Relevance of polyp size for primary endoscopic full-thickness resection of suspected T1 colorectal cancers

INFOGRAPHIC

Endoscopic full-thickness resection for suspected T1 CRC

Retrospective multi-center cohort study

- 136 suspected T1 CRCs
- Median size 15 mm
- Included 75 pT1 CRCs

Technical success: 88%

Histological R0 resection: 80%

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ABSTRACT

Background En bloc local excision of suspected T1 colorectal cancer (CRC) provides optimal tumor risk assessment with curative intent. Endoscopic full-thickness resection (eFTR) with an over-the-scope device has emerged as a local excision technique for T1 CRCs, but data on the upper size limit for achieving a histological complete (R0) resection are lacking. We aimed to determine the influence of polyp size on the R0 rate.

Methods eFTR procedures for suspected T1 CRCs performed between 2015 and 2021 were selected from the endoscopy databases of three tertiary centers. The main outcome was R0 resection, defined as tumor- and dysplasia-free margins (≥ 0.1 mm) for both the deep and lateral resection margins. Regression analysis was performed to
identify risk factors for R1/Rx resection, mainly focusing on endoscopically estimated polyp size.

**Results** 136 patients underwent eFTR for suspected T1 CRC (median size 15 mm [IQR 13–18 mm]; 83.1 % cancer). The rates of technical success and R0 resection were 87.5 % (119/136; 95 %CI 80.9 %–92.1 %) and 79.7 % (106/136; 95 %CI 72.1 %–85.7 %), respectively. Increasing polyp size was significantly associated with R1/Rx resection (risk ratio 2.35 per 5-mm increase, 95 %CI 1.80–3.07; P<0.001). The R0 rate was 89.9 % (80/89) for polyps ≤15 mm, 71.4 % (25/35) for 16–20 mm, and 11.1 % (1/9) for those >20 mm.

**Conclusions** eFTR is associated with a 90 % R0 rate for T1 CRCs of ≤15 mm. Performing eFTR for polyps 16–20 mm should depend on access, their mobility, and the availability of alternative resection techniques. eFTR for >20-mm polyps results in a high R1 rate and should not be recommended.

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**Introduction**

The introduction of national colorectal cancer (CRC) screening programs has resulted in a rising incidence of early (submucosal) invasive cancers (T1 CRC) [1, 2]. The risk of lymph node metastasis (LNM) is low, especially for those cases without histological risk factors such as lymphovascular invasion, tumor budding, and poor differentiation [3]. Because of this low risk of cancer recurrence after local excision, an organ-preserving strategy is recommended [4].

Currently, polyps with a potential risk of submucosal invasion are selected for a local en bloc excision based on their optical features, such as nongranularity, depression, left-sided location, and easy friability [5–7]. When endoscopically optical signs of deep submucosal invasion are present (e.g. JNET 3 or NICE 3 features), primary oncological segmental resection is advocated [8]. However, recent reports have provided evidence that the risk of an adverse outcome for deep submucosal invasive T1 CRC without other histological risk factors is only 1.5%–2.5% [9–14], which is lower than the cumulative mortality and recurrence rates after oncological segmental resection [15, 16]. This legitimizes the strategy of a local excision first as a final staging procedure, followed by completion surgery in patients with a high risk of adverse oncological outcome [17]. As local excision could potentially be curative, an R0 resection should be the aim.

Endoscopic submucosal dissection (ESD) is currently accepted as an en bloc endoscopic resection technique for the removal of T1 CRCs; however, because of the dissection through the submucosa, this technique seems limited to T1 CRCs with superficial submucosal invasion (sm1). With 65%–70% of T1 CRCs being deeply invasive [9, 10,14], additional treatment techniques providing a radical endoscopic resection with free margins in the colon are needed for this group.

