcinoma were identified. This cohort included 64 cases undergoing EFTR after incomplete resection of a malignant polyp (group 1) and 92 non-lifting lesions (group 2). Endpoints of the study were: technical success, R0-resection, adverse events, and successful discrimination of high-risk versus low-risk tumors.

Results: Technical success was achieved in 144 out of 156 (92.3%). Mean procedural time was 42 minutes. R0 resection was achieved in 112 of 156 (71.8%). Subgroup analysis showed a R0 resection rate of 87.5% in Group 1 and 60.9% in Group 2 ($p < .001$). Severe procedure-related adverse events were recorded in 3.9% of patients. Discrimination between high-risk versus low-risk tumor was successful in 155 of 156 cases (99.3%). In Group 1, 84.1% were identified as low-risk lesions, whereas 16.3% in group 2 had low-risk features. In total, 53 patients (34%) underwent oncologic resection due to high-risk features whereas 98 patients (62%) were followed endoscopically.

Conclusions: In early colorectal cancer, EFTR is technically feasible and safe. It allows exact histological risk stratification and can avoid surgery for low-risk lesions. Prospective studies are required to further define indications for EFTR in malignant colorectal lesions and to evaluate long-term outcome. (Gastrointest Endosc 2019;■:1-10.)

Abbreviations: CRC, colorectal cancer; EFTR, endoscopic full-thickness resection; ESD, endoscopic submucosal dissection; FTRD, full-thickness resection device; R0, microscopically complete resection; T1, Tumor stage according to TNM classification.

DISCLOSURE: *A. Caca received lecture fees and study grants from Ovesco Endoscopy. A. Schmidt received lecture fees from Ovesco Endoscopy. All other authors disclosed no financial relationships relevant to this publication.*

*Drs Kuellmer and Mueller contributed equally to this article.

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Reprint requests: Arthur Schmidt, Department of Medicine II, Medical Center, Faculty of Medicine, University of Freiburg, Hugstetter Strasse 55, 79106 Freiburg, Germany.

after R1 EMR

nonlifting lesion

Variable	Entire cohort (n = 156)	Group 1 (n = 64)	Group 2 (n = 92)
Full-thickness resection, no. (%)	135 (86.5%)	54 (84.4%)	81 (88%)
Microscopically complete resection, no. (%)	112 (71.8%)	56 (87.5%)	56 (60.9%)
Histology			
Scar, no. (%)	49 (31.4%)	49 (76.6%)	
Adenoma, no. (%)	1 (0.6%)	1 (1.6%)	
Carcinoma, no. (%)	106 (68%)	14 (21.9%)	92 (100%)
Low risk, no. (%)	68/155 (43.9%)	53/63 (84.1%)	15/92 (16.3%)
High risk, no. (%)	87/155 (56.1%)	10/63 (15.9%)	77/92 (83.7%)

Kuellmer A et al; ***Gastrointest Endosc 2019***; 89(6): 1180

ORIGINAL ARTICLE

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Variable	Entire cohort (n = 156)
Age, mean (± SD), y	72 ± 9.6
Sex, no. (%)	
Female	55 (35.3%)
Male	101 (64.7%)
Indication for EFTR, no. (%)	
Repeat resection of malignant polyp (group 1)	64 (41%)
Non-lifting lesion (group 2)	92 (59%)
Known carcinoma	19 (20.7%)
Initial classified as (benign) adenoma	73 (79.3%)
Location, no. (%)	
Cecum	11 (7.1%)
Ascending colon	17 (10.9%)
Transverse colon	18 (11.5%)
Descending colon	12 (7.69%)
Sigmoid colon	48 (30.8%)
Rectum	50 (32.1%)
Lesion size, median (range), mm	20 (2-45)

Kuellmer A et al; ***Gastrointest Endosc 2019***; 89(6): 1180

Original article

Thieme

Endoscopic full-thickness resection for T1 early rectal cancer: a case series and video report

OPEN ACCESS

Authors

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accepted after revision 14.7.2017

Bibliography

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Endoscopy International Open 2017; 05: E1081–E1086

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ABSTRACT

Background and study aims Endoscopic treatment of malignant colorectal polyps is often challenging, especially for early rectal cancer (ERC) localized close to the dentate line. Conversely, the surgical approach may result in temporary or definitive stoma and in frequent post-surgical complications. The Full-Thickness Resection Device (FTRD®) System (Ovesco Endoscopy, Tübingen, Germany) is a novel system that, besides having other indications, appears to be promising for wall-thickness excision of intestinal T1 carcinoma following incomplete endoscopic resection. However, follow-up data on patients treated with this device are scarce, particularly for ERC.

Patients and methods Six consecutive patients with incomplete endoscopic resection of T1-ERC were treated with the FTRD and their long-term outcomes were evaluated based on a detailed clinical and instrumental assessment.

Results The endoscopic en bloc full-thickness resection was technically feasible in all patients. The histopathologic analysis showed a complete endoscopic resection in all cases, and a full-thickness excision in four. Neither complications, nor disease recurrence were observed during the 1-year follow-up period.

Conclusions The FTRD System is a promising tool for treating ERC featuring a residual risk of disease recurrence after incomplete endoscopic mucosal resection in patients unfit for surgery or refusing a surgical approach.

Introduction

Thanks to the widespread implementation of screening protocols, colorectal malignant lesions are an increasingly detected pathology, being reported in up to 12% of resected polyps [1].

Complete endoscopic resection of rectal lesions can be achieved with snare-polypectomy, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). However, subsequent histopathological examination of the resected specimen may reveal signs of incomplete resection raising the need for additional treatments (▶ **Table 1**) [2].

Limited by post-polypectomy submucosal fibrosis, a rescue endoscopic therapy is often challenging, especially for rectal lesions localized close to the dentate line [3]. On the other hand, major rectal surgery often results in temporary or definitive stoma with a remarkable impact on patients reported outcomes. In addition, post-surgical complications, such as disturbed defecation, sexual and urinary dysfunctions or anasto-

n= 6
FTRD after previous EMR of 6-30mm rectal polyps with ca & R1 histology

Fullthickness: 4/6
Histology FTRD: 1x positive R0

Soriani P et al; ***Endoscopy Int'l Open 2017***; 5: E1081

Resection techniques

- EMR
- FTRD
- ESD
- Hybrid ESD (EMR + ESD)
- EID Endoscopic intermuscular dissection
- TAMIS Transanal minimally invasive surgery
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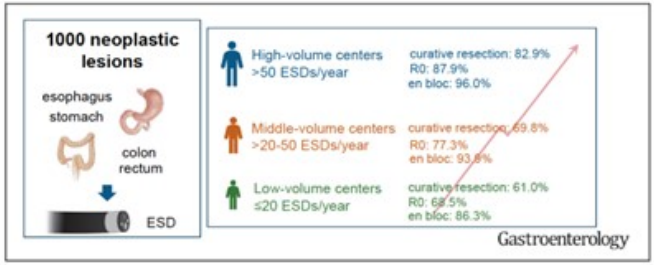
Gastroenterology 2021;161:1168–1178

CLINICAL RE

Endoscopic Submucosal Dissection in Europe: Results of 1000 Neoplastic Lesions From the German Endoscopic Submucosal Dissection Registry

Carola Fleischmann,[1] Andreas Probst,[1] Alanna Ebigbo,[1] Siegbert Faiss,[2] Brigitte Schumacher,[3] H.-P. Allgaier,[4] F.L. Dumoulin,[5] Ingo Steinbrueck,[6] Michael Anzinger,[7] Joerg Marienhagen,[8] Anna Muzalyova,[9] and Helmut Messmann[1]

[1]*Department of Gastroenterology, University Hospital Augsburg, Augsburg, Germany;* [2]*Department of Gastroenterology, Sana Klinikum Lichtenberg, Berlin, Germany;* [3]*Department of Gastroenterology, Elisabeth-Krankenhaus Essen, Essen, Germany;* [4]*Medical Department, Evangelisches Diakoniekrankenhaus, Freiburg, Germany;* [5]*Department of Medicine/Gastroenterology, Gemeinschaftskrankenhaus Bonn, Bonn, Germany;* [6]*Department of Gastroenterology, Asklepios Klinik Barmbek, Hamburg, Germany;* [7]*Department of Gastroenterology, Barmherzige Brüder Krankenhaus München, München, Germany;* [8]*Faculty of Medicine, University of Augsburg, Augsburg, Germany; and* [9]*Chair of Health Care Operations/ Health Information Management, UNIKA-T, University of Augsburg, Augsburg, Germany*



See editorial on page 1101.

BACKGROUND AND AIMS: Endoscopic submucosal dissection (ESD) enables the curative resection of early malignant lesions and is associated with reduced recurrence risk. Due to the lack of comprehensive ESD data in the West, the German ESD registry was set up to evaluate relevant outcomes of ESD. **METHODS:** The German ESD registry is a prospective uncontrolled multicenter study. During a 35-month period, 20 centers included 1000 ESDs of neoplastic lesions. The results were evaluated in terms of en bloc, R0, curative resection rates, and recurrence rate after a 3-month and 12-month follow-up. Additionally, participating centers were grouped into low-volume (≤20 ESDs/y), middle-volume (20–50/y), and high-volume centers (>50/y). A multivariate analysis investigating risk factors for noncurative resection was performed. **RESULTS:** Overall, en bloc, R0, and curative resection rates of 92.4% (95% confidence interval [CI], 0.90–0.94), 78.8% (95% CI, 0.76–0.81), and 72.3% (95% CI, 0.69–0.75) were achieved, respectively. The overall complication rate was 8.3% (95% CI, 0.067–0.102), whereas the recurrence rate after 12 months was 2.1%. High-volume centers had significantly higher en bloc, R0, curative resection rates, and recurrence rates and lower complication rates than middle- or low-volume centers. The lesion size, hybrid ESD, age, stage T1b carcinoma, and treatment outside high-volume centers were identified as risk factors for noncurative ESD. **CONCLUSION:** In Germany, ESD achieves excellent en bloc resection rates but only modest curative resection rates. ESD requires a high level of expertise, and results vary significantly depending on the center's yearly case volume.

Fleischmann C et al; ***Gastroenterology 2021***; 161:1168

Gastroenterology 2021;161:1168–1178

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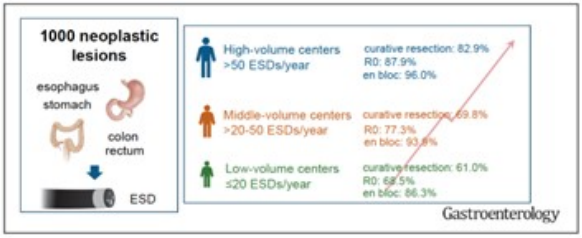

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Rectum ESD n	380 (f130/m250)
Age, median (range), y	69 (30 – 94)
ASA grade 1/2/3/4	174 / 165 / 37 / 4
Specimen size, median (mm)	47 x 37
Treatment naive lesion (%)	347 (91.3%)

Fleischmann C et al; ***Gastroenterology 2021*** ;161:1168

Gastroenterology 2021;161:1168–1178

Endoscopic Submucosal Dissection in Europe: Results of 1000 Neoplastic Lesions From the German Endoscopic Submucosal Dissection Registry

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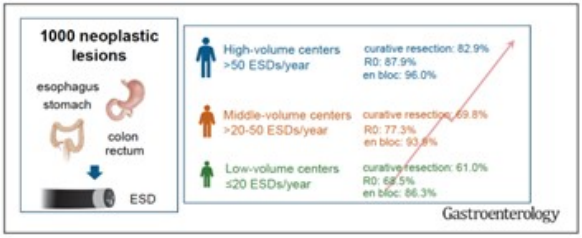

See editorial on page 1101.

