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Training in optical diagnosis in community hospitals is associated with improved recognition and treatment of T1 CRC: a prospective multicenter intervention study (OPTICAL II).

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Abstract:
Background and study aims: Recognition of T1 colorectal cancer (CRC) is difficult, with sensitivities of 35-60% in Western countries. We evaluated the real-life effects of the implementation of the OPTICAL model, a recently developed structured and validated prediction model, in Dutch community hospitals.

Patients and methods: In this prospective multicenter study, 383 endoscopists from 40 hospitals were invited to follow an e-learning on the OPTICAL-model, to increase sensitivity for detecting T1CRC in non-pedunculated polyps. Next, real-life recognition of T1CRC was evaluated in 25 hospitals. Endoscopic and pathologic reports of T1CRCs detected during the next year were collected retrospectively while endoscopists were unaware of this evaluation. Sensitivity for recognition of T1CRC, R0 resection rate, and treatment modality were compared for trained vs. untrained endoscopists and for recognised vs. unrecognised T1CRCs.

Results: Within 1 year after the e-learning 251 endoscopists detected 528 non-pedunculated T1CRCs, 118 (47%) of the endoscopist were trained. T1CRCs had a median size of 20mm and were mainly located in the distal colorectum (66%). Trained endoscopists recognised T1CRCs more frequently than untrained endoscopists (sensitivity 74% vs. 62%; mixed model analysis OR 2.90; 95%CI 1.54-5.45. A higher rate of R0 resection was seen for T1CRCs detected by trained endoscopists (69% vs. 56%, OR 1.73; 95%CI 1.03-2.91).

Conclusion: Training in optical recognition of T1CRCs in community hospitals was associated with an increase in sensitivity for T1CRCs. Recognition led to a higher rate of en bloc local excision, resulting in higher R0-resection rates. This may be an important step towards more organ-preserving strategies.

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Training in optical diagnosis in community hospitals is associated with improved recognition and treatment of T1 CRC: a prospective multicenter intervention study (OPTICAL II).

Short Title: OPTICAL II study

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Abbreviations: T1 CRC: submucosal invasive colorectal cancer; NBI: narrow-band imaging; ESD: Endoscopic Submucosal Dissection; EID: Endoscopic Intermuscular Dissection; eFTR: endoscopic Full-Thickness Resection; TEM: Transanal Endoscopic Microsurgery; TAMIS: Transanal Minimally Invasive Surgery; CELS: Combined Endoscopic Laparoscopic Surgery; PALGA: nationwide network and registry of histo- and cytopathology in the Netherlands; EMR: Endoscopic Mucosal Resection; PPV: positive predictive value; NPV: negative predictive value; CI: confidence intervals; OR: Odds Ratio; IQR: interquartile range;

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ABSTRACT

Background and study aims: Recognition of T1 colorectal cancer (CRC) is difficult, with sensitivities of 35-60% in Western countries. We evaluated the real-life effects of the implementation of the OPTICAL model, a recently developed structured and validated prediction model, in Dutch community hospitals.

Patients and methods: In this prospective multicenter study, 383 endoscopists from 40 hospitals were invited to follow an e-learning on the OPTICAL-model, to increase sensitivity for detecting T1CRC in non-pedunculated polyps. Next, real-life recognition of T1CRC was evaluated in 25 hospitals. Endoscopic and pathologic reports of T1CRCs detected during the next year were collected retrospectively while endoscopists were unaware of this evaluation. Sensitivity for recognition of T1CRC, R0 resection rate, and treatment modality were compared for trained vs. untrained endoscopists and for recognised vs. unrecognised T1CRCs.

Results: Within 1 year after the e-learning 251 endoscopists detected 528 non-pedunculated T1CRCs, 118 (47%) of the endoscopist were trained. T1CRCs had a median size of 20mm and were mainly located in the distal colorectum (66%). Trained endoscopists recognised T1CRCs more frequently than untrained endoscopists (sensitivity 74% vs. 62%; mixed model analysis OR 2.90; 95%CI 1.54-5.45. A higher rate of R0 resection was seen for T1CRCs detected by trained endoscopists (69% vs. 56%, OR 1.73; 95%CI 1.03-2.91).

Conclusion: Training in optical recognition of T1CRCs in community hospitals was associated with an increase in sensitivity for T1CRCs. Recognition led to a higher rate of *en bloc* local excision, resulting in higher R0-resection rates. This may be an important step towards more organ-preserving strategies.

Keywords: T1 CRC, submucosal invasive carcinoma, optical diagnosis, training

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INTRODUCTION

Adequate recognition of submucosal invasive colorectal cancers (T1 CRC) in non-pedunculated colorectal polyps is essential to select polyps for an adequate local resection technique aiming to achieve R0-resection [1]. Unfortunately, optical diagnosis of T1 CRCs is still challenging. with sensitivities ranging between 35-60% [2-5]. Therefore a proportion of T1 CRCs are not recognised until histological assessment, causing difficulties in risk stratification due to improper orientation and fragmentation of the specimen.

While enhanced imaging with either zoom chromoendoscopy, narrow-band imaging, or blue light imaging is essential for the correct diagnosis of T1 CRCs [6, 7], white light features, such as size, location, and surface morphology, are also helpful in stratifying polyps into high and low-risk lesions [8-10] (Figure 1). Models incorporating both enhanced imaging features as well as morphological features have recently been reported [5, 11, 12]. In the Netherlands, the validated OPTICAL model was developed, discriminating T1 CRCs and non-invasive, non-pedunculated polyps of ≥20 mm with a sensitivity and specificity of 78.7% and 94.2% respectively [12]. This model supports endoscopists to apply dedicated local excision techniques for high-risk lesions. However, most of these models are validated on images, included only patients already selected for Endoscopic Submucosal Dissection (ESD), or included only endoscopists interested in polyp characterization [11, 13-18]. It is also unknown whether implementing such a model improves clinical outcomes, such as increased T1 CRC recognition, higher proportions of R0 resection, and whether it will decrease surgery rates after its implementation in community hospitals.

In this multicenter prospective study, we evaluated whether training in the OPTICAL model in community hospitals led to better treatment outcomes for patients with T1 CRC, by comparing outcomes (R0 resection, *en bloc* resection, and treatment strategy) between trained and untrained endoscopists.

MATERIALS & METHODS

Study design and source population

This was a prospective multicenter study from the Dutch T1 CRC Working Group, conducted from January 2019 to August 2020. All 383 endoscopists of 40 Dutch hospitals were invited to partake in this study (Figure 2) and were granted access to voluntarily pass through an e-learning explaining the features of the OPTICAL model [12]. In short, the e-learning consisted of 40 practice cases, an e-course displaying online movies explaining the features of the OPTICAL model, and an explanation of various example cases. The e-learning trained endoscopists in the recognition of T1 CRCs, but also in the selection of cases for a "dedicated *en bloc* resection technique" defined as ESD, Endoscopic Intermuscular Dissection (EID), endoscopic Full-Thickness Resection (eFTR), Transanal Endoscopic Microsurgery (TEM), Transanal Minimally Invasive Surgery (TAMIS), or Combined Endoscopic Laparoscopic Surgery (CELS). Details of the e-learning can be found in Supplementary material 1.

