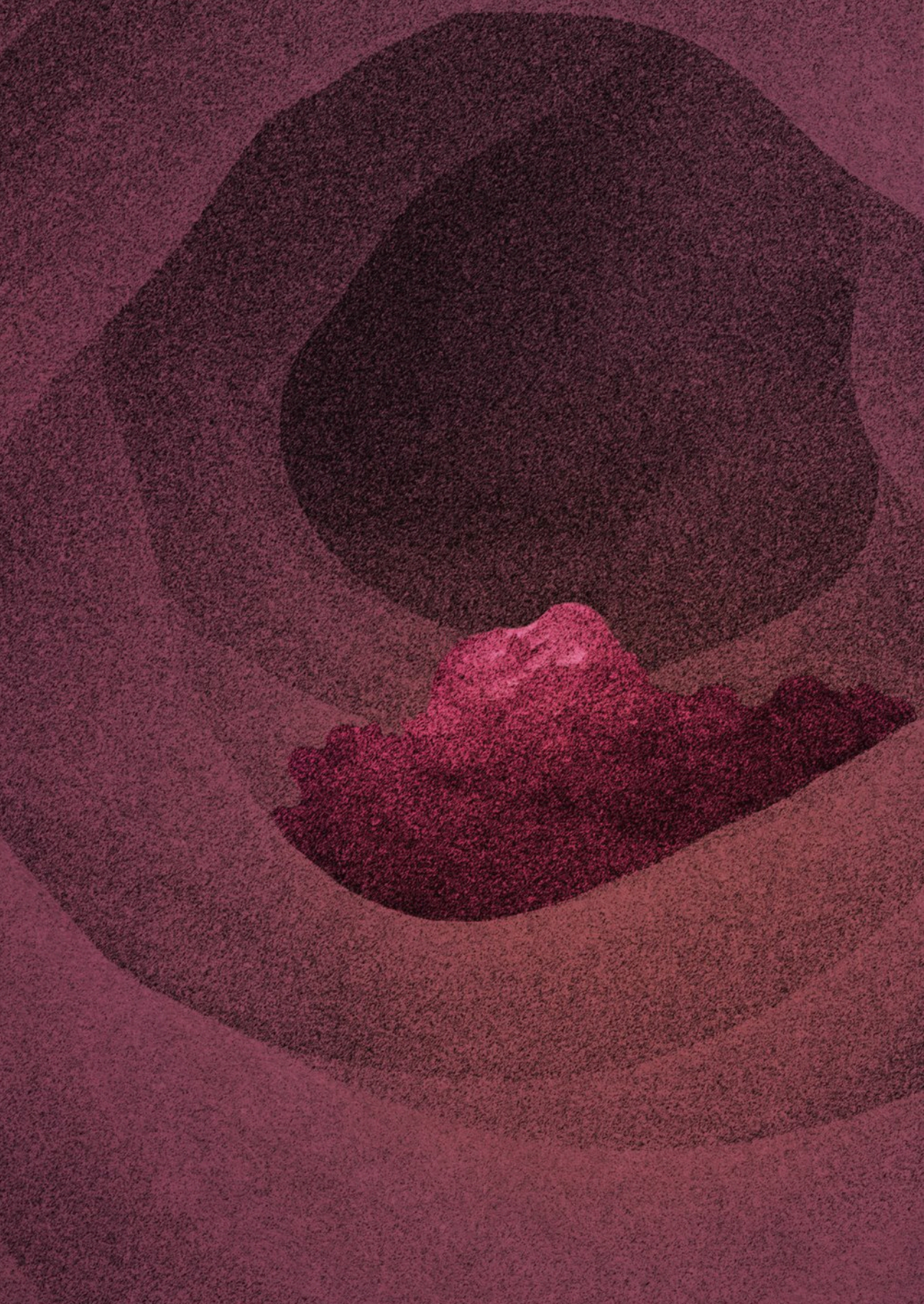
Advancing patient-centered care in the management of large rectal adenomas and T1 colorectal cancer

Dekkers, N.