BACKGROUND AND AIMS: Endoscopic submucosal dissection (ESD) enables the curative resection of early malignant lesions and is associated with reduced recurrence risk. Due to the lack of comprehensive ESD data in the West, the German ESD registry was set up to evaluate relevant outcomes of ESD. **METHODS:** The German ESD registry is a prospective uncontrolled multicenter study. During a 35-month period, 20 centers included 1000 ESDs of neoplastic lesions. The results were evaluated in terms of en bloc, R0, curative resection rates, and recurrence rate after a 3-month and 12-month follow-up. Additionally, participating centers were grouped into low-volume (≤20 ESDs/y), middle-volume (20–50/y), and high-volume centers (>50/y). A multivariate analysis investigating risk factors for noncurative resection was performed. **RESULTS:** Overall, en bloc, R0, and curative resection rates of 92.4% (95% confidence interval [CI], 0.90–0.94), 78.8% (95% CI, 0.76–0.81), and 72.3% (95% CI, 0.69-0.75) were achieved, respectively. The overall complication rate was 8.3% (95% CI, 0.067–0.102), whereas the recurrence rate after 12 months was 2.1%. High-volume centers had significantly higher en bloc, R0, curative resection rates, and recurrence rates and lower complication rates than middle- or low-volume centers. The lesion size, hybrid ESD, age, stage T1b carcinoma, and treatment outside high-volume centers were identified as risk factors for noncurative ESD. **CONCLUSION:** In Germany, ESD achieves excellent en bloc resection rates but only modest curative resection rates. ESD requires a high level of expertise, and results vary significantly depending on the center's yearly case volume.

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En bloc resection	344 (90.5%)
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Fleischmann C et al; ***Gastroenterology 2021*** ;161:1168

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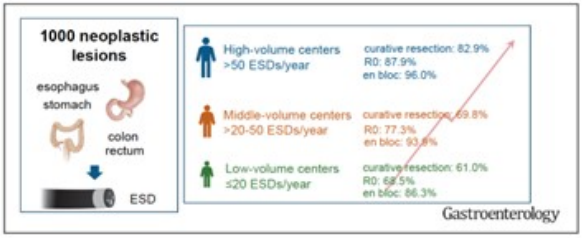

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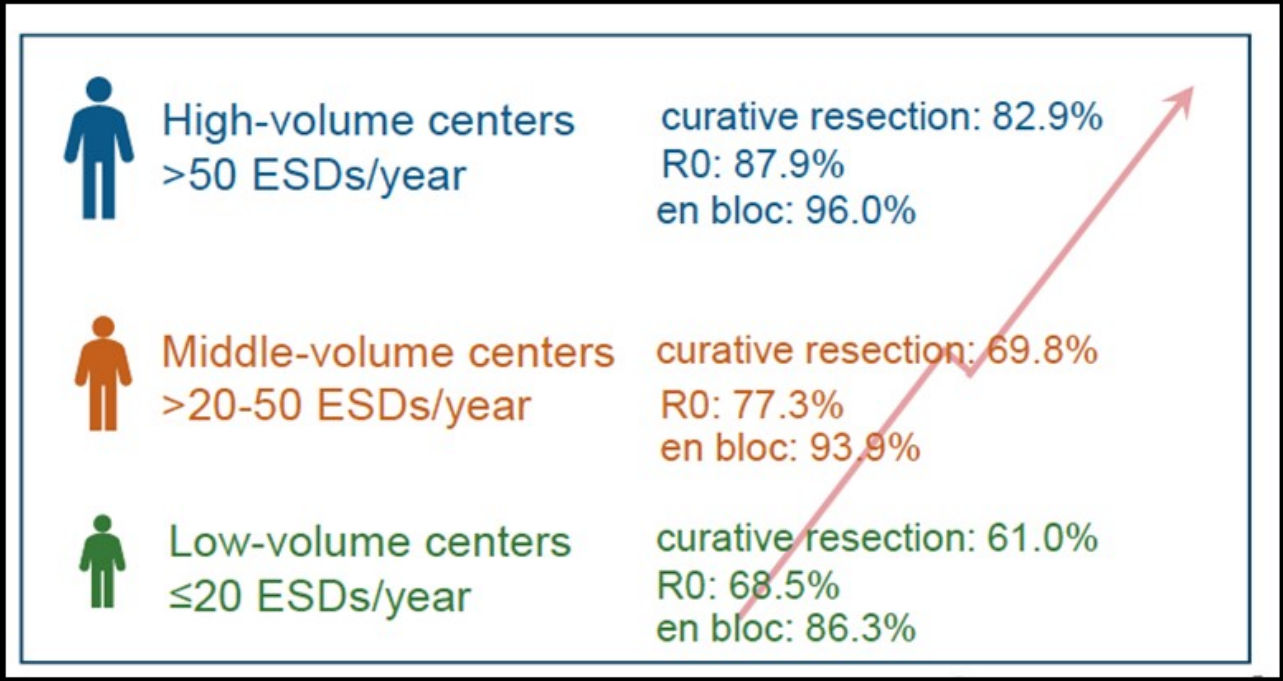

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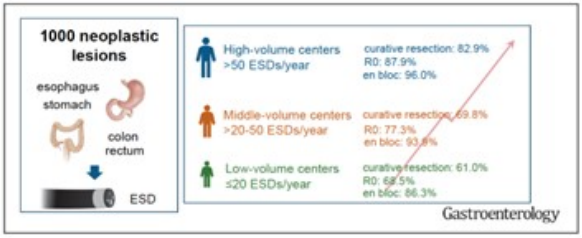

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Procedure time?

Fleischmann C et al; ***Gastroenterology 2021*** ;161:1168

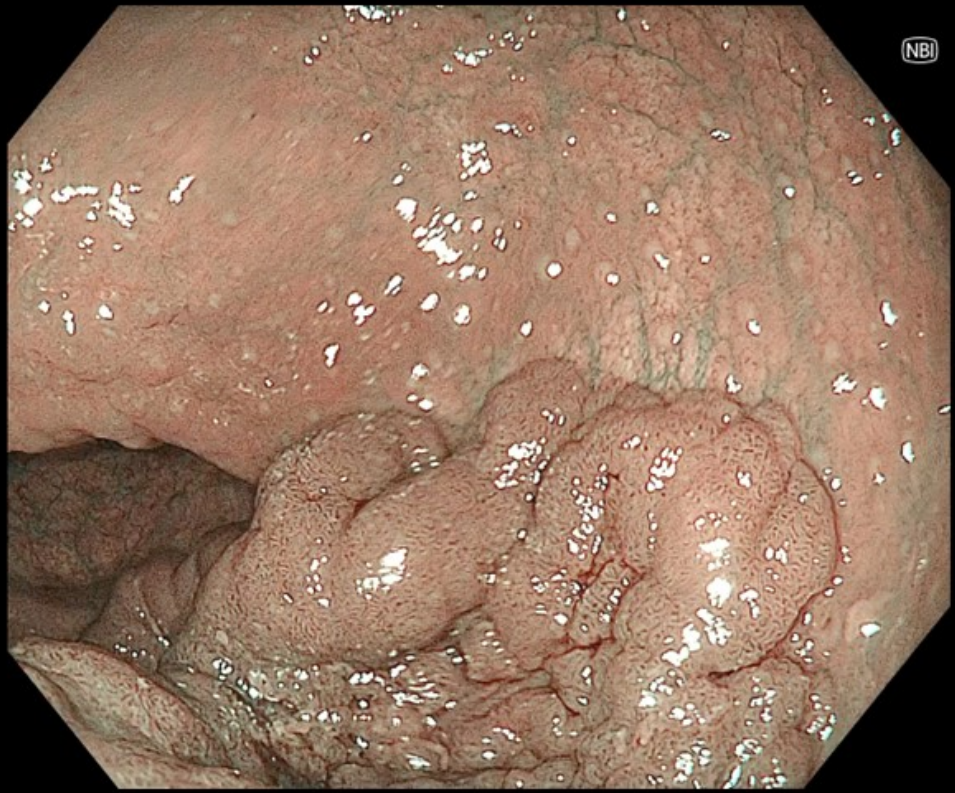
Lesion Size & Procedure Time

Colorectal ESD n (lesion)	171 f76/m95
Mean age ± SD	63.4 ± 11 years
Lesion size median (range)	48 mm (35 – 65)
Mean time (range)	120 min (80 – 176 min)

Yang D et al; ***Endoscopy Int'l Open 2019***; 7: E1714

Colorectal ESD n (lesion)	167 f71/m96
Mean age ± SD	64 ± 11 years
Mean lesion size ± SD (range)	44 ± 20mm (15– 170)
Median time (range)	90 min (10 – 330 min)

Santos-Antunes J et al; ***GE Port J Gastroenterol 2021***; 28:319


NBI

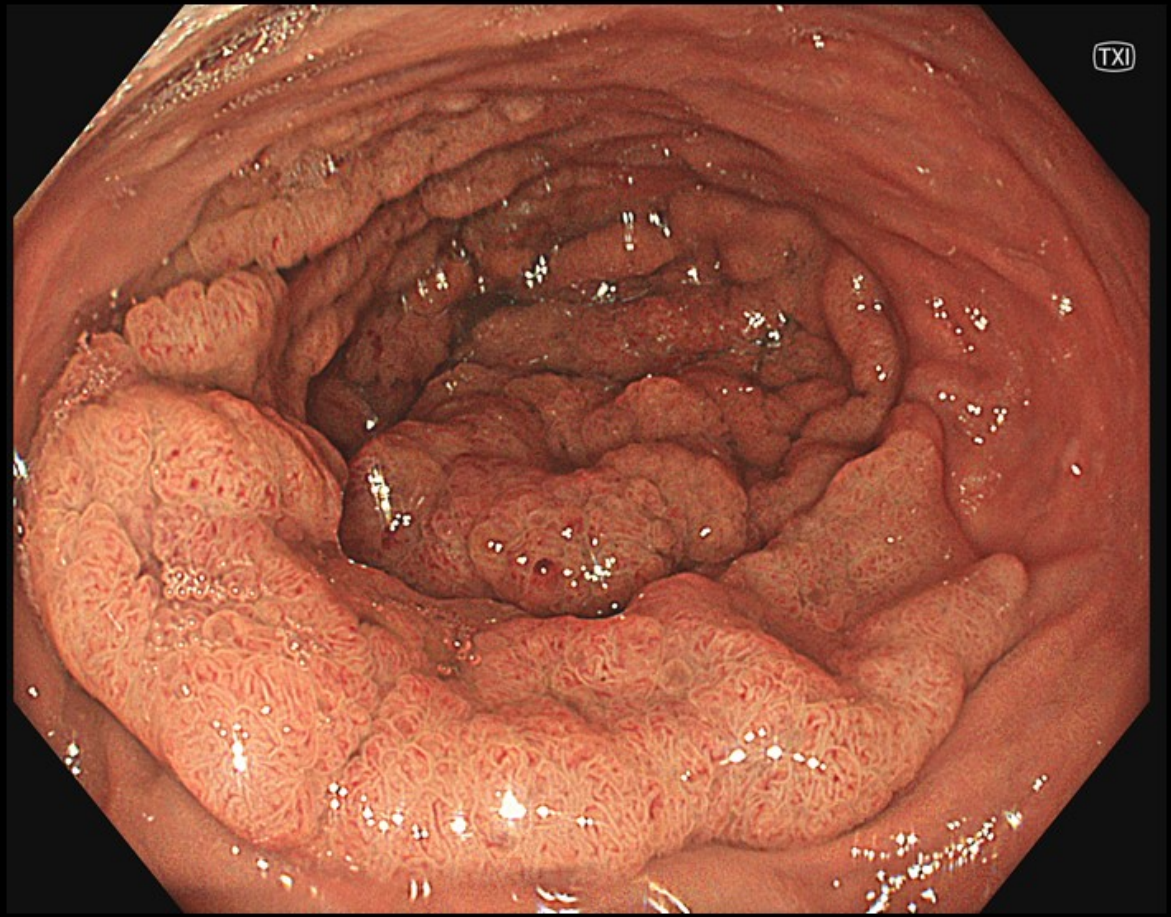
ESD-Rectum

GastroZentrum Hirslanden Zürich

- 1.rectal ESD: 8.5.2009
- n = 160 f79/m81(complex rectal polyps, NET, AIN III, others)
- n = 144 f70/m74(complex rectal polyps)
- Age: 67.8 (27-92)