A trained endoscopist was defined as an endoscopist that completed the preceding practice cases and e-course (Supplementary Figure S1), without the necessary completion of the final practice cases (trained; n=181). We considered endoscopists untrained if they did not participate in the e-learning, or only performed the preceding practice cases (untrained; n=202). Among the trained participants were 136 gastroenterologists, 24 nurse endoscopists, and 21 residents in training. Access to the e-learning was granted until July 2019.

Real-life clinical practice

To evaluate the effect of the e-learning, we collected all pathology reports of T1 CRCs diagnosed after the training period, from August 2019 until August 2020, in a random selection of 25 hospitals with varying participation grades in the e-learning. All consecutive T1 CRCs in this period were identified by performing a search in the nationwide registry of histo- and cytopathology in the Netherlands (PALGA) [19]. To prevent bias, participants were unaware of the inclusion of their encountered T1 CRCs, as such, they were blinded to this part of the study. Data were collected retrospectively, but as we collected all pathologically confirmed T1 CRCs we could include all consecutive T1 CRC lesions encountered by the participating endoscopists irrespective of treatment modality. We evaluated whether the endoscopist had recognised the lesion as at risk for T1 CRC by analyzing the corresponding endoscopy report. There were no standardized report forms, so any statement in the

endoscopy report leading to suspicion of submucosal invasion (e.g., suspicious for T1 CRC, NICE 3, Kudo V, Hiroshima C2-C3, or uncertainty about non-invasiveness) was registered as an adequate recognition of T1 CRC. We chose this approach because we expected that the suspicion of submucosal invasion would lead to the selection of resection techniques as were it a lesion with T1 CRC. One reader extracted all data, and a second reader checked a representative sample of 5/25 centers, corresponding with 16% of all cases. In case of discrepancies between the two readers, this was discussed with the principal investigator of the study. Next, we collected data on the treatment performed (endoscopic, primary, or secondary surgery) and outcome (negative resection margins (R0) and *en bloc* resection). In our cohort, three options were observed in the course of optical diagnosis towards treatment: (1) T1 CRC recognized, biopsies, and referral for primary surgery; (2) recognized T1 CRC, primary local excision performed; (3) uncertainty in optical diagnosis of T1 CRC, biopsies, and afterwards decision of treatment strategy (local excision or surgery). Finally, we compared these outcomes between trained and untrained endoscopists. To correct for a possible selection bias towards already more dedicated endoscopists that finished the e-learning, we obtained additional information on endoscopists characteristics. The principal investigator of each participating center provided details of the following characteristics for both trained and untrained endocopists: prior training in optical diagnosis, certificate to participate in the Dutch population-based CRC screening program, endoscopy experience in years, focus of expertise, use of (virtual) chromoendoscopy, performing Endoscopic Mucosal Resection (EMR) for lesions ≥ 20 mm, performing advanced endoscopic techniques (ESD, eFTR, EID), total colonoscopies per year, dedication in recognition of T1 CRCs, and frequency of consulting an expert colleague during colonoscopy. (Supplementary Table S2). Morphology was defined as “sessile or sessile component” versus “flat” (when no sessile component was described). Morphology was not defined according to the Paris- or LST-classification, because these are not registered in a standardized manner in the Netherlands.

A directed acyclic graph (DAG) was made, to provide insight into parameters influencing T1 CRC recognition and showing which parameters were available in our cohort (Supplementary Figure S3).

The Medical Ethical Review Committee of the Maastricht University Medical Center approved the study and waived the need for informed consent (2021-2719). Patients or public were not involved in the design, conduct, and reporting of this research. We used the STARD checklist when writing our report and followed the the SAGER guidelines for sex and gender reporting [20, 21].

Statistical analysis

For descriptive statistics, categorical variables are presented as numbers and percentages, and numerical variables are presented as medians (interquartile range) or mean (standard deviation). Pearson's χ^2 method and Fisher's exact test were used to assess differences in baseline patient, lesion, and endoscopist characteristics between groups. Generalized linear mixed models with logit link were used to assess differences in (binary) outcomes between T1 CRCs detected by trained vs. untrained endscopists. A random intercept on endoscopist level was included to account for the correlation between T1 CRCs assessed by the same endoscopist. A generalized linear mixed model with logit link and random intercept on endoscopist level was also used to evaluate the independent effect of training on T1 CRC sensitivity, with correction for observed associations as size, morphology, and location of the lesion, the indication of colonoscopy, and the endoscopists' experience or dedication to the treatment of colorectal polyps. The DAG shows for which parameters correction was not possible (Supplementary Figure S3). Sensitivity analysis was performed, in which an additional random intercept on treatment center was included to account for the correlation between T1 CRCs assessed by endoscopists from the same treatment center. Additional sensitivity analysis was performed, in which the intervention was excluded from the model, to investigate whether there was high interaction in the model.

R version 3.5.1 and SPSS version 27.0.0 were used for statistical analysis and figures.

RESULTS

Optical e-learning

Of 383 invited endoscopists 181 (47%) participants completed the e-learning. In this training structure, overall diagnostic accuracy for recognizing T1 CRC (superficially or deeply invasive) vs. adenoma (low-grade or high-grade dysplasia) was high in the online e-module environment as demonstrated by the results of the practice cases. In the preceding practice cases a sensitivity of 82% (95%CI 80-84), specificity of 72% (95%CI 71-74), positive predictive value of 50% (95%CI 48-52%), and negative predictive value of 93% (95%CI 92-93) was observed. In the final practice cases a sensitivity of 82% (95%CI 80-84), specificity of 73% (95%CI 71-74), positive predictive value of 50% (95%CI 48-52), and negative predictive value of 92% (95%CI 92-93) was observed.

Endoscopists scoring high on sensitivity (80-100%) in this training structure were not more experienced, more dedicated to recognition of T1 CRCs, bowel cancer screening program certified, or performing advanced resection techniques more often compared to low performers (<80%).

Further details of the e-learning and practice cases can be found in the supplementary material part 1.

Real-life clinical practice

Study population and included T1 CRCs

In 25 hospitals, we included all consecutively detected T1 CRCs for 1 year after the training period of 118 trained and 133 untrained endoscopists, resulting in a total of 660 T1 CRCs, of which 528 (80%) were non-pedunculated. Two-hundred-eighty (53%) of these non-pedunculated T1 CRCs were identified during colonoscopies performed by endoscopists who were trained in the OPTICAL model, while 248 (47%) were identified during colonoscopies performed by untrained endoscopists.

Characteristics of patients and included T1 CRCs are presented in Table 1 and the characteristics of trained vs. untrained endoscopists are presented in Supplementary Table S2. T1 CRCs were equally distributed between male and female patients (45% female). Registration of all individual OPTICAL parameters in the endoscopy reports was performed in 58/280 (21%) of cases detected by trained endoscopists, against 7/248 (3%) of cases by untrained endoscopists.