CHAPTER 1

General introduction and thesis outline

General introduction

Colorectal cancer

Colorectal cancer (CRC) is one of the most frequently diagnosed cancers, and the second leading cause of cancer-related mortality worldwide.[1] In 2023, approximately 12,000 patients in the Netherlands were diagnosed with CRC, about 3,000 of whom had rectal cancer.[2] CRC develops from benign precursor lesions, following either the adenomatous or, less commonly, the serrated pathway.[3] While all precursor lesions carry malignant potential, only a subset progress to invasive cancer by invading through the muscularis mucosae, potentially extending into the bowel wall, and eventually even metastasizing to other organs. The progression from normal epithelium to CRC typically takes between 10 and 15 years, providing a valuable window for screening and early treatment.[4]

In recent years, many countries have implemented nationwide screening programs to reduce CRC-related morbidity and mortality by detecting and treating disease at an earlier (pre)malignant stage. The Netherlands introduced such a program in 2014, utilizing fecal immunochemical testing to measure hemoglobin levels in stool samples.[5] If these exceed a set threshold, a colonoscopy is performed. Since the start of the program, colorectal lesions have indeed been diagnosed at earlier benign or premalignant stages in all forms and sizes. When CRC is already present in these asymptomatic patients enrolled in screening, it is found at earlier stages compared to patients referred for colonoscopy due to symptoms.[6] Especially the larger premalignant and early-stage cancers present clinical challenges in terms of diagnosis and management.

Optical diagnosis

The variety of colorectal lesions that can be detected during endoscopy can be categorized in different ways. For example based on their anatomical location (colon or rectum), and based on their size, with lesions larger than 2 cm often defined as large. Another way to categorize colorectal lesions is by shape, for example referring to whether a polyp has a stalk (pedunculated) or not (non-pedunculated). In addition, an assessment can be made of the suspected histology of a lesion, distinguishing between benign, superficial submucosal invasion (so-called superficially invasive T1CRC), and deeper invasion (deep invasive T1CRC or more advanced stages of CRC). This assessment is called optical diagnosis. All these classifications are important, as they help determine the most appropriate way of removing a lesion and thereby preventing progression to (more advanced) CRC.

Optical diagnosis has the greatest treatment implications for larger non-pedunculated lesions, as it guides whether a lesion can be removed in multiple pieces (piecemeal) or requires more elaborate local resection techniques to remove it in one piece (en bloc). When cancer is present, piecemeal resection should be avoided as it impairs accurate histological assessment of resection margins and assessment of the oncological risk, potentially leading to unnecessary major surgery with significant morbidity. This is particularly relevant for rectal cancers, where surgery carries the highest risk of requiring a permanent stoma and sexual dysfunction. This topic will be discussed in more detail later, beginning with an overview of the optical diagnosis of these larger non-pedunculated lesions.

For the optical diagnosis of large non-pedunculated rectal lesions, various modalities are available. The first is conventional white-light endoscopy, which employs standard broad-spectrum light to visualize the mucosal surface, during which the endoscopist should be alert to features that may suggest cancer. This approach enables a structured evaluation of the lesion's size, morphology, and surface characteristics. Size can be estimated using instruments with known dimensions, such as biopsy forceps. Although size alone is a poor predictor, it is independently associated with malignant disease.[7] Morphology is commonly described using the Paris classification. According to this system, non-pedunculated lesions are further categorized as: flat (with less than 2.5 millimeters elevation from the mucosa), sessile (showing more pronounced elevation), containing a depressed or even excavated component. Depressed areas warrant specific attention, as they may indicate the presence of (early invasive) cancer and excavation is suggestive for deeper invasion(8).[8] Non-pedunculated lesions that predominantly spread laterally along the bowel wall are also referred to as lateral spreading tumors (LSTs). In LSTs the surface texture, also called granularity, should also be evaluated. LSTs can be categorized into granular types, which includes homogeneous and nodular mixed subtypes, and non-granular types, which include flat elevated and pseudodepressed subtypes. The risk for submucosal invasion is lowest for granular homogeneous LSTs (0.5%) and highest for granular nodular mixed (10.5%) and non-granular pseudodepressed types (31.6%).[9] Optical diagnosis with white-light endoscopy alone has a limited sensitivity ranging between 21 and 46%,[10] and should therefore not be used as the sole method.

Advanced imaging techniques can be used to allow for a more detailed evaluation of the lesion's surface. These techniques include dye-based chromoendoscopy and virtual modalities that utilize different wavelengths of light or optical filters, such as the commonly used Narrow-Band Imaging. Using these methods, both the vascular pattern and the pit pattern, referring respectively to the network of blood vessels and the microscopic openings of the mucosal glands, can be assessed. The regularity of these patterns can be interpreted using one of the available classification systems, such as the Hiroshima classification.[11-16] Regardless of the specific classification used, regular

patterns are suggestive of benign histology, whereas irregular patterns may indicate superficially invasive T1CRC. The disruption or absence of surface patterns is generally associated with deeper invasive carcinomas. Overall, narrow-band imaging has been reported to achieve a sensitivity of approximately 85%.[10] However, this estimate is derived from studies involving various lesion types and is likely overestimated in the context or large non-pedunculated lesions. While combining white-light endoscopy with advanced imaging can improve diagnostic performance,[17] the accuracy in this subgroup remains limited. To better address these limitations, the OPTICAL risk model was developed in the Netherlands. This model integrates observations from both modalities into a structured assessment, yielding a reported sensitivity of 78.7%.[18] Despite these advances, a considerable degree of uncertainty in the optical diagnosis remains, underscoring the need for further improvements.