Endoscopic full-thickness resection (eFTR) is a relatively new, minimally invasive endoscopic resection technique using clip-assisted removal of polyps, with the advantage of facilitating a transmural resection. eFTR may therefore provide very good control of the deep resection margin, especially in the case of deep submucosal invasion. A large German case series of eFTR procedures for mainly benign indications demonstrated an overall histological R0 rate of 77.7 % [18]. However, the R0 resection rate was inversely correlated with the size of the polyp, showing a significant decrease to 58.1 % for polyps larger than 20 mm. Limited data suggest that eFTR also has the potential to facilitate an en bloc R0 resection for malignant colorectal polyps. The same group reported an R0 resection rate of 60.9 % in 92 eFTRs for colon cancers with a median lesion size of 20 mm, while a Dutch registry demonstrated a higher R0 rate of 77.9 % in 71 eFTRs for suspected T1 CRC with a median size of 13 mm [19, 20].

It appears eFTR may be very successful in achieving an R0 resection, but it may also have an upper size limit. We therefore studied the effect of lesion size on the R0 resection rate, with eFTR as the primary treatment of polyps suspected of being T1 CRC.

**Methods**

**Study population**

Hospital-based eFTR registries were screened for eligible subjects treated between December 2015 and March 2021 in three different tertiary referral centers in the Netherlands. The inclusion criteria were: primary eFTR of a colorectal polyp suspected of being T1 CRC based on optical diagnosis (Kudo V pit pattern, Hiroshima C vascular pattern, JNET≥2B classification, presence of a depression and/or easy bleeding). The use of eFTR was decided upon based mainly on the following two indications: (i) nonpedunculated polyps with suspected deep submucosal invasion (Hiroshima C2/V3 vascular pattern); (ii) polyps with suspected superficial invasion or (previous) nonlifting of size up to 15 mm, which were expected to fit easily into the cap. Larger polyps (>15 mm) with anticipated superficial submucosal invasion were generally removed by ESD and not by eFTR. All patients in whom eFTR was intended (i.e. at least anal introduction of the eFTR device occurred) were included.

The exclusion criteria were: polyps removed by a hybrid endoscopic mucosal resection (EMR)–eFTR technique and final histology other than adenocarcinoma, adenoma, or sessile serrated lesion.

All patients provided their consent to undergo eFTR. This study was approved by the Medical Research Ethics Committee of University Medical Center Utrecht (reference number 19/600) and was carried out in accordance with the Helsinki Declaration, but was not subject to the Medical Research involving Human Subjects Act (WMO).
Study outcomes and data collection

Medical records, endoscopy reports, and histological outcomes of all procedures were reviewed. The main outcome was R0 resection, defined as a tumor (malignancy and dysplasia)-free margin (≥ 0.1 mm) at both the deep and lateral resection margins. The secondary outcomes were: (i) technical success, defined as reaching the target area with the eFTR device, successful clip application followed by macroscopically complete en bloc resection; (ii) risk status (described below); (iii) full-thickness resection, defined as the presence of the muscularis propria in the resected specimen; (iv) procedure-related adverse events; (v) determination of risk factors for an R1/Rx resection, with the main focus being on the influence of estimated polyp size at endoscopy.

eFTR procedure

All procedures were performed by endoscopists with significant experience in interventional endoscopy. Management of antiplatelet and anticoagulant therapy was standardized according to current guidelines.

eFTR was conducted using the full-thickness resection device (FTRD; Ovesco Endoscopy, Tübingen, Germany) or using a two-stage technique with the Padlock over-the-scope (OTS) clip (Steris Endoscopy, Mentor, Ohio, USA) (Fig. 1). The FTRD consists of a transparent cap with an inner tip diameter of 13 mm and depth of 23 mm, on which an OTS clip is preloaded, and an integrated 13-mm snare. The Padlock OTS clip has standard and Pro-Select versions with inner tip diameters of 9.5–11 mm and 11.5–14 mm, respectively, with variable depth.