- En bloc resection: 132/144 (91%)
- R0 resection: 114/144 (79%)
- Failed „en bloc“, final piece meal: 7 (4.8%)
- Incomplete ESD: 5 (3.4%) (severe fibrosis:2, tumor infiltration :3)
- Complications: 6 (4.1%) (rebleeding: 5, perforation: 1)

- Procedure time: 177 min (40-480)
- Specimen size: 5.9 cm (2-17cm)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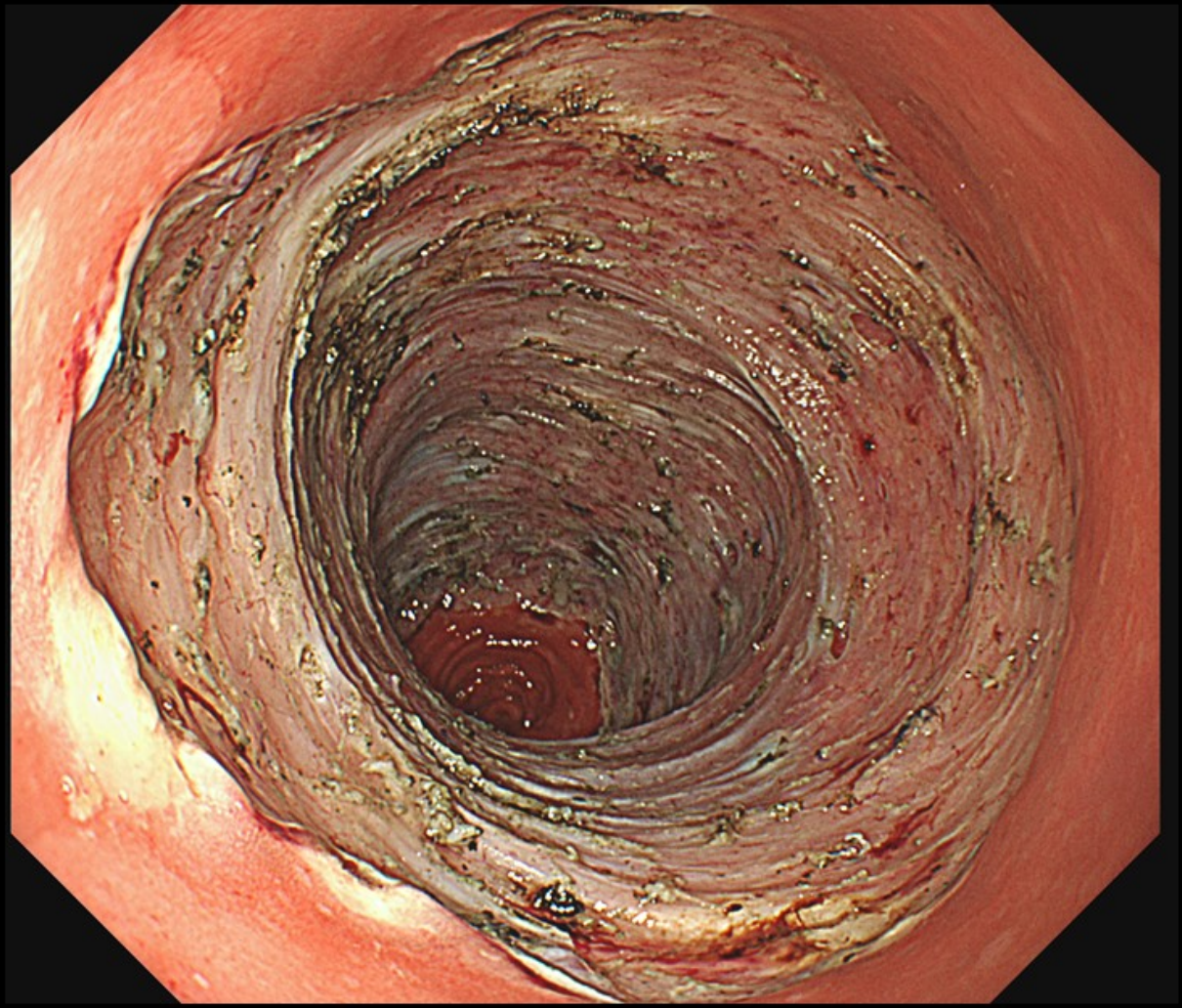
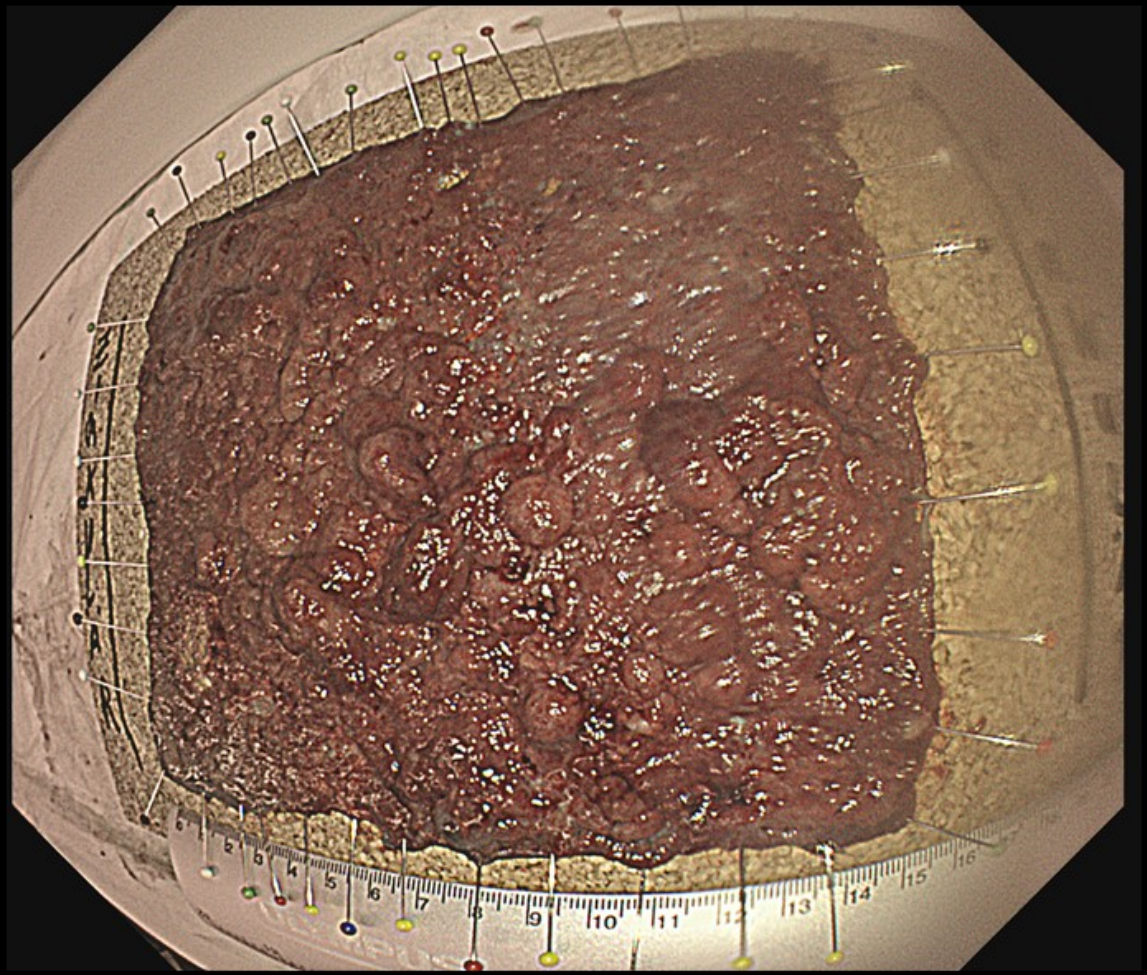
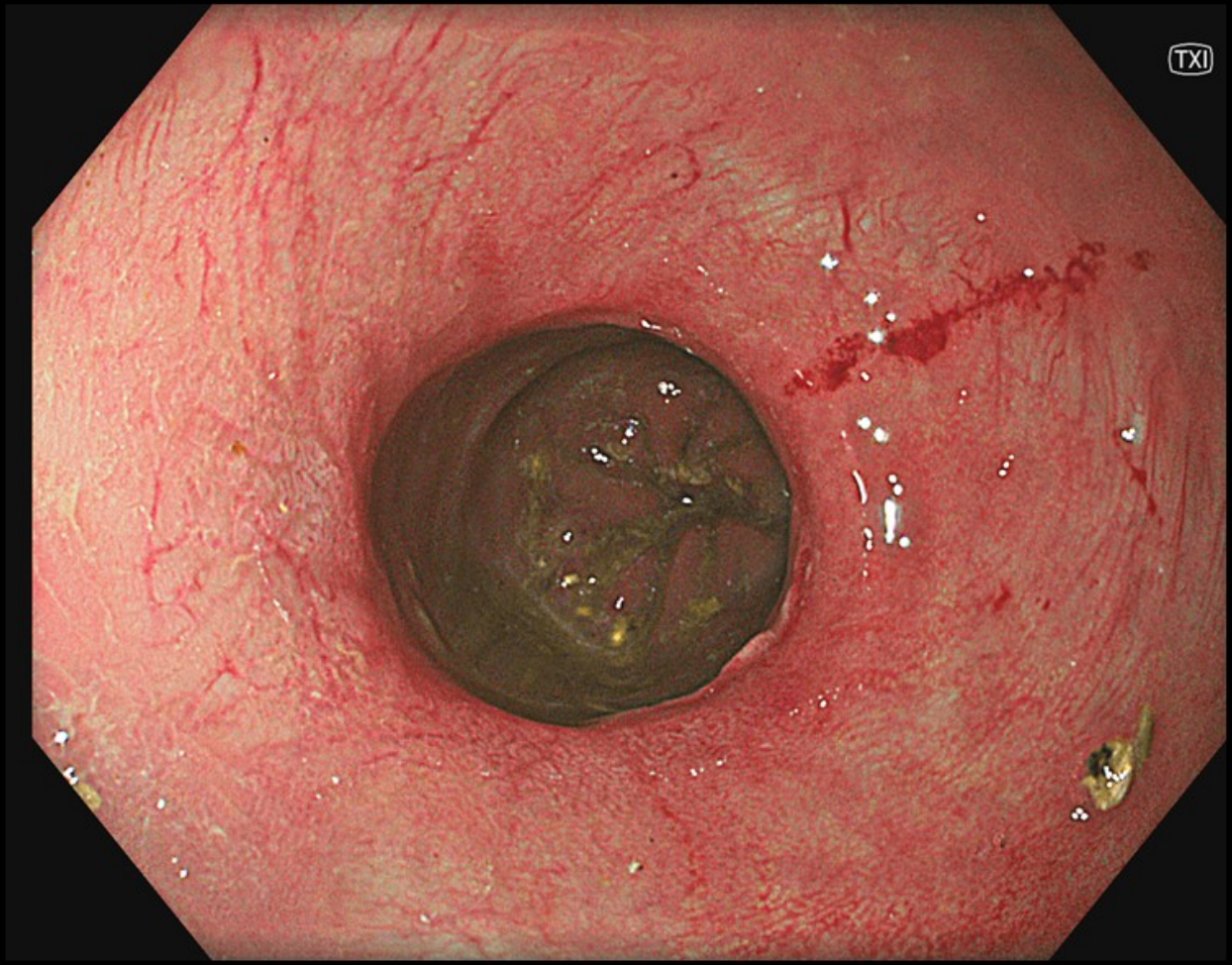




17 x 14 cm, LGIN (80%) HGIN (20%), R0



Follow up 6 Mo later

ESD-Rectum

GastroZentrum Hirslanden Zürich

- n = 144 (complex rectal polyps)
- Histology:
    - Low Grade Dysplasia: 63 (43 %)
    - High Grade Dysplasie: 49 (34%)
    - Invasive Cancer: 32 (22%)

ESD-Rectum

GastroZentrum Hirslanden Zürich

- n = 144 (complex rectal polyps)
- Invasive Cancer : 32 (22%)
  - R0 resection: 25 (78%)
  - Curative resection (pT1 sm1 L0 V0 G1-2 R0) : 11 (34%)
  - Noncurative R0 resection (pT1 sm2-3 LX VX GX R0) : 13 (40%)
  - Lymphovascular invasion: 7 (21%)
  - Deep sm invasion R1: 7 (21%)
  - Surgery: 12 (37%)

J Gastroenterol
https://doi.org/10.1007/s00535-019-01566-y

The Japanese Society of Gastroenterology

ORIGINAL ARTICLE—ALIMENTARY TRACT

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

Chihiro Yasue[1] · Akiko Chino[1] · Manabu Takamatsu[2] · Ken Namikawa[1] · Daisuke Ide[1] · Shoichi Saito[1] · Masahiro Igarashi[1] · Junko Fujisaki[1]

Received: 13 December 2018 / Accepted: 20 February 2019

Abstract

Background Determining the depth of invasion of early stage colorectal cancer has been emphasized as a means of improving endoscopic diagnostic accuracy. Recent studies have focused on other pathological risk factors for lymph node metastasis (LNM). We investigated the significance of depth of invasion and predictive properties of other endoscopic findings.