Adding other imaging modalities, such as magnetic resonance imaging or endoscopic ultrasound, appears to be of little added value, as these techniques tend to overstage lesions and thereby increase the risk of overtreatment.[19] Improving education and training may contribute to better diagnostic performance of optical diagnosis, particularly given the substantial variability observed between community level endoscopists and experts.[20] However, even studies conducted in expert centers with dedicated endoscopists have demonstrated a significant risk of optically missed cancers, ranging from 11-22%.[18, 21, 22] This observation suggests that education alone will not be sufficient to achieve adequate diagnostic accuracy. Moreover, this suggests some T1CRCs may lack clear visual signs and therefore remain undetected with current techniques, so-called covert cancers.[23] Besides educational initiatives, new technologies are therefore needed to improve optical diagnosis.

In light of the uncertainty surrounding optical diagnosis, caution is warranted when treating large non-pedunculated lesions, particularly in the rectum, where incorrect piecemeal removal of a cancerous lesion has the most serious consequences for the patient. Accordingly, the current Dutch guideline discourages piecemeal resection for all large rectal lesions, except for homogenous granular lesions where it may be considered, as these carry a negligible risk of malignancy.[24] In such benign lesions, piecemeal removal by piecemeal endoscopic mucosal resection may offer advantages such as the lower complication rates and generally shorter procedure times compared to en bloc resections.[25, 26] However, piecemeal resections are associated with higher recurrence rates ranging between 19 and 29%,[27-29] necessitating more stringent surveillance, which can also justify an en bloc resection of these homogeneous granular type lesions, a strategy that may even be the most cost-effective.[30-32] All other large non-pedunculated rectal lesions should in any case be treated with an en bloc resection, effectively managing them as if they were T1CRC.

T1 colorectal cancer

Early-stage CRC, or T1CRC, is defined according to commonly accepted Western criteria as cancer with histologically confirmed invasion through the muscularis mucosae into, but not beyond, the submucosa. Due to their limited invasion, most T1CRCs can still be removed completely by local, organ-preserving, resections. However, T1CRCs still have the potential to metastasize, primarily to locoregional lymph nodes. If lymph node metastases (LNM) are present, a local resection alone is considered non-curative. Instead, current guidelines recommend a more extensive surgical resection, that includes removal of the affected bowel segment along with the draining lymph nodes, followed by adjuvant systemic therapy in case of colon cancer with histologically confirmed LNM.[33] In rectal cancer, LNM similarly requires more extensive treatment, which may involve (chemo)radiotherapy, radical surgery, or both.

Ideally, preoperative staging would allow for accurate detection of LNM. However, current staging techniques, including optical endoscopic imaging, endoscopic ultrasound, computed tomography and magnetic resonance imaging for rectal lesions, are insufficiently accurate, even when used in combination. The most commonly used risk-model is histology based and can only be applied after resection. This has led to a two-step approach in the management of T1CRC. The local resection, aimed at achieving a complete en bloc resection, is the first step and can be considered a "diagnostic resection". Pathological analysis of the locally resected specimen is then used to determine the need for additional oncological resection, based on the risk of residual disease and LNM. This oncological risk must be carefully weighed against the potential risks associated with additional treatment, or completion surgery, on an individual basis. There is an increased oncological risk if resection margins are positive or uncertain, suggesting potential incomplete resection, or if so-called high-risk features for LNM are present. These features include poor tumor differentiation, high-grade tumor budding, lymphovascular invasion, and deep submucosal invasion.[34] Although not yet included in formal guidelines, a recent study suggests that deep submucosal invasion alone may not be a strong predictor, potentially not justifying additional oncological surgery on its own.[35]

By adopting this two-step approach, extensive surgery and its associated morbidity and mortality can be avoided in patients with a radically resected low-risk T1CRC (i.e., absence of all high-risk features), which is the case in approximately 65-85% of patients with superficially invasive carcinomas and 30-50% of those with deep invasion.[36, 37] Multiple studies have shown the long-term safety of this strategy;[38-40] however, the short-term effects of local endoscopic resections, such as their impact on surgical morbidity, have not been thoroughly investigated. For prior local surgical resections, available literature suggests that they might increase complexity of completion surgery and thereby increase procedure times and complication rates.[41]

Since complete risk stratification requires a complete en bloc resection specimen and incomplete resection always necessitates additional treatment, it is crucial to select an advanced local resection technique that enables complete en bloc removal of lesions suspected to have submucosal invasion.