First, diagnostic endoscopy was performed to identify the polyp. The size of the polyp was estimated at endoscopy. The lateral margins of the polyp were circumferentially marked with coagulation. The endoscope was then equipped with the FTRD system or the Padlock device. After the fitted endoscope was re-introduced, the polyp was pulled into the cap using a grasping forceps. When the target area was assumed to be fully captured in the cap, the clip was deployed. Subsequently, the polyp was resected by the integrated snare using the FTRD system or by a standard polypectomy snare after placement of the Padlock clip.

From August 2017, we performed ESD-assisted eFTR for large (in particular ≥ 15 mm) malignant polyps. Our hypothesis was that this strategy would improve control of the lateral margin, resulting in higher overall R0 rates. Circumferential incision was performed with an ESD knife after submucosal lifting, followed by partial dissection until nonlifting was encountered and eFTR was then performed as described above.

The resected specimen was pinned onto cork before immersion in formalin. The resection site was inspected endoscopically for macroscopic completeness, positioning of the clip, and adverse events.

▶ Fig. 1 Images from endoscopic full-thickness resection (eFTR) of a flat polyp in the ascending colon using the Padlock clip showing: a,b endoscopic narrow-band imaging of a 18-mm polyp with features of malignancy and deep submucosal invasion (Paris 0-IIa + IIc, Hiroshima C3 vascular pattern); c correct positioning of the clip; d full-thickness resection; e histological appearance consistent with a low risk T1b CRC with deep submucosal invasion (sm3), without the presence of lymphovascular invasion or high grade budding; free margins were present indicating the malignancy had been radically removed.
Histological outcome

Histological assessment was carried out by an experienced gastrointestinal pathologist. The histological evaluation was performed according to the Vienna classification of gastrointestinal neoplasms and the 8th TNM classification of malignant tumors [21]. After primary eFTR, T1 CRCs were classified on the basis of the presence or absence of the following histological risk factors for lymph node metastasis or local recurrence: lymphovascular invasion (LVI; defined as tumor cells in an endothelial-lined channel, including lymphatic and blood vessels); poor differentiation (assessed according to the WHO) [22]; high grade tumor budding (Bd2–3; assessed according to the International Tumor Budding Consensus Conference recommendations) [23]; ≥ T2 CRC; and deep submucosal invasion (defined as submucosal invasion depth ≥ 1000 µm [Sm2/3]). Tumors were considered to be low risk T1 CRCs when all features were absent; low risk T1b CRCs when only deep invasion was present; and high risk T1 CRCs if any of LVI, tumor budding, poor differentiation, or ≥ T1 CRC resection margins were present. An curative resection was defined as an R0 resection for a low risk T1 CRC, low risk T1b CRC, or a benign adenoma, which is as recommended by the current Dutch and European Society for Medical Oncology (ESMO) guidelines [4].

Table 1  Patient and polyp characteristics of 136 endoscopic full-thickness resection (eFTR) procedures.

<table>
<thead>
<tr>
<th>Patient and polyp characteristics</th>
<th>Final histological outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td>Adenoma with LGD 12 (8.8)</td>
</tr>
<tr>
<td>Male 83 (61.0)</td>
<td>Adenoma with HGD 11 (8.1)</td>
</tr>
<tr>
<td>Female 53 (39.0)</td>
<td>Adenocarcinoma 113 (83.1)</td>
</tr>
<tr>
<td>Age, median (IQR), years 72 (67–76)</td>
<td>T1 CRC 75 (55.1)</td>
</tr>
<tr>
<td>ASA score, n (%)</td>
<td>– T1Sm1 20 (26.7)</td>
</tr>
<tr>
<td>≥ 2 105 (77.8)</td>
<td>– T1Sm2 21 (28.0)</td>
</tr>
<tr>
<td>≥ 3 31 (22.8)</td>
<td>– T1Sm3 32 (42.7)</td>
</tr>
<tr>
<td>Polyp size, median (IQR), mm 15 (13–18)</td>
<td>– T1Smx 50 (2.7)</td>
</tr>
<tr>
<td>Location of polyp, n (%)</td>
<td>– Lymphovascular invasion (present) 21 (28.0)</td>
</tr>
<tr>
<td>Cecum 9 (6.6)</td>
<td>– Budding</td>
</tr>
<tr>
<td>Ascending colon 25 (18.4)</td>
<td>Low-grade (Bd1) 50 (66.7)</td>
</tr>
<tr>
<td>Hepatic flexure 12 (8.8)</td>
<td>High-grade (Bd2–3) 18 (24.0)</td>
</tr>
<tr>
<td>Transverse colon 30 (22.1)</td>
<td>Not available 7 (9.3)</td>
</tr>
<tr>
<td>Splenic flexure 6 (4.4)</td>
<td>Differentiation</td>
</tr>
<tr>
<td>Descending colon 6 (4.4)</td>
<td>Well/Moderate 68 (90.7)</td>
</tr>
<tr>
<td>Sigmoid 37 (27.2)</td>
<td>Poor 7 (9.3)</td>
</tr>
<tr>
<td>Rectum 11 (8.1)</td>
<td>≥ T2 CRC 38 (27.9)</td>
</tr>
</tbody>
</table>