Methods We retrospectively investigated 846 patients with submucosal invasive (T1) colorectal cancer who received an accurate pathological diagnosis and were treated between January 2005 and December 2016. Pathological risk factors associated with LNM were reviewed. We divided patients into groups: low-risk T1 colorectal cancer (LRC; no risk factors) and high-risk T1 colorectal cancer (HRC; exhibiting lymphovascular invasion, tumor budding grade of 2/3, and/or poor differentiation) and studied predictive endoscopic factors for HRC.

Results Significant risk factors for LNM in multivariate analysis were lymphovascular invasion [odds ratio (OR) 8.09; 95% confidence interval (CI) 3.84–17.1], tumor budding (OR 1.89; 95% CI 1.09–3.29), and histological differentiation (OR 2.09; 95% CI 1.12–3.89). The LNM-positive rate with only deep submucosal invasion was 1.6%. Significant predictive factors for HRC in multivariate analysis identified rectal tumor location (OR 1.92; 95% CI 1.35–2.72, depression (OR 2.73; 95% CI 1.96–3.80), protuberance within the depression (OR 2.58; 95% CI 1.39–4.78), expansiveness (OR 2.39; 95% CI 1.27–4.50), and loss of mucosal patterns (OR 1.90; 95% CI 1.20–3.01) as significant factors.

Conclusions Rectal tumor location, depression, protuberance within the depression, expansiveness, and loss of mucosal patterns could be predictive factors for HRC.

Keywords Lymph node metastasis · T1 colorectal cancer · Risk factors for lymph node metastasis

Introduction

Progress in endoscopic systems and technology in recent years has enabled safe and reliable en bloc resection of submucosal invasive (T1) colorectal cancer with a resulting increase in the number of such procedures [1–3]. In Japan, when performing complete en bloc resection with negative resection margins as the treatment plan after endoscopic therapeutic resection for T1 colorectal cancer, additional surgical resection with lymph node dissection is considered if one of the following is found: (1) depth of invasion (DI) ≥ 1000 μm; (2) lymphovascular invasion (LVI) positive; (3) tumor budding (TB) grade 2/3; and/or (4) poorly differentiated adenocarcinoma/signet-ring cell carcinoma/mucinous carcinoma (POR) histological differentiation [4–11]. However, the overall rate of lymph node metastasis (LNM) with T1 colorectal cancer is about 10%; therefore, additional surgical resection may be unnecessary for most patients [12–17].

According to recent reports, the frequency of LNM is about 1–2%, even with DI ≥ 1000 μm, as long as the other risk factors are negative; the risk factors for DI should be

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Risk factors for LNM

1. LV invasion
   - OR 8.09; 95% CI 3.84 - 17.1
2. Tumor budding
   - OR 1.89 ; 95% CI 1.09 - 3.29
3. Histological differentiation
   - OR 2.09; 95% CI 1.12 - 3.89

LNM + rate w/ only deep sm invasion: 1.6%

n = 846

Yasue C et al; ***J Gastroenterol 2019***; 54: 708

ORIGINAL ARTICLE

Lymphovascular Infiltration, Not Depth of Invasion, is the Critical Risk Factor of Metastases in Early Colorectal Cancer

Retrospective Population-based Cohort Study on Prospectively Collected Data, Including Validation

Carl-Fredrik Rönnow, MD, PhD, Victoria Arthursson, MD,* Ervin Toth, MD, PhD,† Peter-Martin Krarup, MD, PhD,‡ Ingvar Syk, MD, PhD,* and Henrik Thorlacius, MD, PhD*✉*

Objective: To identify clinical and histopathological risk factors of LNM in T1 CRC.

Summary of Background Data: The requisite of additional surgery after locally resected T1 CRC is dependent on the risk of LNM. Depth of submucosal invasion is used as a key predictor of lymphatic metastases although data are conflicting on its actual impact.

Methods: Retrospective population-based cohort study on prospectively collected data on all patients with T1 CRC undergoing surgical resection in Sweden, 2009–2017 and Denmark 2016–2018. The Danish cohort was used for validation. Potential risk factors of LNM investigated were; age, sex, tumor location, submucosal invasion, grade of differentiation, mucinous subtype, lymphovascular, and perineural invasion.

Results: One hundred fifty out of the 1439 included patients (10%) had LNM. LVI ($P < 0.001$), perineural invasion ($P < 0.001$), mucinous subtype ($P = 0.006$), and age <60 years ($P < 0.001$) were identified as independent risk factors whereas deep submucosal invasion was only a dependent ($P = 0.025$) risk factor and not significant in multivariate analysis ($P = 0.075$). The incidence of LNM was 51/882 (6%) in absence of the independent risk factors. The Danish validation cohort, confirmed our findings regarding the role of submucosal invasion, LVI, and age.

Conclusions: This is a large study on LNM in T1 CRC, including validation, showing that LVI and perineural invasion, mucinous subtype, and low age constitute independent risk factors, whereas depth of submucosal invasion is not an independent risk factor of LNM. Thus, our findings provide a useful basis for management of patients after local excision of early CRC.

Keywords: colorectal cancer, endoscopic resection, lymph node metastases

(*Ann Surg* 2022;275:e148–e154)

Implementation of screening programs and advances in minimal invasive techniques, such as flexible endoscopic resection and transanal endoscopic microsurgery, have increased the proportion of early colorectal cancers (CRCs) amenable to local excision.[1,2] For example, endoscopic submucosal dissection has been shown to allow a high degree of R0 resections of early malignant lesions in the colon and rectum.[3,4] Local excision is associated with decreased morbidity, mortality, and reduced overall costs and better functional outcome in comparison to surgical resection.[5–8] Local excision of early CRC poses a significant challenge for the clinicians to predict risk of lymph node metastases (LNM), which influences the decision to perform additional surgery. However, these advantages must be weighed against the potential risk of leaving involved lymph nodes behind. In general, studies have shown that the incidence of LNM in T1 CRC ranges between 6% and 17%.[9–12] Thus, identification of clinical and histopathological features determining risk of metastatic disease in regional lymphatics is critical in management of patients after local excision of malignant lesions in the colon and rectum.

The European Society of Gastrointestinal Endoscopy recommends additional surgery after radical local excision of T1 CRC if 1 or more of the following histopathological features are present; deep submucosal invasion (>Sm1), lymphovascular involvement (LVI), tumor budding, and poor differentiation.[13] These recommendations are based on studies containing relatively few patients and only 3 studies contained more than 300 patients.[14] Based on the European Society of Gastrointestinal Endoscopys recommendations, one of the most commonly used factors to guide decision making after removal of T1 CRC has been depth of submucosal invasion according to the Sm classification (Sm1–3).[13,15] Thus, invasion beyond Sm1 or deeper than 1000 μm has become standard to recommend surgery after local R0 resection of T1 CRC. This concept has recently been questioned by studies reporting that depth of submucosal invasion is not an independent risk factor of LNM in T1 CRC.[12,16–19] Moreover, several studies have reported very low incidence of LNM regardless of depth of submucosal invasion in lesions lacking other histopathological risk factors.[20–24] In this context, it is interesting to note that depth of submucosal invasion might be of limited clinical value knowing that more than 60% of T1 CRC without LNM have invaded more than 1000 μm into the submucosa.[25] New research has revealed that width and area of submucosal invasion might be better predictors of LNM than depth of invasion, which could be related to the vascular anatomy of the submucosal space.[26,27]

Based on the considerations above, the aim of this study was to determine clinical and histopathological factors related to LNM in a large nationwide cohort using multivariate analysis to provide valid support for management of patients with early CRC.

METHODS

Patients

The Swedish Colorectal Cancer Registry (SCRCR) is a national quality registry containing prospectively collected data on rectal cancers from 1995 and colon cancers from 2007 and onwards.

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	Sm1	Sm2	Sm3	Total
Sm invasion only	17 / 336 (5.1%)	21 / 240 (8.8%)	36 / 424 (8.5%)	74 / 1000 (7.4%)
LVI only	7 / 21 (33.3%)	5 / 11 (45.5%)	16 / 40 (40%)	28 / 72 (38.9)
Perineural invasion only	1 / 1 (100%)	1 / 2 (50%)	2 / 4 (50%)	4 / 7 (57.1%)
Mucinous subtype only	1 / 16 (6.3%)	2 / 10 (20%)	5 / 30 (16.7)	8 / 56 (14.3%)
High-grade only	1 / 17 (5.9%)	0 / 11 (0%)	2 / 25 (8%)	3 / 53 (5.7%)

n=1439

Rönnow CF et al; ***Ann Surg 2022***; 275(1): 83e148

ORIGINAL ARTICLE

Lymphovascular Infiltration, Not Depth of Invasion, is the Critical Risk Factor of Metastases in Early Colorectal Cancer

Retrospective Population-based Cohort Study on Prospectively Collected Data, Including Validation

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Objective: To identify clinical and histopathological risk factors of LNM in T1 CRC.

Summary of Background Data: The requisite of additional surgery after locally resected T1 CRC is dependent on the risk of LNM. Depth of submucosal invasion is used as a key predictor of lymphatic metastases although data are conflicting on its actual impact.

Methods: Retrospective population-based cohort study on prospectively collected data on all patients with T1 CRC undergoing surgical resection in Sweden, 2009–2017 and Denmark 2016–2018. The Danish cohort was used for validation. Potential risk factors of LNM investigated were; age, sex, tumor location, submucosal invasion, grade of differentiation, mucinous subtype, lymphovascular, and perineural invasion.

Results: One hundred fifty out of the 1439 included patients (10%) had LNM. LVI ($P < 0.001$), perineural invasion ($P < 0.001$), mucinous subtype ($P = 0.006$), and age <60 years ($P < 0.001$) were identified as independent risk factors whereas deep submucosal invasion was only a dependent ($P = 0.025$) risk factor and not significant in multivariate analysis ($P = 0.075$). The incidence of LNM was 51/882 (6%) in absence of the independent risk factors. The Danish validation cohort, confirmed our findings regarding the role of submucosal invasion, LVI, and age.

Conclusions: This is a large study on LNM in T1 CRC, including validation, showing that LVI and perineural invasion, mucinous subtype, and low age constitute independent risk factors, whereas depth of submucosal invasion is not an independent risk factor of LNM. Thus, our findings provide a useful basis for management of patients after local excision of early CRC.

Keywords: colorectal cancer, endoscopic resection, lymph node metastases

(*Ann Surg* 2022;275:e148–e154)

Implementation of screening programs and advances in minimal invasive techniques, such as flexible endoscopic resection and transanal endoscopic microsurgery, have increased the proportion of early colorectal cancers (CRCs) amenable to local excision.[1,2] For example, endoscopic submucosal dissection has been shown to allow a high degree of R0 resections of early malignant lesions in the colon and rectum.[3,4] Local excision is associated with decreased morbidity, mortality, and reduced overall costs and better functional outcome in comparison to surgical resection.[5–8] Local excision of early CRC poses a significant challenge for the clinicians to predict risk of lymph node metastases (LNM), which influences the decision to perform additional surgery. However, these advantages must be weighed against the potential risk of leaving involved lymph nodes behind. In general, studies have shown that the incidence of LNM in T1 CRC ranges between 6% and 17%.[9–12] Thus, identification of clinical and histopathological features determining risk of metastatic disease in regional lymphatics is critical in management of patients after local excision of malignant lesions in the colon and rectum.