En bloc resection techniques for large non-pedunculated colorectal lesions

Several flexible endoscopic and local surgical resection techniques are available, allowing for the complete en bloc removal of large non-pedunculated lesions, even with submucosal invasion. The selection of the preferred technique depends on factors such as the lesion's location, size, and available local expertise. Additionally, the expected invasion depth plays a crucial role in determining the technique, as the dissection plane varies between methods.

Endoscopic techniques

Endoscopic submucosal dissection (ESD) is a technique that involves injecting fluid into the submucosa to lift the lesion, making a circumferential incision around the target area, and performing dissection within the submucosal layer just above and parallel to the muscularis propria using an electrosurgical knife introduced via a flexible endoscope.[42, 43] ESD enables radical en bloc resections, even for larger lesions, but its effectiveness is limited for deeply invasive T1CRCs due to the constraints of its dissection plane.[44-46] ESD can technically be performed throughout the entire colon, but in the West, it is primarily used in the rectum due to its relatively higher perforation rate of approximately 4%.[47] The thicker submucosa of the rectum and the typically limited clinical consequences of perforations (i.e., unintended full-thickness defects), which are often manageable with conservative treatment alone, make it a safer site than the proximal colon.[48] In Western countries, ESD is mainly performed in expert centers by dedicated endoscopists, as the lack of adequate training, and perhaps financial compensation, has limited its widespread adoption.[48, 49]

Endoscopic full-thickness resection (eFTR) is a technique that uses a full-thickness resection device that allows for transmural resection of the colonic wall, extending as deep as the serosa.[50] Unlike ESD, eFTR has a clear size limitation of 15-20 mm,[51] making it unsuitable for large lesions. Additionally, maneuvering in the rectum is challenging, making other techniques preferable in this location. Consequently, eFTR is primarily used for smaller non-lifting lesions or those in technically challenging locations, such as near the appendix.[52] Furthermore, eFTR can be used in a hybrid approach in combination with a piecemeal resection for larger lesions, enabling complete removal of the most suspicious part of a larger lesion.[53]

Endoscopic intermuscular dissection (EID), is a relatively new endoscopic resection technique that involves dissection at the deeper intermuscular plane, present in the rectum, as performed more frequently in local surgical resections in the rectum, while still using a flexible endoscope. The first three-year follow-up study shows promising results that EID may offer a viable alternative to radical surgery for some patients with deep invasive carcinomas.[22]

Local surgical techniques

The most commonly used local surgical resection technique in the Netherlands is transanal minimally invasive surgery (TAMIS). For this procedure, a transanal single-incision laparoscopic surgery (SILS) port, CO_2 insufflation to create a pneumorectum, and standard laparoscopic instruments are used to lift and dissect the lesion. TAMIS is exclusively intended for treatment of rectal lesions and can be used to remove those located up to 15-20 cm from the anal verge, allowing for complete en bloc resection regardless of the lesion's size.[54, 55] Ideally, the dissection plane is partial thickness, following the intermuscular plane between the circular and longitudinal layers of the muscularis propria, using a diathermic hook. This approach preserves the integrity of the mesorectal fascia and does not compromise surgical resection planes should completion surgery be required. For lesions near the dentate line, the distal margin can be incised without a port using standard transanal retractors. Transanal endoscopic microsurgery (TEM) is a comparable videoscopic transanal excision technique that is used to a lesser extent due to its reliance on specialized, costly instruments including a TEM scope, and angled instruments.[56] In contrast to TEM, TAMIS allows for more distal dissections due to its shorter port, offers a greater working angle, and may be less traumatic to the anal sphincter.[57, 58]

Preferred techniques for large non-pedunculated rectal lesions

For large non-pedunculated rectal lesions in which submucosal invasion cannot be excluded with certainty based on optical diagnosis, or when (superficially invasive) T1CRC is suspected, the preferred technique is either ESD or TAMIS. Both are considered standard of care and have demonstrated satisfactory long-term outcomes.[59, 60] Due to the lack of large-scale head-to-head comparative trials, these techniques are currently used interchangeably in the Netherlands and the choice between ESD and TAMIS is based more on the clinical team's preference and available expertise than on scientific evidence.