IQR, interquartile range; ASA, American Society of Anesthesiologists; LGD, low grade dysplasia; HGD, high grade dysplasia; CRC, colorectal cancer. 1 Includes 26 endoscopic submucosal dissection-assisted eFTR procedures.
Table 2. Details of the procedures and outcomes for the 136 endoscopic full-thickness resections (eFTRs) performed for suspected T1 colorectal cancer (CRC).

<table>
<thead>
<tr>
<th>Procedural details and outcomes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical success, n (%)</td>
<td>119 (87.5)</td>
</tr>
<tr>
<td>pT1 CRC</td>
<td>68/75 (90.7)</td>
</tr>
</tbody>
</table>

Reason for technical failure, n
- Polyp not reached with eFTR device: 3
- Insufficient suction/traction into eFTR cap: 4
- Macroscopic incomplete resection: 10

Procedure performed, n
- Standard eFTR: 110
- Endoscopic submucosal dissection-assisted eFTR: 26

eFTR device used, n (%)
- Full-thickness resection device: 114 (83.8)
- Padlock: 22 (16.2)

Histological outcome
Full-thickness resection, n (%): 118/129 (91.5)
Histological R0 resection (n = 133), n (%): 106 (79.7)
- Free deep margin: 124 (93.2)
- Free lateral margin: 108 (81.2)

For histological type
- Adenoma: 20/22 (90.9)
- pT1 CRC: 61/73 (83.6)
- ≥pT2 CRC: 25/38 (65.8)

<table>
<thead>
<tr>
<th>Table 2</th>
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<tbody>
<tr>
<td>Details of the procedures and outcomes for the 136 endoscopic full-thickness resections (eFTRs) performed for suspected T1 colorectal cancer (CRC).</td>
</tr>
</tbody>
</table>

Statistical analysis
Patient demographics and clinical, polyp, and procedural characteristics were analyzed using descriptive statistics. Categorical data were described with counts and/or percentages; for the main eFTR outcomes, 95% CIs were also determined using the Wilson procedure. Numerical variables were expressed as median and interquartile range (IQR) after testing for normality. A Poisson regression analysis with robust SEs was performed to evaluate the multivariable risk ratios for size, morphology, location, type of device, and depth of invasion for the dependent variable R1/Rx resection. The selection of available parameters was made on a directed acyclic graph based on all potential risk factors for an R1/Rx resection (Fig. 1s, see online-only Supplementary material). Multivariable risk analyses were performed using IBM SPSS Statistics, version 25 (Armonk, New York, USA).

Results
Patient and polyp characteristics
A total of 136 eFTR procedures in 136 patients (83 men [61%]; median [IQR] age, 72 [67–76]) were included. Baseline patient and polyp characteristics are shown in Table 1. Median polyp size based on endoscopic assessment was 15 mm (IQR 13–18 mm), evenly distributed between the right- and left-sided colon. Hiroshima classification type C and Kudo pit-pattern type V were reported in 97.5% and 63.3% of the reported cases, respectively. A vascular pattern of suspected deep submucosal (Hiroshima C3) was reported in 36.9%. In addition, a morphological depression was seen in 66.2% of cases.