Recognition of T1 CRCs

Primary outcomes are presented in Table 2. Trained endoscopists showed better recognition of non-pedunculated T1 CRCs compared to untrained endoscopists (74% vs. 62%, *p=0.006*; OR 1.74; 95%-CI 1.18-2.56). No clinically relevant differences in baseline cancer characteristics were observed between T1 CRCs detected by trained endoscopists vs. untrained endoscopists (Table 1). Trained endoscopists were more experienced, performing advanced resection techniques more often (EMR for lesions >20mm, ESD or eFTR), and more frequent screening program certified as compared to untrained endoscopists (Supplementary Table S2). To correct for potential selection bias of pre-existent level of training and dedication, multivariable regression analysis was performed correcting for both lesion characteristics (the indication of the colonoscopy, size, morphology, and location of the lesion), and endoscopist characteristics (the experience, the focus of expertise, screening program certification, and dedication to lesion characterization of the endoscopist) (Table 3). This showed that training in the OPTICAL model remained significantly associated with a higher sensitivity for T1 CRCs in clinical practice (OR 2.90; 95%CI 1.54-5.45). Other independent factors influencing sensitivity for T1 CRCs were lesion size and morphology. Sessile morphology was associated with lower sensitivity for T1 CRCs compared to flat morphology (56% vs. 81%; OR 0.29; 95%CI 0.16-0.52). Lesion size of <20mm or >40mm was associated with lower sensitivity for T1 CRC compared to a lesion size of 20-40mm (61% in <20mm lesions; OR 0.44; 95%CI 0.26-0.76; 78% in 20-40mm lesions; 58% in >40mm lesions; OR 0.26; 95%CI 0.12-0.58). Recognition of T1 CRCs was similar for endoscopists that reported the OPTICAL parameters in their endoscopy reports, compared to endoscopists that did not (76% vs. 73%; OR 1.05; 95%CI 0.56-1.97; p=0.877). Sensitivity analysis, including treatment center, showed similar outcomes. Sensitivity analysis, excluding the intervention, also showed similar outcomes for other variables in the model, indicating absence of an interaction effect.

Local excision outcomes for T1 CRCs

Although no differences existed in the proportion of *en bloc* resections, trained endoscopists more often selected a dedicated *en bloc* resection technique for recognised T1 CRCs (50% vs. 40%; OR 1.59; 95%CI 0.95-2.67; p=0.078; Table 2). Furthermore, the R0-resection rate after local excision of T1 CRCs was higher in trained vs. untrained endoscopists (69% vs. 56%; OR 1.73; 95%CI 1,03-2.91; *p=0.038*).

With increasing size of the lesion, the *en bloc* resection rate decreased (84% in <20mm, 79% in 20-40mm, and 56% in ≥40mm), and the primary surgery referral percentage increased (from 22% in <20mm to 54% in 20-40mm, and 44% in ≥40mm).

Variability of outcomes between participating centers

To assess whether the amount of uptake of the e-learning per center (i.e., which percentage of all endoscopists in a specific center had finished the e-learning) influenced T1 CRC diagnosis and treatment outcomes, participating centers were compared regarding the outcomes (Supplementary Figures S4 & S5). While a variation between centers was seen for T1 CRC recognition (mean 68% ± 46.5, range 29-91%), the proportion of R0-resection (mean 78% ± 41.7, range 33-100%), and proportion of primary surgery (mean 43% ± 16.8, range 11-75%), these differences were not observed when centers were categorized according to the percentage of endoscopists participating in the OPTICAL e-learning (<30% of centers' endoscopists vs. 30-70% of centers' endoscopists vs ≥70% of centers' endoscopists). In mixed model analysis, the difference in T1 CRC recognition between centers appeared to be caused by endoscopist and polyp characteristics. Addition of treatment center did not lead to a better discrimination (random effect 0,000).

DISCUSSION

In this prospective, multicenter study, we evaluated the effects of nationwide training in optical diagnosis on sensitivity for detecting T1 CRCs. Training was shown to be an independent predictor for better optical recognition of non-pedunculated T1 CRCs (OR 2.70; 95%CI 1.48-4.85). Furthermore, this study showed that the recognition of T1 CRCs leads to a better treatment strategy, reflected by more frequent use of dedicated local excision techniques, and a higher percentage of R0-resections of T1 CRCs identified by trained endoscopists (69% vs. 56%, OR 1.73; 95%CI 1,03-2.91; *p=0.038*).

An R0-resection not only optimises histological risk stratification and identification of a group at low risk of lymph node metastasis, but it can also be the starting point of an organ-preserving treatment strategy even in the presence ≥1 risk factors [22]. Optimising the chance of an R0 resection by selecting the most appropriate resection technique, should be the major aim of pre-resection assessment. In our cohort, however, EMR was still chosen as a resection technique for small T1 CRCs frequently, despite being recognised as early cancer. The R0 resection rate of only 46% after treatment of a T1 CRC with EMR irrespective of size is in line with the previous reported R0-resection rate of 59% after intentional EMR for T1 CRCs [23]. The R0 resection potential of EMR is likely being overestimated in smaller sized T1 CRCs. Consequently, EMR should be discouraged as a first-line treatment of suspected T1 CRCs.

The difference in R0 resection rates for detected T1 CRCs between trained and untrained endoscopists was more prominent in colonic than rectal T1 CRCs. This was partly due to more frequent selection of *en bloc* resection technique for large polyps in the rectum independent of the recognition of T1 CRCs.

In contrast to Vleugels et al, who observed that recognised T1 CRCs were less frequently referred for surgery, increased recognition did not result in a decrease of surgery in our study (data not shown) [2]. Although the suspected depth of invasion was not registered in the endoscopy report, more obvious signs of cancer, and therefore increased risk of deeper submucosal invasion, may have been the main reason for surgerical referral. However, depth of submucosal invasion has recently been recognised as a weak predictor of LNM, with an absolute risk of only 2.6% when deep submucosal invasion is the sole risk factor present [24]. It should therefore be considered to first use *en bloc* resection techniques,

such as eFTR [25], TAMIS, CELS [26], or EID [27], to remove deeply invasive T1 CRCs instead of primary surgery. By performing *en bloc* resections for all T1 CRC, including those with deep submucosal invasion, another subgroup may be recognised as eligible for intensive follow-up or adjuvant chemoradiotherapy.

Several limitations of our study should be acknowledged. The selection of more dedicated endoscopists may have occurred in the trained group. Given the voluntary nature of participation in this study, there might be a bias towards endoscopists already dedicated to T1 CRC recognition. Comparing trained and untrained endoscopists' characteristics, showed more dedication to T1 CRC recognition, CRC screening program certification, and more use of advanced endoscopy techniques among trained endoscopists.However, after correction for these differences, training in the OPTICAL model remained an independent predictor for T1 CRC recognition. Therefore, we believe that although dedicated endoscopists were more likely to complete the training, the training still leads to improved T1 CRC recognition, and, more importantly, a better treatment strategy. Furthermore, the DAG (Supplementary Figure S3) shows some unmeasured confounders we could not correct for in our analysis. However, we believe the influence of these unmeasured confounders is limited, since these parameters are related to other parameters (eg. number of screening colonoscopies is related to years of experience and screening certification) or very unlikely to be different between groups (eg. time pressure), or might be a mediator instead of a confounder (eg. sufficient cleaning of the polyp). Thus, while a part of the effect might be explained by these unmeasured differences between endoscopists or procedural differences, it is highly unlikely that the complete training effect might be explained by unmeasured confounders.