Patient involvement in T1 colorectal cancer care

Medical decision-making is often complex, especially in cancer care, as it involves uncertain evidence, the weighing of potential benefits against possible harms and consideration of the likelihood of different outcomes,[61] while also aligning choices

with individual patient values and preferences. Because of this complexity and the heterogeneity in both clinical factors and personal preferences, it is essential for healthcare providers to actively involve patients in the decision-making process.

Shared decision-making is a collaborative process in healthcare that involves both clinicians and patients working together to make informed treatment decisions. It entails healthcare providers sharing relevant medical information, including potential benefits, risks, and uncertainties, while patients contribute their values, preferences and lifestyle factors.[62] A prerequisite is thus that patients receive clear and comprehensible information, which can be challenging in practice for various reasons. Medical information is often complex, involving multiple considerations and nuances that can be difficult for non-experts to grasp. In addition, the information provided by physicians may not always align with patients' preferences,[63, 64] and in cancer care medical details can be emotionally charged, especially when discussing aspects such as survival or the risk of recurrence.[65]

Although the patient journey of T1CRC involves several complex decisions, such as the choice to perform additional treatment or not after local resection, information provision and decision-making has never been evaluated. Evaluating these processes from patients' perspective can help to identify unmet informational needs and guide more patient-centered care in T1CRC.

Thesis outline

The main goal of the various chapters presented in this thesis is to improve the management of patients with non-pedunculated rectal adenomas and T1CRC through a patient-centered approach. To achieve this, various challenges in optical diagnosis, local treatment, completion surgery, follow-up and decision-making were studied and educational resources were developed for healthcare providers and patients. Firstly, in **Chapter 2** we developed an educational module for endoscopists, covering key aspects of a polypectomy, based on the national guideline. The remainder of this thesis is subdivided into three parts.

Part I: Optical diagnosis & Local treatment

In part I, the focus lies on optical diagnosis and local treatment. Regarding optical diagnosis, **Chapter 3** introduces a potential novel technique to enhance optical imaging of T1CRC: tumor-targeted fluorescence-guided endoscopy. This preparatory study investigates the most suitable imaging target for this approach in vitro. **Chapter 4** describes the study protocol of the randomised controlled TRIASSIC trial, which

compares transanal minimally invasive surgery to endoscopic submucosal dissection for the resection of larger rectal adenomas and T1 rectal cancers. **Chapter 5** presents the results of an ancillary study of this trial, comparing the physical recovery of both procedures using wearable accelerometers to assess physical activity.

Part II: Treatment strategies after local treatment

In part II, the focus lies on treatment strategies after local resection. In **Chapter 6** we evaluated the results of completion surgery after ESD, comparing the morbidity and mortality of primary oncological resections with those of completion surgery following ESD in patients with suspected T1 CRC. In **Chapter 7**, a meta-analysis was conducted to evaluate the risk and time patter of cancerous recurrence after local resection of T1 rectal cancer, comparing endoscopic and local surgical resection techniques.

Part III: Patient empowerment

In part III, the focus lies on patient empowerment. **Chapter 8** presents an evaluation of T1CRC patients' perspectives on information provision, including their information needs, and experience on the decision-making process. In **Chapter 9** educational videos on T1CRC for patients are presented. The videos highlight key aspects of the T1CRC patient journey, including the complex decision to either proceed with additional treatment after local resection of refrain from further treatment.

Finally, **Chapter 10** provides a summary of the findings in this thesis, and elaborates on future perspectives.

References:

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229–63.
2. Integraal Kankercentrum Nederland (IKNL): http://nkr-cijfers.iknl.nl [Acces date 20 november 2024]
3. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. The Lancet. 2019;394(10207):1467–80.
4. Nguyen LH, Goel A, Chung DC. Pathways of Colorectal Carcinogenesis. Gastroenterology. 2020;158(2):291–302.
5. Brenner H, Tao S. Superior diagnostic performance of faecal immunochemical tests for haemoglobin in a head-to-head comparison with guaiac based faecal occult blood test among 2235 participants of screening colonoscopy. Eur J Cancer. 2013;49(14):3049–54.
6. Toes-Zoutendijk E, van Leerdam ME, Dekker E, van Hees F, Penning C, Nagtegaal I, et al. Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-Off Levels. Gastroenterology. 2017;152(4):767–75.e2.
7. Wieszczy P, Kaminski MF, Franczyk R, Loberg M, Kobiela J, Rupinska M, et al. Colorectal Cancer Incidence and Mortality After Removal of Adenomas During Screening Colonoscopies. Gastroenterology. 2020;158(4):875–83.e5.
8. Participants in the Paris W. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointestinal Endoscopy. 2003;58(6, Supplement):S3–S43.
9. Bogie RMM, Veldman MHJ, Snijders L, Winkens B, Kaltenbach T, Masclee AAM, et al. Endoscopic subtypes of colorectal laterally spreading tumors (LSTs) and the risk of submucosal invasion: a meta-analysis. Endoscopy. 2018;50(3):263–82.
10. Backes Y, Moss A, Reitsma JB, Siersema PD, Moons LMG. Narrow Band Imaging, Magnifying Chromoendoscopy, and Gross Morphological Features for the Optical Diagnosis of T1 Colorectal Cancer and Deep Submucosal Invasion: A Systematic Review and Meta-Analysis. Official journal of the American College of Gastroenterology | ACG. 2017;112(1):54–64.
11. Kudo S, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc. 1996;44(1):8–14.
12. Sano Y, Tanaka S, Kudo SE, Saito S, Matsuda T, Wada Y, et al. Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. Dig Endosc. 2016;28(5):526–33.
13. Uraoka T, Saito Y, Ikematsu H, Yamamoto K, Sano Y. Sano's capillary pattern classification for narrow-band imaging of early colorectal lesions. Dig Endosc. 2011;23 Suppl 1:112–5.
14. Hewett DG, Kaltenbach T, Sano Y, Tanaka S, Saunders BP, Ponchon T, et al. Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. Gastroenterology. 2012;143(3):599–607.e1.
15. Wada Y, Kashida H, Kudo SE, Misawa M, Ikehara N, Hamatani S. Diagnostic accuracy of pit pattern and vascular pattern analyses in colorectal lesions. Dig Endosc. 2010;22(3):192–9.

16. Kanao H, Tanaka S, Oka S, Hirata M, Yoshida S, Chayama K. Narrow-band imaging magnification predicts the histology and invasion depth of colorectal tumors. Gastrointest Endosc. 2009;69(3 Pt 2):631–6.

17. Ikehara H, Saito Y, Matsuda T, Uraoka T, Murakami Y. Diagnosis of depth of invasion for early colorectal cancer using magnifying colonoscopy. J Gastroenterol Hepatol. 2010;25(5):905–12.

18. Backes Y, Schwartz MP, Ter Borg F, Wolfhagen FHJ, Groen JN, de Vos Tot Nederveen Cappel WH, et al. Multicentre prospective evaluation of real-time optical diagnosis of T1 colorectal cancer in large non-pedunculated colorectal polyps using narrow band imaging (the OPTICAL study). Gut. 2019;68(2):271–9.

19. Detering R, van Oostendorp SE, Meyer VM, van Dieren S, Bos A, Dekker JWT, et al. MRI cT1-2 rectal cancer staging accuracy: a population-based study. Br J Surg. 2020;107(10):1372–82.

20. Meulen LWT, van de Wetering AJP, Debeuf MPH, Mujagic Z, Masclee AAM. Optical diagnosis of T1 CRCs and treatment consequences in the Dutch CRC screening programme. Gut. 2020;69(11):2049–51.

21. Barendse RM, Musters GD, de Graaf EJR, van den Broek FJC, Consten ECJ, Doornebosch PG, et al. Randomised controlled trial of transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND Study). Gut. 2018;67(5):837–46.

22. van der Schee L, Albers SC, Didden P, Lacle MM, Farina Sarasqueta A, Richir MC, et al. Results of endoscopic intermuscular dissection for deep submucosal invasive rectal cancer: a three-year follow-up study. Gut. 2025.

23. Burgess NG, Hourigan LF, Zanati SA, Brown GJ, Singh R, Williams SJ, et al. Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. Gastroenterology. 2017 Sep;153(3):732-742.e1.

24. Nederlandse Vereniging van Maag-Darm-Leverartsen (NVMDL). Richtlijn colorectaal carcinoom. 2024.

25. Jacques J, Schaefer M, Wallenhorst T, Rösch T, Lépilliez V, Chaussade S, et al. Endoscopic En Bloc Versus Piecemeal Resection of Large Nonpedunculated Colonic Adenomas : A Randomized Comparative Trial. Ann Intern Med. 2024;177(1):29–38.

26. Fujiya M, Tanaka K, Dokoshi T, Tominaga M, Ueno N, Inaba Y, et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointestinal endoscopy. 2015;81(3):583–95.

27. Michielan A, Merola E, Vieceli F, Rogger TM, Crispino F, Sartori C, et al. Recurrence rates after piecemeal endoscopic mucosal resection of large colorectal laterally spreading tumors. Ann Gastroenterol. 2023;36(2):195–202.