Histology
Final histology of the entire cohort demonstrated malignancy in 83.1% (113/136), including 75 T1 CRCs and 38 ≥T2 CRCs, and benign histology in 16.9% (23/136) (Table 1). T1 CRC with deep submucosal invasion (sm2/3) was present in 53 T1 CRCs (70.7%). LVI was the most frequent unfavorable histological feature in the T1 CRC subgroup (21/75; 28%) and its presence was strongly related to the depth of invasion (sm1, 10%; sm2/3, 34.0%; P = 0.04). High grade budding (Bd2 = 3) was seen in 24% of all T1 CRCs: 16.7% in T1sm1 and 31.3% in T1sm2/3 (P = 0.24).

Technical success
eFTR procedures were performed using the FTRD system and Padlock clip strategy in 114 and 22 procedures, respectively. An ESD-assisted eFTR technique was used in the removal of 26 polyps (19.1%; see later section). Technical success in the entire cohort was 87.5% (119/136; 95% CI 80.9%–92.1%) (Table 2). In 10 cases, polyps were removed by eFTR, but resection was macroscopically incomplete with visible residual neoplastic tissue. In addition, four polyps could not be removed by eFTR because of insufficient polyp capture (including three ≥T2 CRCs and one T1sm3, as identified in the final surgical resection specimen) and three because of inability to reach the polyp with the eFTR device. The latter three cases were excluded from further analysis. Larger polyp size resulted in a higher technical failure rate: ≤ 15 mm, 6.7% (6/89); 16–20 mm, 11.4% (4/35); > 20 mm, 44.4% (4/9); P = 0.002.

R0 resection and effect of polyp size
An overall R0 resection was achieved in 79.7% (106/133; 95% CI 72.1%–85.7%) (Table 2). For pT1 CRCs, R0 was achieved in 83.6% (61/73; 95% CI 73.4%–90.3%). Resection margins were reported tumor-positive in lateral, vertical, or both directions in 18.8%, 6.8%, and 5.3%, respectively.
Multivariable regression analysis showed that polyp size determined at endoscopy was significantly associated with R1/Rx resection (risk ratio [RR] 2.35 per 5-mm increase, 95%CI 1.80–3.07; P < 0.001) (▶Table 3). The R0 resection rate was 89.9% (80/89; 95%CI 81.9%–94.6%) for polyps ≤15 mm, 71.4% (25/35; 95%CI 55.0%–83.7%) for polyps 16–20 mm, and 11.1% (1/9; 95%CI 2.0%–43.5%) for polyps >20 mm. The equivalent R0 rates for pT1 CRCs specifically were 89.9%, 81.0%, and 0%, respectively (▶Fig. 2; Table 1s).

Clinical outcome and follow-up
According to the previously described diagnosis and risk classification, eFTR was associated with a curative resection rate of 42.1% (56/133). Treatment strategies after eFTR are depicted in the flowchart (▶Fig. 3). Endoscopic follow-up was available in 26 of 36 patients with a low risk T1 CRC or low risk T1b CRC, and none showed local recurrence after a median follow-up period of 12 months (IQR 8–13 months). Only two patients with low risk T1bCRC underwent oncological surgery.

### Table 3
Univariable and multivariable regression analysis of variables associated with histological R1/Rx resection after 133 endoscopic full-thickness resection (eFTR) procedures for suspected T1 colorectal cancer (CRC).