Sensitivity for detecting T1 CRCs in clinical practice found in our study (68% overall, 74% for trained endoscopists, and 62% for untrained endoscopists) is high compared to reported sensitivities of 35-60% in previous cohort studies, especially for untrained endoscopists [2-5]. This high sensitivity of detecting T1 CRC of untrained endoscopists may be explained by several causes. First,some studies were performed in the early years after implementation of the CRC screening programs (2015-2017) [2, 3, 5]. Given the 6 years of experience within the CRC screening program at the time of our study period, we might be observing a natural learning curve for T1 CRC recognition. Second, due to self-education, cross-contamination between trained and untrained endoscopists, and consultation with

expert endoscopists, the untrained group may have been exposed to some level of training and could therefore have shown better outcomes than expected.

Given the blinded, retrospective analysis of T1 CRC recognition, extracted from the national pathology database, we were not able to calculate specificity. Information regarding total amount of benign lesions treated in the different centers cannot be retrieved due to the lack of a national/regional registry.

The observed sensitivity in the image-based practice cases of the e-learning (82.4 and 82.1) was higher than the sensitivity observed in real-life practice. High-quality images and videos, unlimited assessment time, and optimal visualization of the area of interest could have contributed to this high performance. This contradicts real-life circumstances, where polyp cleaning, scope positioning, and time pressure may interfere with optimal assessment conditions. The dictated structured approach during the practice cases may also not have been applied during live endoscopies. A Hawthorne effect could also have contributed to better optical diagnosis in the e-module compared to real-life practice. While this part of the study was initially designed as a tool to measure the effect of training in the optical model on recognition of T1 CRCs, this appeared not to be appropriate to estimate the baseline sensitivity for T1 CRCs, given the fact that participating endoscopists studied beforehand and used study materials during the practice cases. Altogether, this suggests that endoscopists might be good at diagnosing T1 CRCs under the right circumstances, but these circumstances might not be reached during real-time clinical practice, resulting in a lower sensitivity for T1 CRCs. Since endoscopists were unaware of the clinical part of our study, our data reflect real-time endoscopic practice for T1 CRCs on a community level.

Given the pragmatic nature of this study, aiming to include as many Dutch centers as possible to evaluate the effects of training in optical diagnosis of T1 CRCs on a national level, no sample size calculation was performed. Post-hoc sample size analysis showed a minimum inclusion of 154. Given the 528 inclusions in this study, it is assumed that we have more than enough power to support our findings.

In conclusion, in this prospective multicenter intervention study, it was shown that training in optical recognition of T1 CRCs was associated with an increase in sensitivity for recognition of T1 CRCs in clinical practice. Better recognition led to a higher selection rate of an appropriate *en bloc* local

excision technique, resulting in higher R0-resection rates. There is however still room for significant improvement as recognition only resulted in the selection of a dedicated resection technique in 50% of cases, and referral for primary surgery in 41%. The focus should therefore not only be on recognition, but also on appropriate treatment. This may be an important step towards more organ-preserving strategies.

REFERENCES

1. Bahin FF, Heitman SJ, Rasouli KN et al. Wide-field endoscopic mucosal resection versus endoscopic submucosal dissection for laterally spreading colorectal lesions: a cost-effectiveness analysis. Gut 2018; 67: 1965-1973. doi:10.1136/gutjnl-2017-313823
2. Vleugels JLA, Koens L, Dijkgraaf MGW et al. Suboptimal endoscopic cancer recognition in colorectal lesions in a national bowel screening programme. Gut 2020; 69: 977-980. doi:10.1136/gutjnl-2018-316882
3. Meulen LWT, van de Wetering AJP, Debeuf MPH et al. Optical diagnosis of T1 CRCs and treatment consequences in the Dutch CRC screening programme. Gut 2020; 69: 2049-2051. doi:10.1136/gutjnl-2019-320403
4. Denis B, Gendre I, Perrin P et al. Management of large polyps in a colorectal cancer screening program with fecal immunochemical test: a community- and population-based observational study. Endosc Int Open 2021; 9: E1649-E1657. doi:10.1055/a-1551-3306
5. Puig I, Lopez-Ceron M, Arnau A et al. Accuracy of the Narrow-Band Imaging International Colorectal Endoscopic Classification System in Identification of Deep Invasion in Colorectal Polyps. Gastroenterology 2019; 156: 75-87. doi:10.1053/j.gastro.2018.10.004
6. Backes Y, Moss A, Reitsma JB et al. 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. The American journal of gastroenterology 2017; 112: 54-64. doi:10.1038/ajg.2016.403
7. Zhang QW, Teng LM, Zhang XT et al. Narrow-band imaging in the diagnosis of deep submucosal colorectal cancers: a systematic review and meta-analysis. Endoscopy 2017; 49: 564-580. doi:10.1055/s-0043-103014
8. Burgess NG, Hourigan LF, Zanati SA et al. Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. Gastroenterology 2017; 153: 732-742 e731. doi:10.1053/j.gastro.2017.05.047
9. D'Amico F, Amato A, Iannone A et al. Risk of Covert Submucosal Cancer in Patients With Granular Mixed Laterally Spreading Tumors. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2021; 19: 1395-1401. doi:10.1016/j.cgh.2020.07.024
10. Vosko S, Shahidi N, Sidhu M et al. Optical Evaluation for Predicting Cancer in Large Nonpedunculated Colorectal Polyps Is Accurate for Flat Lesions. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2021; 19: 2425-2434 e2424. doi:10.1016/j.cgh.2021.05.017
11. Bonniaud P, Jacques J, Lambin T et al. Endoscopic characterization of colorectal neoplasia with different published classifications: comparative study involving CONECCT classification. Endosc Int Open 2022; 10: E145-E153. doi:10.1055/a-1613-5328
12. Backes Y, Schwartz MP, Ter Borg F 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: 271-279. doi:10.1136/gutjnl-2017-314723
13. Fabritius M, Gonzalez JM, Becq A et al. A simplified table using validated diagnostic criteria is effective to improve characterization of colorectal polyps: the CONECCT teaching program. Endosc Int Open 2019; 7: E1197-E1206. doi:10.1055/a-0962-9737
14. Brule C, Pioche M, Albouys J et al. The COlorectal NEoplasia Endoscopic Classification to Choose the Treatment classification for identification of large laterally spreading lesions lacking submucosal carcinomas: A prospective study of 663 lesions. United European gastroenterology journal 2022; 10: 80-92. doi:10.1002/ueg2.12194
15. Hirata D, Kashida H, Iwatate M et al. Effective use of the Japan Narrow Band Imaging Expert Team classification based on diagnostic performance and confidence level. World J Clin Cases 2019; 7: 2658-2665. doi:10.12998/wjcc.v7.i18.2658