28. Moss A, Williams SJ, Hourigan LF, Brown G, Tam W, Singh R, et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut. 2015;64(1):57–65.

29. Tate DJ, Desomer L, Klein A, Brown G, Hourigan LF, Lee EY, et al. Adenoma recurrence after piecemeal colonic EMR is predictable: the Sydney EMR recurrence tool. Gastrointest Endosc. 2017;85(3):647–56.e6.

30. Stéphane S, Timothée W, Jérémie A, Raphael O, Martin D, Emmanuelle P, et al. Endoscopic submucosal dissection or piecemeal endoscopic mucosal resection for large superficial colorectal lesions: A cost effectiveness study. Clin Res Hepatol Gastroenterol. 2022;46(6):101969.

31. Sekiguchi M, Igarashi A, Mizuguchi Y, Takamaru H, Yamada M, Sakamoto T, et al. Cost-effectiveness analysis of endoscopic resection for colorectal laterally spreading tumors: Endoscopic submucosal dissection versus piecemeal endoscopic mucosal resection. Dig Endosc. 2022;34(3):553–68.

32. Bahin FF, Heitman SJ, Rasouli KN, Mahajan H, McLeod D, Lee EYT, et al. Wide-field endoscopic mucosal resection versus endoscopic submucosal dissection for laterally spreading colorectal lesions: a cost-effectiveness analysis. Gut. 2018;67(11):1965–73.

33. Ganapathi AM, Speicher PJ, Englum BR, Castleberry AW, Migaly J, Hsu DS, et al. Adjuvant chemotherapy for t1 node-positive colon cancers provides significant survival benefit. Dis Colon Rectum. 2014;57(12):1341–8.

34. Hashiguchi Y, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. Int J Clin Oncol. 2020;25(1):1–42.

35. Zwager LW, Bastiaansen BAJ, Montazeri NSM, Hompes R, Barresi V, Ichimasa K, et al. Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis. Gastroenterology. 2022;163(1):174–89.

36. Ikematsu H, Yoda Y, Matsuda T, Yamaguchi Y, Hotta K, Kobayashi N, et al. Long-term outcomes after resection for submucosal invasive colorectal cancers. Gastroenterology. 2013;144(3):551–9; quiz e14.

37. Spadaccini M, Bourke MJ, Maselli R, Pioche M, Bhandari P, Jacques J, et al. Clinical outcome of non-curative endoscopic submucosal dissection for early colorectal cancer. Gut. 2022;71(10):1998–2004.

38. Overwater A, Kessels K, Elias S, Backes Y, Spanier B, Seerden T, et al. Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes. Gut. 2018;67(2):284–90.

39. Yamashita K, Oka S, Tanaka S, Nagata S, Hiraga Y, Kuwai T, et al. Preceding endoscopic submucosal dissection for T1 colorectal carcinoma does not affect the prognosis of patients who underwent additional surgery: a large multicenter propensity score-matched analysis. Journal of Gastroenterology. 2019;54:897–906.

40. Oh EH, Kim N, Hwang SW, Park SH, Yang D-H, Ye BD, et al. Comparison of long-term recurrence-free survival between primary surgery and endoscopic resection followed by secondary surgery in T1 colorectal cancer. Gastrointestinal Endoscopy. 2021;94(2):394–404.

41. Wyatt JNR, Powell SG, Altaf K, Barrow HE, Alfred JS, Ahmed S. Completion Total Mesorectal Excision After Transanal Local Excision of Early Rectal Cancer: A Systematic Review and Meta-analysis. Dis Colon Rectum. 2022;65(5):628–40.

42. Fujishiro M. Endoscopic submucosal dissection for stomach neoplasms. World J Gastroenterol. 2006;12(32):5108–12.

43. Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, et al. Outcomes of Endoscopic Submucosal Dissection for Colorectal Epithelial Neoplasms in 200 Consecutive Cases. Clinical Gastroenterology and Hepatology. 2007;5(6):678–83.

44. Draganov PV, Aihara H, Karasik MS, Ngamruengphong S, Aadam AA, Othman MO, et al. Endoscopic Submucosal Dissection in North America: A Large Prospective Multicenter Study. Gastroenterology. 2021;160(7):2317–27.e2.

45. Watanabe D, Toyonaga T, Ooi M, Yoshizaki T, Ohara Y, Tanaka S, et al. Clinical outcomes of deep invasive submucosal colorectal cancer after ESD. Surg Endosc. 2018;32(4):2123–30.