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>R1/Rx resection, n/N (%)</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk ratio (95%CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Age, per 1-yr increase</td>
<td></td>
<td>1.004 (0.97–1.05)</td>
<td>0.84</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18/83 (21.7)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>9/50 (18)</td>
<td>0.83 (0.40–1.70)</td>
<td>0.61</td>
</tr>
<tr>
<td>Polyp size, per 5–mm increase</td>
<td>2.22 (1.84–2.68)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Polyp size, mm&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤15</td>
<td>9/89 (10.1)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>16–20</td>
<td>10/35 (28.6)</td>
<td>2.83 (1.26–6.36)</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;20</td>
<td>8/88 (9.9)</td>
<td>8.79 (4.54–17.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gross morphology&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat elevated</td>
<td>10/67 (14.9)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Protruded</td>
<td>17/66 (25.7)</td>
<td>1.73 (0.85–3.49)</td>
<td>0.13</td>
</tr>
<tr>
<td>Invasion depth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤T1sm1</td>
<td>5/42 (11.9)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>T1sm2/3</td>
<td>9/53 (17.0)</td>
<td>1.43 (0.52–3.94)</td>
<td>0.49</td>
</tr>
<tr>
<td>≥T2</td>
<td>13/38 (34.2)</td>
<td>2.87 (1.13–7.31)</td>
<td>0.03</td>
</tr>
<tr>
<td>eFTR device</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTRD</td>
<td>22/111 (19.8)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Padlock</td>
<td>5/22 (22.7)</td>
<td>1.15 (0.49–2.70)</td>
<td>0.75</td>
</tr>
<tr>
<td>Polyp location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>22/122 (18.0)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>5/11 (45.5)</td>
<td>2.5 (1.19–5.34)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<sup>1</sup> Estimated endoscopically.

<sup>2</sup> Polyps with flat elevated morphology were 0-IIa lesions and protruded morphology were 0-IIs lesions (according to the Paris classification), irrespective of the presence of a depression (IIc).

**ESD-assisted eFTR**

ESD-assisted eFTR was used for removal of 26 suspected T1 CRCs. The median polyp size of 20 mm (IQR 17–25 mm) was larger compared with polyps removed by primary eFTR (15 mm [IQR 12–15 mm]; P<0.001). Technical success was achieved in 76.9% (20/26) and failure was related to residual neoplasia visible after resection (n=4) or inability to pull the polyp into the cap (n=2). R1/Rx resection was reported in 50% (13/26), which was also related to the polyp size. Detailed outcomes are described in Table 2s.
Adverse events

Procedure-related adverse events occurred in 6.6% (9/136). Seven perforations were encountered, including three delayed perforations and four transmural defects. The latter four cases were diagnosed during the procedure and related to snaring without application of the OTS clip (n = 2), traumatic injury while advancing through a diverticular sigmoid (n = 1), and perforation during dissection with the ESD knife in an ESD-assisted eFTR procedure (n = 1). Urgent surgery was required in two patients, while the remaining patients could be managed conservatively, with endoscopic closure using through-the-scope clips and antibiotics.

Other adverse events were: post-procedural fever treated with antibiotics (n = 1) and self-limiting delayed hemorrhage (n = 1).

Discussion

In this cohort of 136 eFRs for colorectal polyps suspected of being T1 CRCs, it was shown that complete histological resection could be achieved in the vast majority (90%) of polyps that were endoscopically sized up to 15 mm. However, the R0
resection rate decreased for larger polyps, a decline also seen in proven pT1 CRCs.

The upper size limit, anticipated depth of invasion, risk of complications, local expertise, and proportion of potential curative resections are important to the clinician when deciding to select the optimal local resection technique for the treatment of a patient with lesions suspected of being T1 CRCs. eFTR has emerged as a very promising new excision tool, especially for T1 CRCs with deep submucosal invasion (T1b). It is relatively easy to apply and less difficult to learn compared with ESD; however, the perforation risk is not inconsiderable, the device is more expensive, and long-term follow-up data are still lacking [18, 20].

It is currently unclear which local excision technique should be preferred as the first-line treatment modality for small T1 CRCs. eFTR could be considered for suspected T1 colon cancers ≤ 15 mm, independent of the depth of invasion. In studies on ESD and underwater EMR for polyps with signs of superficial submucosal invasive CRC only, approximately 50% of the removed T1 CRCs turned out to be T1b CRCs [24, 25] and the proportion of R0 resections has been shown to drop in T1b CRCs to 41%–65% [24, 26, 27]. Future comparative studies are needed to determine the optimal treatment strategy for ≤ 15-mm T1 CRCs.