The European Society of Gastrointestinal Endoscopy recommends additional surgery after radical local excision of T1 CRC if 1 or more of the following histopathological features are present; deep submucosal invasion (>Sm1), lymphovascular involvement (LVI), tumor budding, and poor differentiation.[13] These recommendations are based on studies containing relatively few patients and only 3 studies contained more than 300 patients.[14] Based on the European Society of Gastrointestinal Endoscopys recommendations, one of the most commonly used factors to guide decision making after removal of T1 CRC has been depth of submucosal invasion according to the Sm classification (Sm1–3),[13,15] Thus, invasion beyond Sm1 or deeper than 1000 μm has become standard to recommend surgery after local R0 resection of T1 CRC. This concept has recently been questioned by studies reporting that depth of submucosal invasion is not an independent risk factor of LNM in T1 CRC.[12,16–19] Moreover, several studies have reported very low incidence of LNM regardless of depth of submucosal invasion in lesions lacking other histopathological risk factors.[20–24] In this context, it is interesting to note that depth of submucosal invasion might be of limited clinical value knowing that more than 60% of T1 CRC without LNM have invaded more than 1000 μm into the submucosa.[25] New research has revealed that width and area of submucosal invasion might be better predictors of LNM than depth of invasion, which could be related to the vascular anatomy of the submucosal space.[26,27]

Based on the considerations above, the aim of this study was to determine clinical and histopathological factors related to LNM in a large nationwide cohort using multivariate analysis to provide valid support for management of patients with early CRC.

METHODS

Patients

The Swedish Colorectal Cancer Registry (SCRCR) is a national quality registry containing prospectively collected data on rectal cancers from 1995 and colon cancers from 2007 and onwards.

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	LN metastasis
No significant risk factors	77 / 1053 (7.3%)
Adjusted for age	
< 50 yr	8 / 48 (16.7%)
50 – 59 yr	18 / 123 (14.6%)
60 – 69 yr	15 / 264 (5.7%)
70 – 79 yr	22 / 391 (5.6%)
≥ 80 yr	14 / 227 (6.2%)

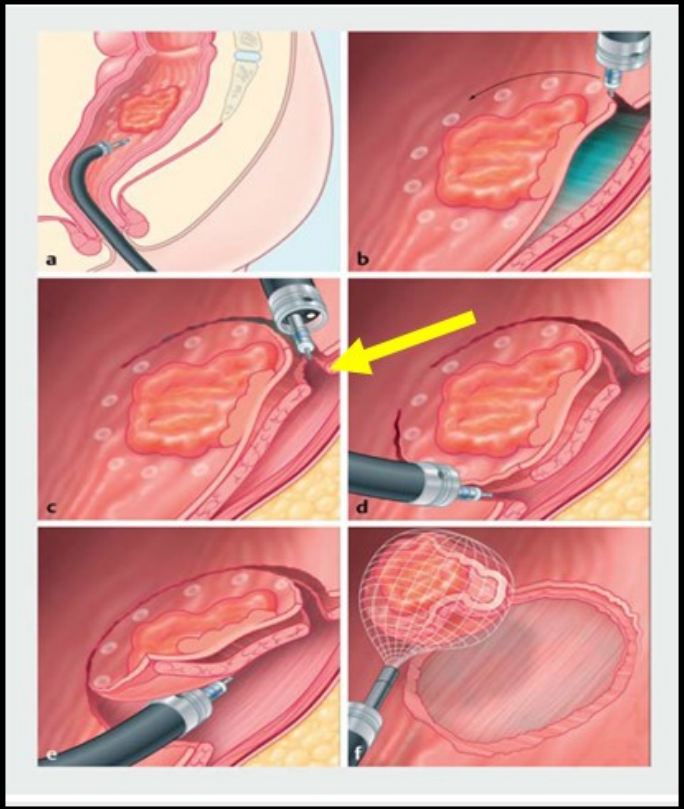
n=1439

Rönnow CF et al; ***Ann Surg 2022***; 275(1): 83e148

Resection techniques

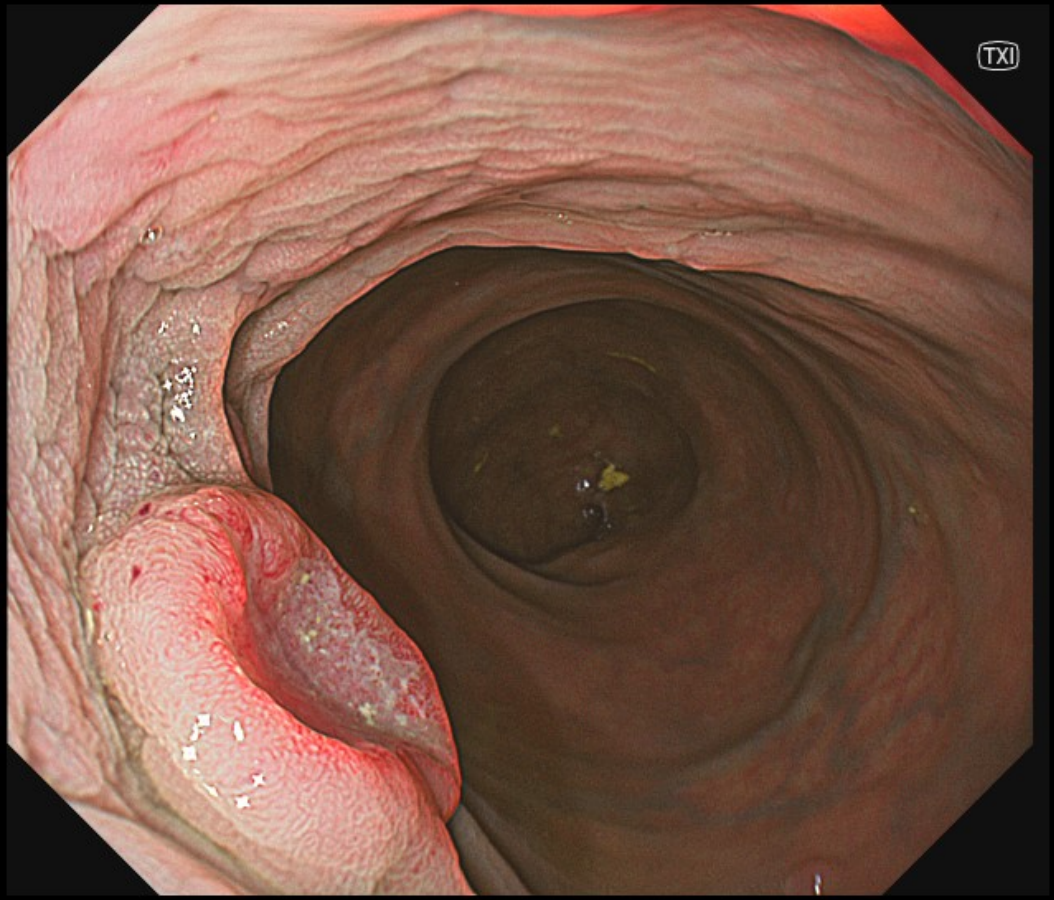
- EMR
- FTRD
- ESD
- Hybrid ESD (EMR + ESD)
- EID Endoscopic intermuscular dissection
- TAMIS Transanal minimally invasive surgery
- TEM Trananal endoscopic microsurgery
- TEO Transanal endoscopic operation

Endoscopic intermuscular dissection EID

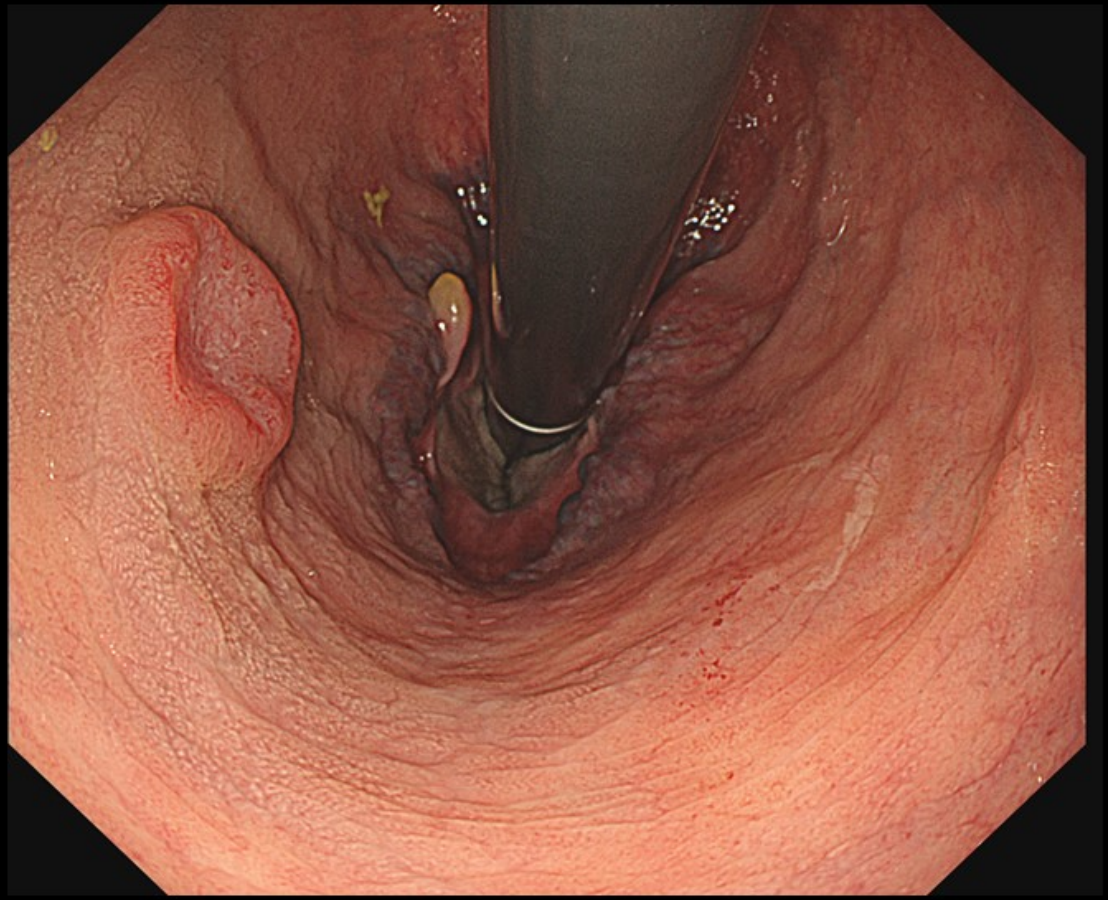


- Risk of LN metastasis associated with deep sm invasion should be balanced against mortality and morbidity of TME
- Dissection between the circular & the longitunal part of M. propria
- R0 resection of deep sm ca is possible with intact rectal wall