46. Akintoye E, Kumar N, Aihara H, Nas H, Thompson CC. Colorectal endoscopic submucosal dissection: a systematic review and meta-analysis. Endosc Int Open. 2016;4(10):E1030–e44.

47. Singh S, Mohan BP, Vinayek R, Dutta S, Dahiya DS, Inamdar S, et al. Underwater versus conventional endoscopic submucosal dissection for colorectal lesions: systematic review and meta-analysis. Gastrointestinal Endoscopy. 2025;101(3):551–7.e5.

48. Singh RR, Nanavati J, Gopakumar H, Kumta NA. Colorectal endoscopic submucosal dissection in the West: A systematic review and meta-analysis. Endosc Int Open. 2023;11(11):E1082–e91.

49. Draganov PV, Wang AY, Othman MO, Fukami N. AGA Institute Clinical Practice Update: Endoscopic Submucosal Dissection in the United States. Clinical Gastroenterology and Hepatology. 2019;17(1):16–25.e1.

50. Schmidt A, Bauerfeind P, Gubler C, Damm M, Bauder M, Caca K. Endoscopic full-thickness resection in the colorectum with a novel over-the-scope device: first experience. Endoscopy. 2015;47(8):719–25.

51. Didden P, van Eijck van Heslinga RAH, Schwartz MP, Arensman LR, Vleggaar FP, de Graaf W, et al. Relevance of polyp size for primary endoscopic full-thickness resection of suspected T1 colorectal cancers. Endoscopy. 2022;54(11):1062–70.

52. Zwager LW, Bastiaansen BAJ, van der Spek BW, Heine DN, Schreuder RM, Perk LE, et al. Endoscopic full-thickness resection of T1 colorectal cancers: a retrospective analysis from a multicenter Dutch eFTR registry. Endoscopy. 2022;54(5):475–85.

53. Meier B, Elsayed I, Seitz N, Wannhoff A, Caca K. Efficacy and safety of combined EMR and endoscopic full-thickness resection (hybrid EFTR) for large nonlifting colorectal adenomas. Gastrointest Endosc. 2023;98(3):405–11.

54. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc. 2010;24(9):2200–5.

55. Barendse RM, Doornebosch PG, Bemelman WA, Fockens P, Dekker E, de Graaf EJR. Transanal Employment of Single Access Ports Is Feasible for Rectal Surgery. Annals of Surgery. 2012;256(6):1030–3.

56. de Graaf EJ, Burger JW, van Ijsseldijk AL, Tetteroo GW, Dawson I, Hop WC. Transanal endoscopic microsurgery is superior to transanal excision of rectal adenomas. Colorectal Dis. 2011;13(7):762–7.

57. Martin-Perez B, Andrade-Ribeiro GD, Hunter L, Atallah S. A systematic review of transanal minimally invasive surgery (TAMIS) from 2010 to 2013. Tech Coloproctol. 2014;18(9):775–88.

58. Maglio R, Muzi GM, Massimo MM, Masoni L. Transanal minimally invasive surgery (TAMIS): new treatment for early rectal cancer and large rectal polyps—experience of an Italian center. Am Surg. 2015;81(3):273–7.

59. Ohata K, Kobayashi N, Sakai E, Takeuchi Y, Chino A, Takamaru H, et al. Long-term Outcomes After Endoscopic Submucosal Dissection for Large Colorectal Epithelial Neoplasms: A Prospective, Multicenter, Cohort Trial From Japan. Gastroenterology. 2022;163(5):1423–34.e2.

60. Maeda K, Koide Y, Katsuno H, Tajima Y, Hanai T, Masumori K, et al. Long-term results of minimally invasive transanal surgery for rectal tumors in 249 consecutive patients. Surg Today. 2023;53(3):306–15.

61. Reyna VF, Nelson WL, Han PK, Pignone MP. Decision making and cancer. Am Psychol. 2015;70(2):105–18.

62. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: a model for clinical practice. J Gen Intern Med. 2012;27(10):1361–7.

63. Mesters I, van den Borne B, De Boer M, Pruyn J. Measuring information needs among cancer patients. Patient Educ Couns. 2001;43(3):253–62.

64. Lowenstein LM, Volk RJ, Cuddy A, Hempstead AP, You YN, Van Loon K, et al. Patients' information needs and attitudes about post-treatment surveillance for colorectal cancer in the United States: a multi-perspective, mixed methods study. BMJ Open. 2019;9(8):e025888.

65. Mulcare H, Schofield P, Kashima Y, Milgrom J, Wirth A, Bishop M, et al. Adjustment to cancer and the information needs of people with lung cancer. Psycho-Oncology. 2011;20(5):488–96.