As eFTR is the only endoscopic local excision technique for deep submucosal invasive cancers in the colon, larger lesions up to 20 mm may be resected if deemed suitable for complete traction and suction into the cap, such as a mobile lesion located on the top of a fold. Owing to its size limit and costs, eFTR seems less suitable as a first-choice technique for deep invasive submucosal rectal cancers, where transanal minimally invasive surgery (TAMIS) and endoscopic intermuscular dissection (EID) are both very good and cheaper alternatives, and most importantly are independent of polyp size [28].

Local treatment is recommended for T1 CRCs that are considered at low risk of LNM or recurrent disease [29]. A recent meta-analysis has reported this risk to be 0.7% in patients with a low risk T1 CRC [3]. If a histological risk factor is present, patients who are considered at high risk of LNM or local recurrence, if sufficiently fit, should be referred for segmental colectomy. In this respect, high risk is defined as all risks higher than 0.7%. However, in the presence of only deep submucosal invasion without other unfavorable histological features, there is growing evidence that the risk of LNM or local recurrence is between 2% and 2.5%, which almost equals the mortality rate of 1.7% for colorectal surgery for T1 CRCs [9, 10, 14, 16]. Population-based cohort studies indicate that the proportion in this low risk T1b CRC group ranges between 26.6% to 46.1% of all T1 CRCs [9–14]. In our study, low risk T1b CRC was finally diagnosed in one-third of all T1 CRCs resected by eFTR. Although follow-up was relatively short, recurrent disease in low risk T1b CRCs removed by eFTR was not observed. Prospective studies are required to confirm the long-term oncological safety of a conservative management strategy for these patients.

Several limitations of our study should be acknowledged. First, one limitation is the measurement of polyp size, which was subjectively estimated by the endoscopist. Not only may this lead to over- or underestimation of the exact size, but it is also prone to terminal digit preference [30]. Indeed, the preferred end-digits 5 or 0 (i.e. 10, 15, and 20 mm) were more frequently reported in our cohort. However, our strategy most closely resembles current practice where measurement tools are not routinely used. It probably induces only a small source of error and does not seem to influence our main findings. We decided not to focus on the pathologically measured polyp size post-eFTR, because this does not play any role in deciding which resection modality is most appropriate from a clinical perspective. Furthermore, measurement after formalin fixation is prone to inaccuracy because of difficulty in determining the lateral polyp margins, coagulation effects, tissue fixation, and measurement bias [31].

Second, the number of polyps > 20 mm included in our study is relatively low compared with the other size categories. Although this limits the statistical power, we believe that polyp size ≥ 20 mm is a strong argument to refrain from eFTR for suspected T1 CRCs. The absolute difference in R0 between ≤ 20-mm and > 20-mm polyps was considerable. A hybrid ESD-assisted eFTR approach was introduced for larger polyps, and almost all > 20-mm polyps were removed with this technique. However, this modified approach does not seem to have the potential to expand the upper size limit for eFTR. In contrast to our expectations, R0 rates were unacceptable, still showing low rates of free lateral margins. Third, two eFTR devices with minor technical differences were used in this study. Both techniques were shown to be equally effective.

In conclusion, our study shows that eFTR is an effective resection technique to resect lesions suspected of being a T1 CRC; however, the effectiveness decreases with increasing polyp diameter. Polyps < 15 mm can be removed effectively; poor radical resection rates are achieved for polyps ≥ 20 mm. For polyps between 15 and 20 mm, mobility, accessibility, wall flexibility, and depth of submucosal invasion should guide the decision on whether to perform eFTR or switch to another local excision technique.

Competing interests

L.M.G. Moons, F.P. Vleggaar, and P. Didden are consultants for Boston Scientific. The remaining authors declare that they have no conflict of interest.

References