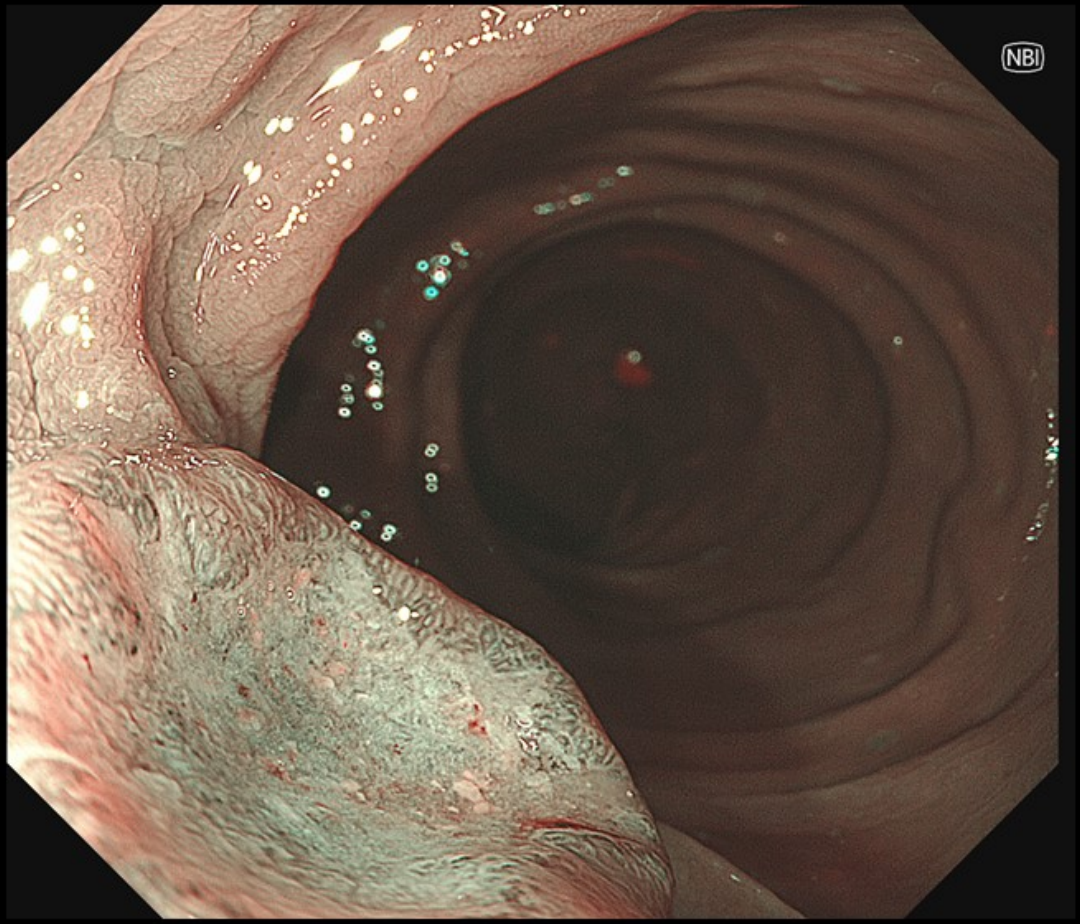
Toyonaga T et al. ***Endoscopy 2018***; 50: 813
Moons L et al. ***Endoscopy 2022***; 54: 993
Dang H et al; ***VideoGIE 2022***; 7(8): 273