16. Hosotani K, Imai K, Hotta K et al. Diagnostic performance for T1 cancer in colorectal lesions >/=10 mm by optical characterization using magnifying narrow-band imaging combined with magnifying chromoendoscopy; implications for optimized stratification by Japan Narrow-band Imaging Expert Team classification. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society 2021; 33: 425-432. doi:10.1111/den.13766
17. Komeda Y, Kashida H, Sakurai T et al. Magnifying Narrow Band Imaging (NBI) for the Diagnosis of Localized Colorectal Lesions Using the Japan NBI Expert Team (JNET) Classification. Oncology 2017; 93 Suppl 1: 49-54. doi:10.1159/000481230
18. Iwatate M, Sano Y, Tanaka S et al. Validation study for development of the Japan NBI Expert Team classification of colorectal lesions. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society 2018; 30: 642-651. doi:10.1111/den.13065
19. Casparie M, Tiebosch AT, Burger G et al. Pathology databanking and biobanking in The Netherlands, a central role for PALGA, the nationwide histopathology and cytopathology data network and archive. Cell Oncol 2007; 29: 19-24. doi:10.1155/2007/971816
20. Bossuyt PM, Reitsma JB, Bruns DE et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ 2015; 351: h5527. doi:10.1136/bmj.h5527
21. Heidari S, Babor TF, De Castro P et al. Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev 2016; 1: 2. doi:10.1186/s41073-016-0007-6
22. van Oostendorp SE, Smits LJH, Vroom Y et al. Local recurrence after local excision of early rectal cancer: a meta-analysis of completion TME, adjuvant (chemo)radiation, or no additional treatment. The British journal of surgery 2020; 107: 1719-1730. doi:10.1002/bjs.12040
23. Fukuda H, Takeuchi Y, Shoji A et al. Curative value of underwater endoscopic mucosal resection for submucosally invasive colorectal cancer. Journal of gastroenterology and hepatology 2021; 36: 2471-2478. doi:10.1111/jgh.15513
24. Zwager LW, Bastiaansen BAJ, Montazeri NSM 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: 174-189. doi:10.1053/j.gastro.2022.04.010
25. Didden P, van Eijck van Heslinga RAH, Schwartz MP et al. Relevance of polyp size for primary endoscopic full-thickness resection of suspected T1 colorectal cancers. Endoscopy 2022; 54: 1062-1070. doi:10.1055/a-1790-5539
26. Leicher LW, Huisman JF, van Grevenstein WMU et al. Colonoscopic-Assisted Laparoscopic Wedge Resection for Colonic Lesions: A Prospective Multicenter Cohort Study (LIMERIC-Study). Ann Surg 2022; 275: 933-939. doi:10.1097/SLA.0000000000005417
27. Moons LMG, Bastiaansen BAJ, Richir MC et al. Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum: a new endoscopic approach. Endoscopy 2022; 54: 993-998. doi:10.1055/a-1748-8573

FIGURES AND TABLES

Figure 1: Three T1 CRCs in white light and advanced imaging

Figure 2: Flowchart of study design and inclusions

Legend: *Trained endoscopists completed the e-learning module (with or without post-test). Untrained endoscopists did not register or dropped out during the e-learning module.

SUPPLEMENTARY MATERIALS

Supplement to:

"Training in optical diagnosis in community hospitals improves recognition and treatment of T1 colorectal carcinomas: a prospective multicenter intervention study (OPTICAL II)."

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Supplementary material 1: Details of e-learning for OPTICAL training

Before starting the e-learning participants provided consent for the usage of their results for this study and filled in a baseline questionnaire about their experience as an endoscopist, supplemented with information about the endoscopists provided by the principal investigators of each center. Progression through the e-learning was logged, and only after completion, participants could proceed to the post-test, scheduled 4-6 weeks after the e-learning.

Practice cases

The practice cases consisted of 40 real-time cases of LNPCPs selected from a large prospective database of registered LNPCPs in a tertiary hospital (University Medical Center Utrecht). Polyps contained either low-grade dysplasia (LGD; n=19), high-grade dysplasia (HGD; n=11), or T1 CRC (n=10) as determined by the golden standard; pathology reports. All cases containing T1 CRC were revised to determine the level of submucosal invasiveness; deep invasion was defined as invasion depth ≥1000 µm or Kikuchi SM2-3. Three cases were classified as superficial T1 CRC and seven cases as deep invasive T1 CRC. Cases in the preceding and final practice set were equal but arranged in different order. None of these cases were used in the e-learning itself.

For each case, we provided multiple images and/or video material of the whole polyps in both white-light and advanced imaging (narrow-band imaging [NBI]). We selected cases on which all features of the OPTICAL-model could be assessed. Size and location were provided in a textbox. Also, if spontaneous bleeding was unlikely to be adequately assessed on the imagery, this feature was stated in the text box. For each case, participants were asked ten questions, for which they had to give a predefined answer (Table S1). First, seven questions concerning the characterization of the polyp by features associated with a risk of invasive cancer were asked. Second, participants had to predict their optical diagnosis (LGD, HGD, superficial T1 CRC, or deep-invasive T1 CRC) and give their recommended therapy: piecemeal resection, en-bloc resection, or surgical resection. Finally, they had to provide the risk of invasive carcinoma in the assessed polyp (0-100%).

For the golden standard of the polyp features, we used the answers provided by previously trained endoscopists (participants in the original OPTICAL study) to reach a consensus. Questions reaching <70% consensus were reviewed and the final decision for the answer key was made by an expert

endoscopist and developer of the e-learning (LMM). The risk of carcinoma was calculated by using the OPTICAL-model with the features of the answer key as input. (Figure S1)

To evaluate the lasting effect of the e-learning, participants were asked to wait 4-6 weeks after finishing the e-learning before proceeding to the finale practice cases.

Design of e-learning

The e-learning was designed to explain the necessity of optical diagnosis in LNPCPs and to explain in detail all aspects of the OPTICAL model. (Figure S3) It consisted of three chapters and six subchapters: I) Why is optical diagnosis important for your practice, II) The making of the OPTICAL model, and III) Features of the OPTICAL model. This last chapter was subdivided into a) Stepwise approach for optical diagnosis, b) Surface morphology, c) White light features of malignancy: Depression & Spontaneous bleeding, d) Advanced Imaging: Narrow-Band Imaging, e) Advanced Imaging: Pit pattern analysis and f) Combined approach of all features: Using the Optical model. All chapters were video lectures interrupted with interactive case-based questions. The total duration of the e-learning was approximately 3 hours.

Supplementary Figure S1: E-module participation

Supplementary Table S1: Questions and answer options asked in practice cases

Question	Option 1	Option 2	Option 3	Option 4	Option 5
Question 1 *Surface morphology*	Homogenous granular	Granular with large nodule > 10mm	Granular with non-erythematous area	Non-granular	-
Question 2 *Depression*	Yes, well demarcated	Yes, not well demarcated	No depression	-	
Question 3 *Spontaneous Bleeding*	Yes	No	Cannot be assessed	-	
Question 4 *Vessel distribution*	Regular	Irregular	Absent	-	
Question 5 *Vessel diameter*	Even	Uneven	Absent	-	
Question 6 *Hiroshima*	A	B	C1	C2	C3
Question 7 *NICE*	NICE 1	NICE 2	NICE 3	-	
Question 8 *Optical diagnosis*	LGD	HGD	T1 superficial	T1 deep	-
Question 9 *Therapy*	Endoscopic resection (piecemeal)	En-bloc resection	Surgery	-	
Question 10 *OPTICAL %*	% (0-100)	-			

Supplementary Figures S2 A-B: Examples of e-learning in an online web-based module

Supplementary material 2: Clinical cohort

Supplementary Figure S3: Directed acyclic graph T1 CRC recognition

Green: data available in cohort

Orange: data not available in cohort

Supplementary Table S2. Baseline characteristics of trained and untrained endoscopists

	Overall N=251	Trained N=118	Untrained N=133	P-value
Endoscopy experience in years, median (IQR)	10 (6-16)	9 (6-15)	12 (6-19)	0.120
Focus area, n (%)				*0.003*
- Colorectal	39 (16%)	31 (27%)	8 (6%)	
- Liver	19 (8%)	8 (7%)	11 (8%)	
- HPB	23 (9%)	12 (10%)	11 (8%)	
- Esophagus/Stomach	7 (3%)	3 (3%)	4 (3%)	
- Functional	7 (3%)	3 (3%)	4 (3%)	
- IBD	41 (16%)	14 (12%)	27 (20%)	
- General	49 (20%)	22 (19%)	26 (20%)	
- Oncology	2 (1%)	1 (1%)	1 (1%)	
- Unknown	64 (26%)	22 (19%)	41 (31%)	
Screening program endoscopist, n (%)	160 (64%)	89 (77%)	70 (53%)	*<0.001*
Uses (virtual) chromoendoscopy, n (%)	152 (61%)	88 (76%)	64 (47%)	*<0.001*
Performs EMR ≥20mm, n (%)	90 (36%)	57 (49%)	32 (24%)	*<0.001*
Frequently using advanced endoscopy techniques, n (%)	34 (14%)	28 (24%)	6 (5%)	*<0.001*
Dedicated in recognition of T1 CRCs, n (%)	104 (41%)	62 (53%)	42 (32%)	*<0.001*
Total colonoscopies performed, median (IQR)	3500 (2112-5570)	3478 (2463-5000)	3600 (1600-6000)	0.757
Frequently consulting expert, n (%)	184 (73%)	92 (79%)	91 (68%)	*0.002*

Supplementary Figures S4 A-D; Variability between centers regarding optical diagnosis and treatment outcomes of T1 CRCs.

Supplementary Figures S5 A-D; Distribution between centers regarding optical diagnosis and treatment outcomes of T1 CRCs.

Table 1. Patient and lesion characteristics of non-pedunculated T1 CRCs detected by trained and untrained endoscopists

	Overall T1 CRCs (n=528)	T1 CRCs detected by trained endoscopists (n=280)	T1 CRCs detected by untrained endoscopists (n=248)	P-value
Patient characteristics				
Female sex, n (%)	238 (45%)	116 (41%)	122 (49%)	0.074
Age, mean (SD)	69 (9.1)	68 (9.5)	70 (8.7)	0.152
ASA-classification, n (%)				0.740
- ASA I	101 (19%)	53 (19%)	48 (19%)	
- ASA II	354 (67%)	184 (66%)	170 (69%)	
- ASA III	71 (13%)	42 (15%)	29 (12%)	
- ASA IV	2 (1%)	1 (0%)	1 (0%)	
Lesion characteristics				
Size in mm, median (IQR)	20 (15)	20 (15)	20 (15)	0.863
Size groups, n (%)				0.597
- 1-5 mm	6 (1%)	5 (2%)	1 (0%)	
- 6-9 mm	26 (5%)	16 (6%)	10 (4%)	
- 10-19 mm	174 (33%)	88 (31%)	86 (35%)	
- 20-29 mm	170 (32%)	91 (33%)	79 (32%)	
- 30-39 mm	79 (15%)	42 (15%)	37 (15%)	
- ≥40 mm	73 (14%)	38 (14%)	35 (14%)	
Morphology, n (%)				*0.048*
- Sessile or sessile component	341 (65%)	193 (69%)	149 (60%)	
- Flat	187 (35%)	87 (31%)	99 (40%)	
Location, n (%)				0.312
- Proximal	182 (34%)	91 (33%)	91 (37%)	
- Distal	346 (66%)	189 (67%)	157 (63%)	
Location rectum, n (%)	214 (41%)	111 (40%)	103 (42%)	0.659
Indication colonoscopy, n (%)				*0.041*
- Screening	252 (48%)	131 (47%)	121 (49%)	
- Surveillance	42 (8%)	22 (8%)	20 (8%)	
- Diagnostic	195 (37%)	99 (35%)	96 (39%)	
- Therapeutic	29 (5%)	23 (8%)	6 (2%)	
- Missing	10 (2%)	5 (2%)	5 (2%)	
Treatment, n (%)				0.485
- Local excision	234 (44%)	127 (45%)	107 (43%)	
- Primary surgery	211 (40%)	114 (41%)	97 (39%)	
- Secondary surgery	83 (16%)	39 (14%)	44 (18%)	

Legend: Proximal location is defined as cecum, ascending colon, and tranversum including the splenic flexure. Secondary surgery is defined as surgery following a local excision of a T1 CRC.

Table 2. Diagnosis and treatment outcomes of non-pedunculated T1 CRCs

	Overall T1 CRCs (n=528)	**ICC^**	**T1 CRCs detected by trained endoscopists (n=280)**	**T1 CRCs detected by untrained endoscopists (n=248)**	**Odds ratio with 95%CI #**	**p-value**
Recognition (sensitivity), n (%)	361 (68%)	0.06	207 (74%)	154 (62%)	*1.74 (1.18-2.56)*	*0.006*
Proportion of en bloc resections (local excised T1 CRCs)	239/317 (75%)	0.08	128/166 (77%)	111/151 (73.5%)	0.82 (0.48-1.41)	0.474
Dedicated local en bloc resection technique used*	143/317 (45%)	0.19	83/166 (50%)	60/151 (40%)	1.59 (0.95-2.67)	0.078
R0 resection rate (local excised T1 CRCs)	200/317 (63%)	0.16	115/166 (69%)	85/151 (56%)	*1.73 (1.03-2.91)*	*0.038*
Proportion of primary surgery	211 (40%)	0.10	114 (41%)	97 (39%)	1.11 (0.76-1.62)	0.599

^ Intraclass coefficient reflects the correlation between the outcomes of patients within the same endoscopist
# Generalized linear mixed model with a random intercept on endoscopist to correct for clustering.
* Dedicated local en bloc resection technique defined as: Endoscopic Submucosal Dissection (ESD), Endoscopic Intermuscular Dissection (EID), endoscopic Full-Thickness Resection (eFTR), Transanal Endoscopic Microsurgery (TEM), Transanal Minimally Invasive Surgery (TAMIS), or Combined Endoscopic Laparoscopic Surgery (CELS).
Abbreviations: CRC: colorectal carcinoma;ICC: intraclass coefficient; CI: Confidence Interval

Table 3. Mixed model analysis on recognition of T1 CRCs.