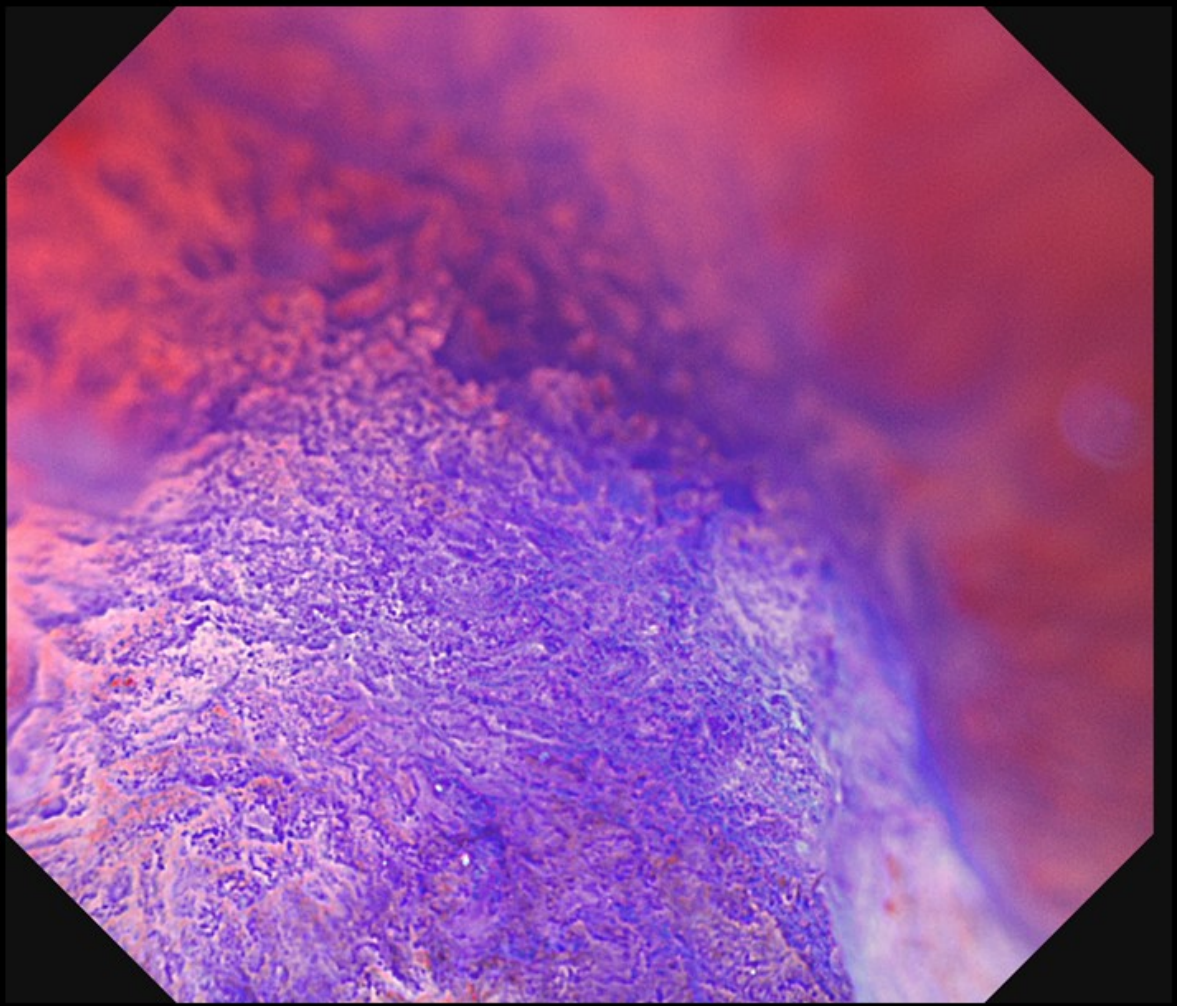
0-IIc lesion



0-IIc lesion

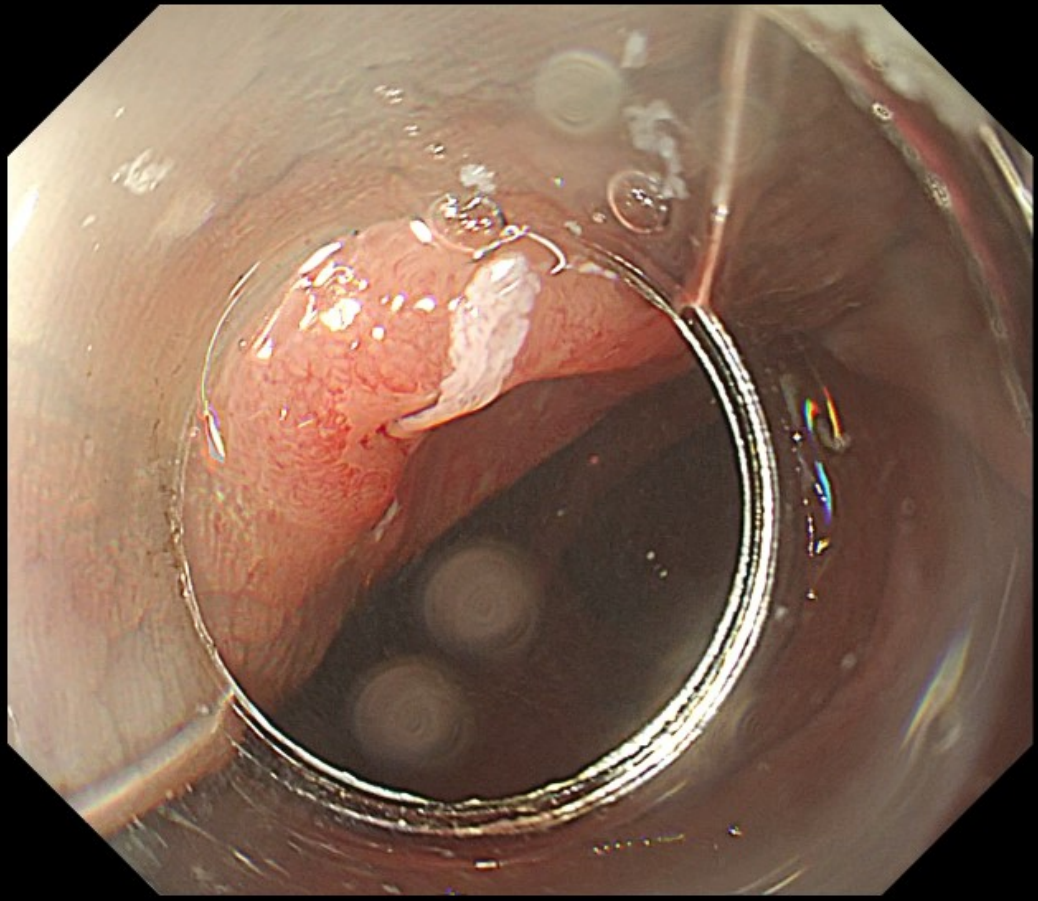


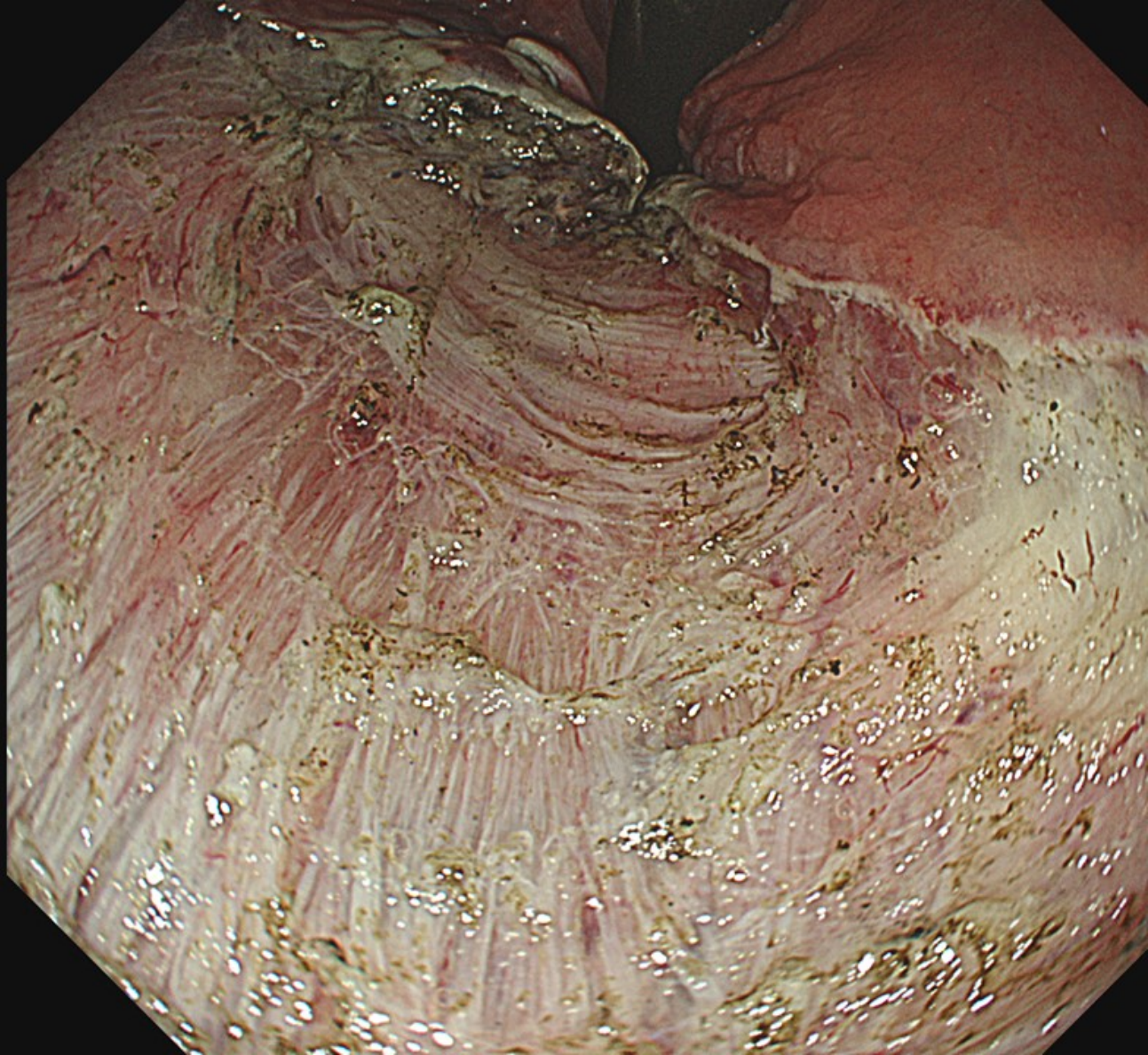
0-IIc lesion, JNET Typ 2B

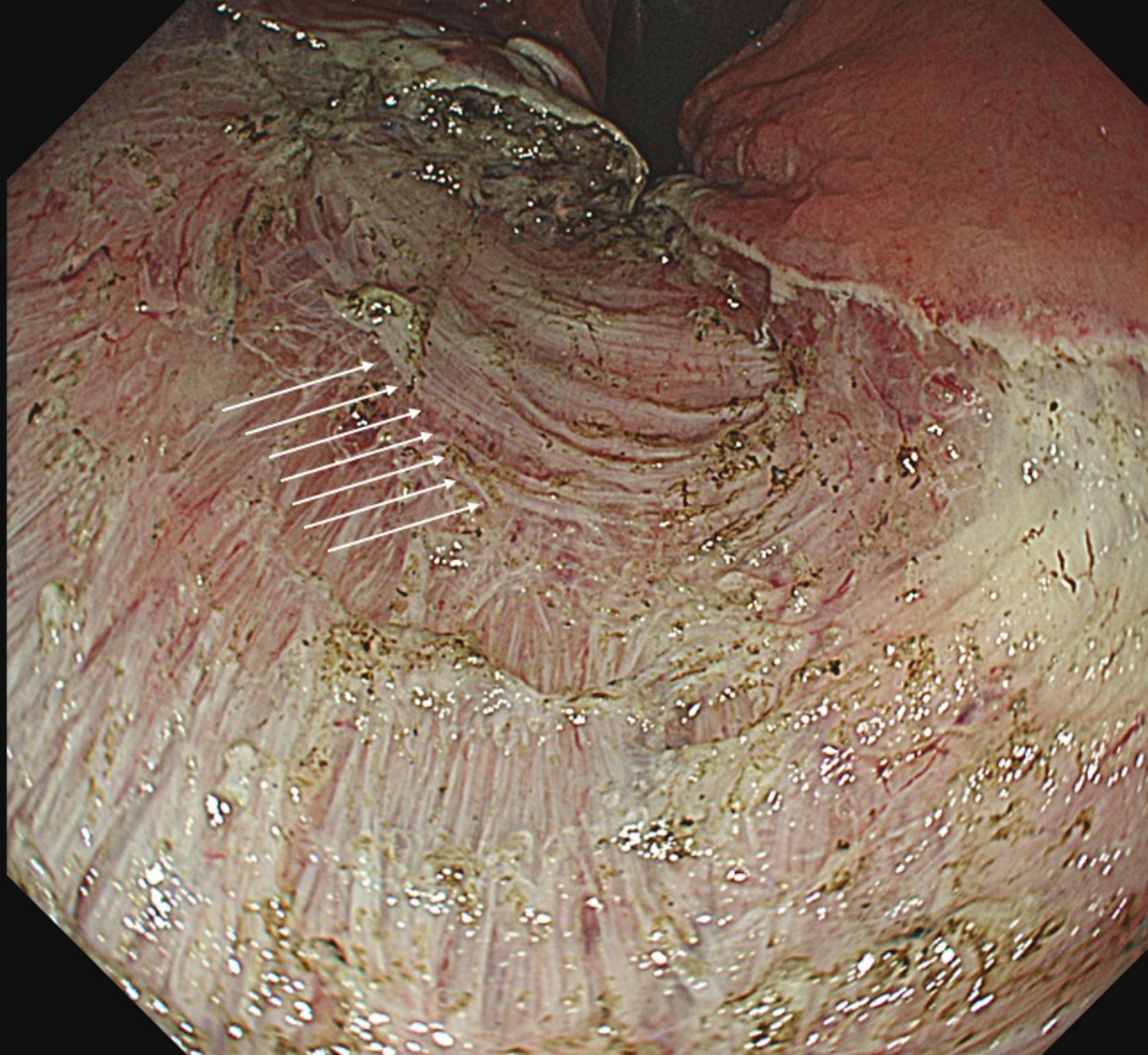


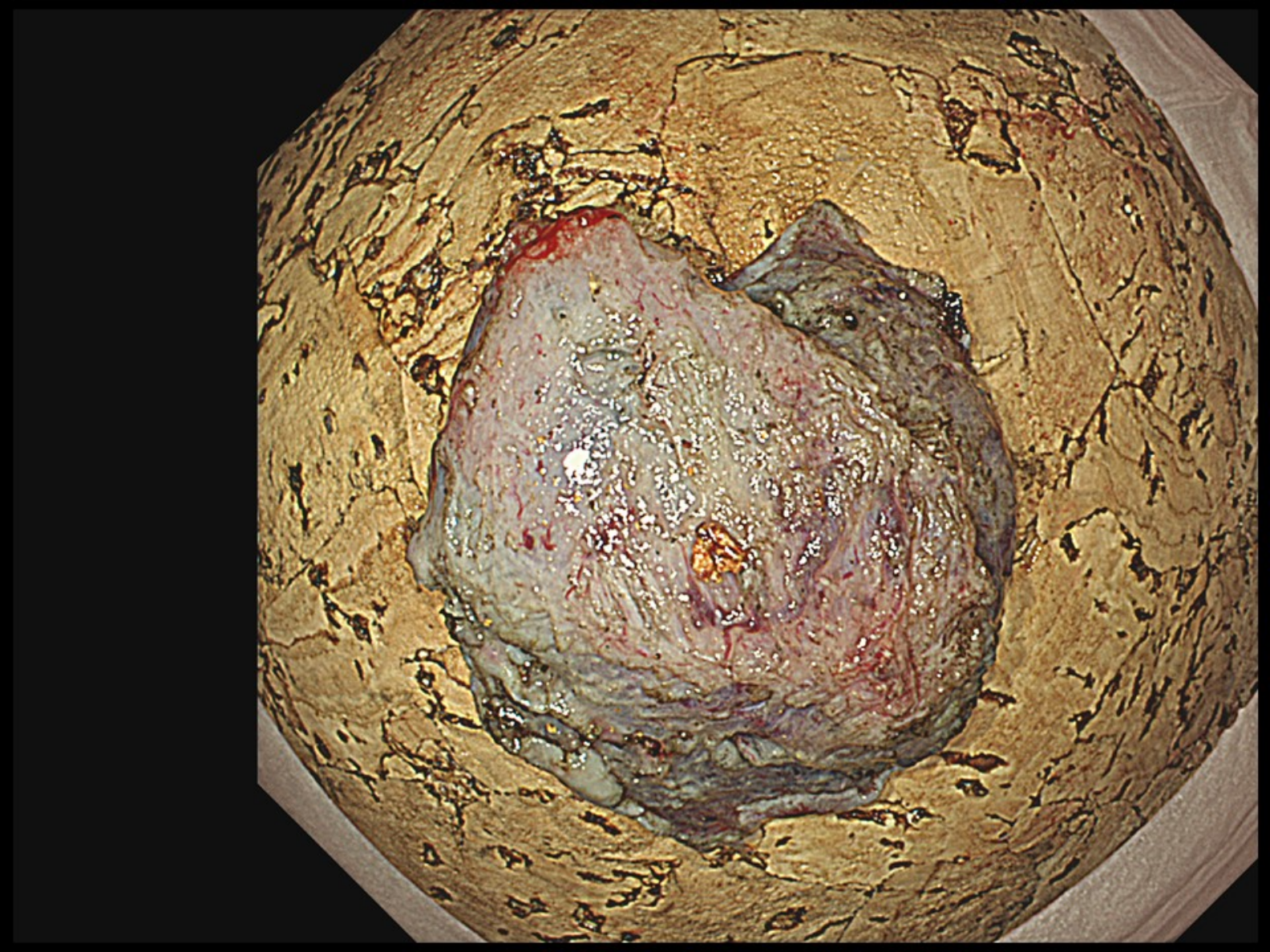
0-IIc lesion, JNET Typ 2B, V_N

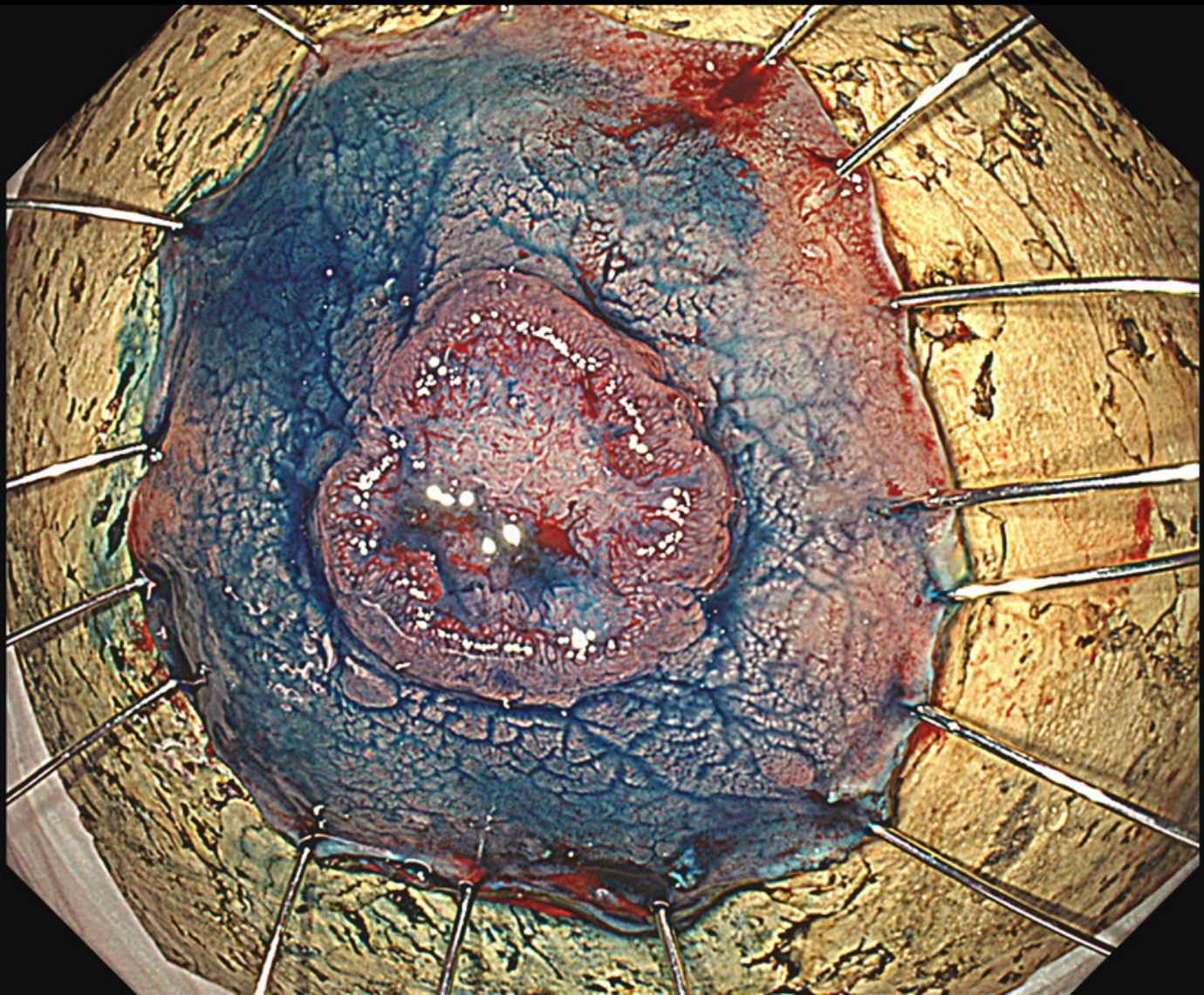
Endoscopic intermuscular dissection EID



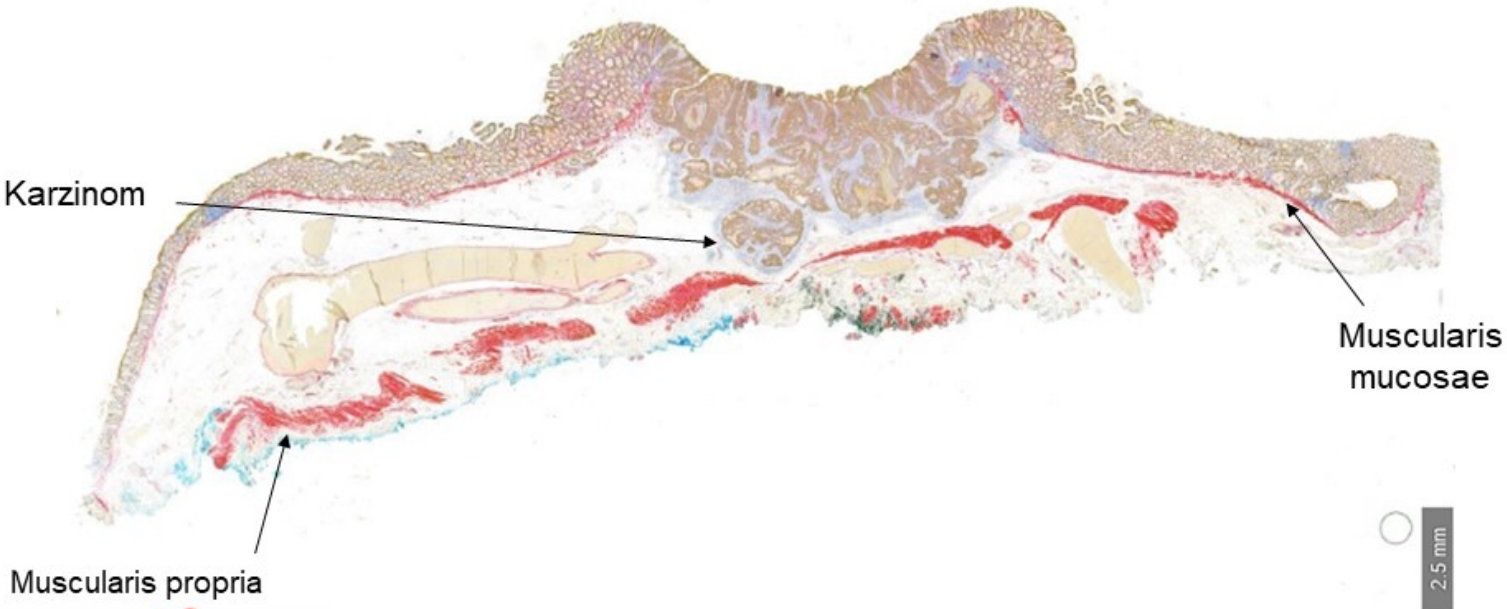








Histology



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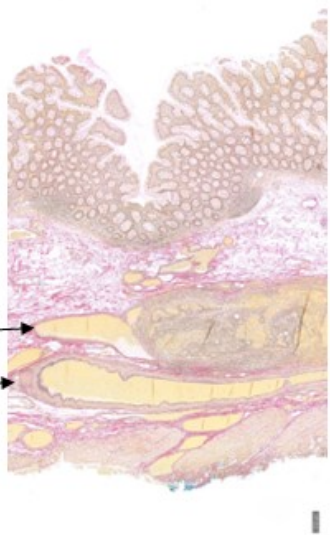
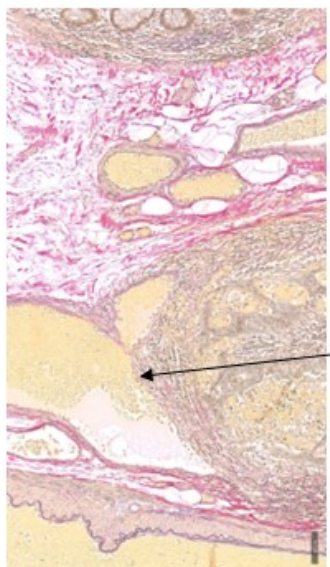
Panzytokeratin braun
(epithelialer Marker)

Desmin Rot
(muskulärer Marker)

PD Dr. Ewerton Maggio

Histology





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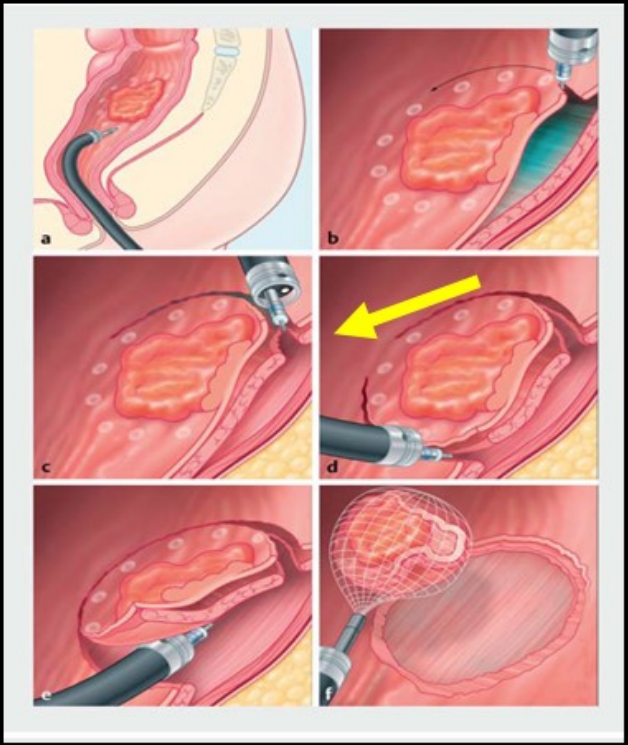
Elastin van Gieson

pT1 (sm3) (4000 µm) G2 L0 V1 Pn0 R0 (narrow) (VM-, HM-)

PD Dr. Ewerton Maggio

Endoscopic intermuscular dissection EID



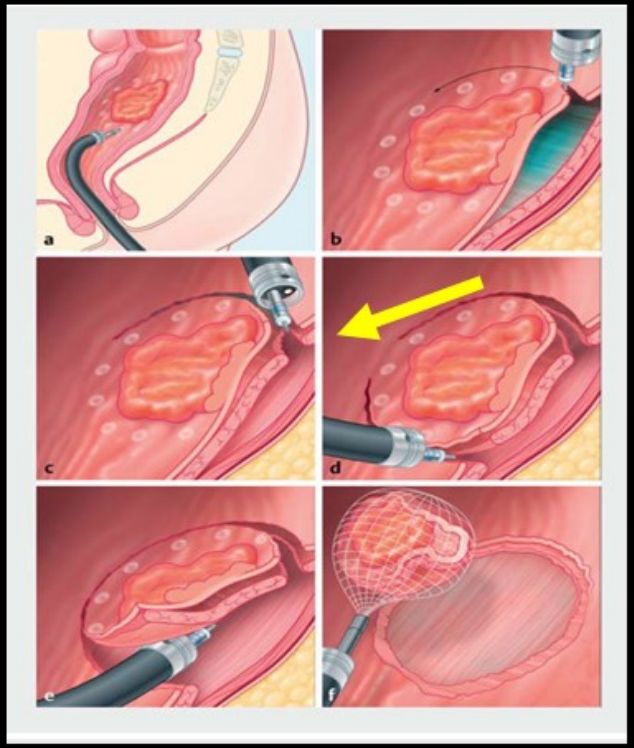
- n=67
- median lesion size: 25 mm (20-33)
- Technical success (en bloc): 96%

- EID achieved in 56/64 (88%)
- Failure to indentify the intermuscular plane: 3 (4%)

- Partial full thickness resection: 8 (12%)
- Focal accidental injury of longitunal muscles: 8 (12%)
- Minor adverse events: 8 (12%)

Moons L et al. ***Endoscopy 2022***; 54: 993

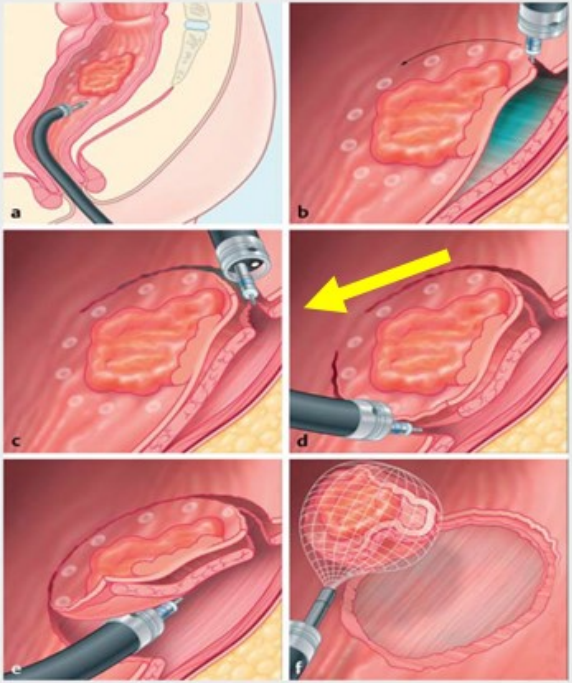
Endoscopic intermuscular dissection EID



Parameters	n/N (%)
Depth of invasion	
• Tis	8 / 67 (12%)
• sm1	5 / 67 (8%)
• sm2	13 / 67 (19%)
• sm3	27 / 67 (40%)