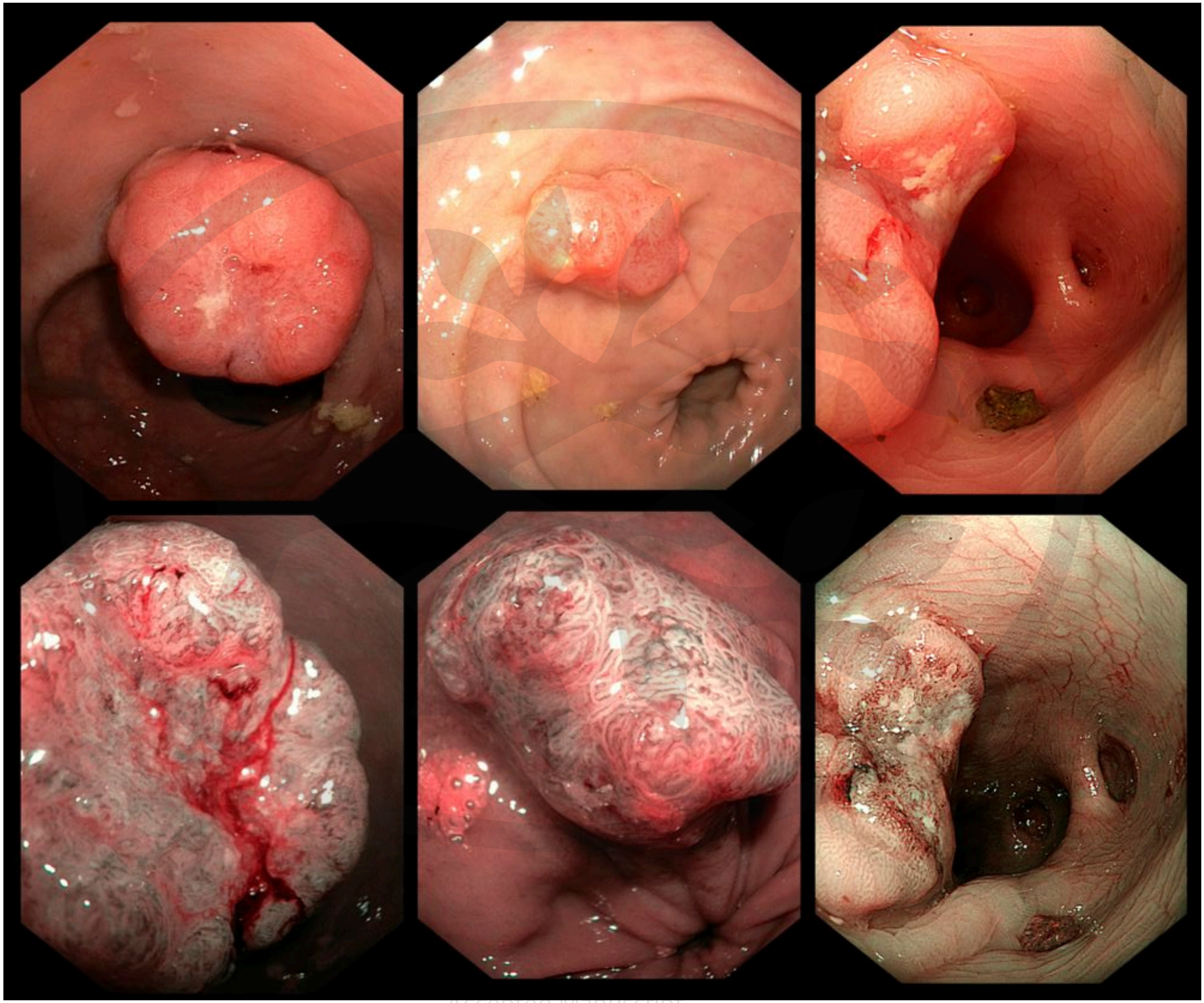
	Coefficient	S.E.	p-value[#]	Odds Ratio	95%-CI
Trained in Optical model	1.064	0.321	*0.001*	*2.90*	*1.54-5.45*
Size of lesion					
- <20 mm	-0.816	0.274	*0.003*	*0.44*	*0.26-0.76*
- 20-40 mm	Ref				
- >40 mm	-1.347	0.409	*0.001*	*0.26*	*0.12-0.58*
Location, rectum	0.049	0.269	0.855	1.05	0.62-1.78
Indication colonoscopy					
- Screening	Ref				
- Surveillance	0.345	0.461	0.454	1.41	0.57-3.49
- Diagnostic (symptomatic)	0.404		0.197	1.50	0.81-2.77
- Therapeutic (referred)	-0.280	0.313	0.621	0.76	0.25-2.30
- Diagnostic (other)	0.501	0.567	0.384	1.65	0.53-5.12
		0.575			
Morphology, sessile or sessile component	-1.241	0.295	*<0.001*	*0.29*	*0.16-0.52*
Boston Bowel Preparation Score ≥2 per segment*	0	-	-	-	-
Endoscopist screening program certified	-0.332	0.422	0.432	0.72	0.31-1.65
Endoscopist EMR≥20mm	-0.496	0.402	0.211	0.61	0.38-1.34
Endoscopist advanced endoscopy technique	0.089	0.419	0.833	1.09	0.48-2.49
Endoscopists focus area colorectal	-0.210	0.387	0.587	0.81	0.38-1.73
Endoscopist use (virtual) chromoendoscopy	-0.426	0.392	0.277	0.65	0.30-1.41
Endoscopist dedicated T1 CRC recognition	0.503	0.426	0.238	1.65	0.72-3.82
Endoscopist frequently consulting expert	0.263	0.465	0.575	1.30	0.52-3.25
Endoscopist experience in years					
- 0-5 years	Ref				
- 6-10 years	-0.535	0.410	0.193	0.59	0.26-1.31
- >10 years	-0.314	0.399	0.432	0.73	0.33-1.60

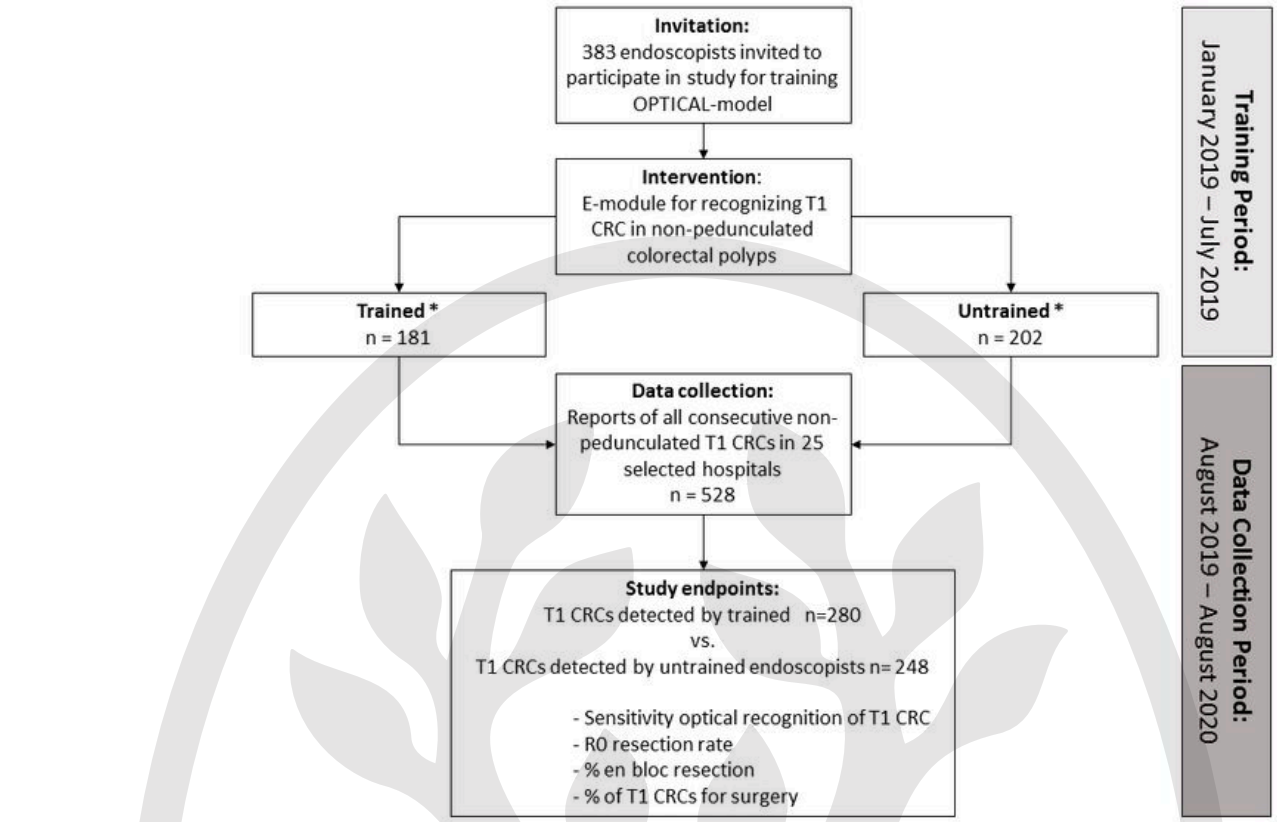
Intercept	1.975	0.772	0.011		

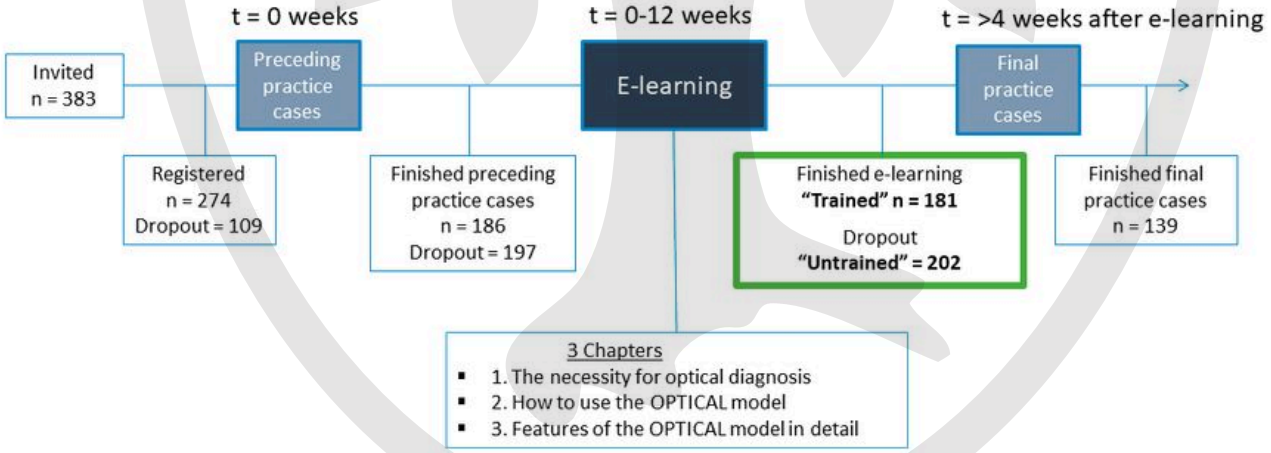
[#]Generalized linear mixed models (with logit link), with random intercept on endoscopist level.

* Boston Bowel Preparation score (BBPS) was ≥2 for all cases.

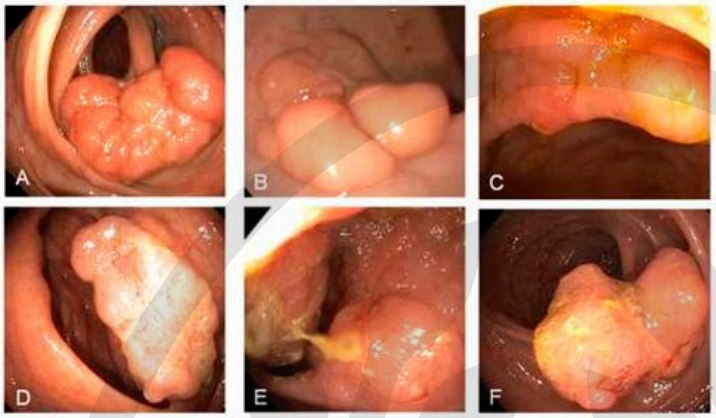
Abbreviations: CRC: colorectal carcinoma; S.E.: Standard Error; CI: Confidence Interval; mm: millimeters; EMR: Endoscopic Mucosal Resection







Which polyp contains an submucosal invasive cancer



Case information:

Optical e-learning #1_1

Question 1

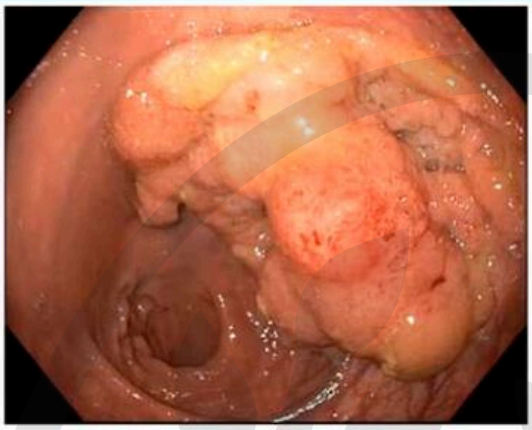
Which polyp contains a submucosal invasive cancer?

- Polyp A
- Polyp B
- Polyp C
- Polyp D
- Polyp E
- Polyp F

Previous case | Next case

Dashboard > Optical E-learning - Chapter 3 > Optical e-learning #3_6_1 Menu

A real life case- A polyp in the rectum



Case information:

Optical e-learning #3_6_1

Optical e-learning Chapter 3 - The OPTICAL I model Please watch the video before answering the question

Question 1

What is your most likely optical diagnosis?

- ○ Adenoma
- ○ Adenoma with superficial cancer or high grade dysplasia
- ○ Adenoma with a deeply invasive cancerous component
- ○ I do not know

Previous case | Next case