• T2	14 / 67 (21%)
Histological risk factors	
• Lymphovascular invasion	30 / 67 (45%)
• High grade tumor budding	19 / 67 (28%)
• Poor differentiation	7 / 67 (7%)

Moons L et al. ***Endoscopy 2022***; 54: 993

Endoscopic intermuscular dissection EID



R0 rate	
• Overall	54 / 67 (81%)
• Technical successful cases	54 / 64 (84%)
• pT1	41 / 45 (91%)
• pT1 w/ deep Sm invasion	36 / 40 (90%)
Curative resection rate	
• Overall	30 / 67 (45%)
• Technical successful cases	30 / 64 (47%)
• pT1	22 / 45 (49%)
• pT1 w/ deep sm invasion	18 / 40 (45%)

Moons L et al. ***Endoscopy 2022***; 54: 993

Intermuscular dissection

- EIS or TAMIS
- Promising technique for deep sm invasive T1ca
- T1 - clear margins and potentially curative
- Superficial T2 - deep margin still adequate
- Rectum wall keeps intact
- No risk of compromising the surgical plane

Spinelli A Dis Colon Rectum 2021;64: 17-18

Rectal cancer in 2023

How far can we go with local resection?

Prospective multicenter data collections necessary

Controversy questions:

- R0 resected case with deep sm invasion L0 V0?
- R0 resected cases with L0 V1?
- R1 resected cases in elderly?*

*Spadaccini M et al. ***GUT 2022***;71:1998

Rectal cancer in 2023

How far can we go with local resection?

Challanges for diagnostic endosocpy

- Prediction of lymphovascular invasion
- Optical diagnosis for differentiation of T1 and T2
- AI? *

*Kudo S et al. ***Gastroenterology 2021***;160:1075

More infos coming soon!

EndoSwiss Live

23.-24 June 2023 Zurich