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Systematic review and meta-analysis on effectiveness and safety of the full-thickness resection device (FTRD) in the colon

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Systematic review and meta-analysis on effectiveness and safety of the full-thickness resection device (FTRD) in the colon

Metaanalyse zur endoskopischen Vollwandresektion im Kolon

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ZUSAMMENFASSUNG

Hintergrund Die endoskopische Vollwandresektion erweitert die Möglichkeiten endoskopischer Resektionen. Sie basiert auf der Resektion der Läsion einerseits und dem sicheren Verschluss des Resektionsdefekts andererseits. Das Full-Thickness Resection Device (FTRD, Ovesco Endoscopy, Tübingen) vereint beide Schritte in einem Gerät. Typische Indikationen sind sogenannte schwierige oder Non-lifting-Adenome im Kolon.

Methodik Systematisches Review und Metaanalyse zur Effektivität und Sicherheit der endoskopischen Vollwandresektion im Kolon mit dem FTRD-System.

Ergebnisse Insgesamt wurden 26 Studien eingeschlossen, darunter 12 Volltextpublikationen und 14 Kongressbeiträge. Die Gesamtzahl der analysierten FTRD-Prozeduren betrug 1538. Die Zielläsion wurde mit einer Rate von 96,1 % (95 %-Konfidenzintervall (95 %-KI): 94,6–97,1) erreicht. Die Resektion war in 90,0 % (95 %-KI: 87,0–92,3) technisch erfolgreich. und eine R0-Resektion gelang mit einer Rate von 77,8 % (95 %-KI: 74,7–80,6). Komplikationen traten bei 8,0 % (95 %-KI: 5,8–10,4) der Prozeduren auf; die Rate der Nachblutungen und Perforationen lag bei 1,5 % (95 %-KI: 0,3–3,3) bzw. 0,3 % (95 %-KI: 0,0–0,9). Die Rate komplikationsbedingter Operationen betrug 1,0 % (95 %-KI: 0,4–1,8).

Schlussfolgerung Die endoskopische Vollwandresektion im Kolon mittels FTRD ist effektiv und sicher. Eine R0-Resektion gelingt in vielen Fällen, und insbesondere schwerwiegende Komplikationen mit der Notwendigkeit einer Notfalloperation sind sehr selten.

ABSTRACT

Background Endoscopic full-thickness resection (EFTR) has expanded the possibilities of endoscopic resection. The full-thickness resection device (FTRD, Ovesco Endoscopy, Tübingen, Germany) combines a clip-based defect closure and snare resection in a single device.

Methods Systematic review and meta-analysis on effectiveness and safety of the FTRD in the colon.

Results A total of 26 studies (12 published as full-text articles and 14 conference papers) with 1538 FTRD procedures were included. The pooled estimate for reaching the target lesion was 96.1 % (95 % confidence interval [95 % CI]: 94.6–97.1) and 90.0 % (95 % CI: 87.0–92.3) for technically successful resection. Pooled estimate of histologically complete resection was 77.8 % (95 % CI: 74.7–80.6). Adverse events occurred at a pooled estimate rate of 8.0 % (95 % CI: 5.8–10.4). Pooled estimates for bleeding and perforation were 1.5 % (95 % CI: 0.3–3.3) and 0.3 % (95 % CI: 0.0–0.9), respectively. The rate for need of emergency surgery after FTRD was 1.0 % (95 % CI: 0.4–1.8).

Conclusion The use of the FTRD in the colon shows very high rates of technical success and complete resection (R0) as well as a low risk of adverse events. Emergency surgery after colonic FTRD resection is necessary in single cases only.

ABBREVIATIONS

95 % CI	95 % confidence interval
EFTR	endoscopic full-thickness resection
EMR	endoscopic mucosal resection
ESD	endoscopic submucosal dissection
FTRD	full-thickness resection device
PI	prediction interval

Introduction

Over the last few years, endoscopic full-thicknesses resection (EFTR) has emerged as new and promising resection technique [1, 2]. It has led to an expansion of indications for endoscopic resection, and several different techniques for EFTR have meanwhile been developed for use in the upper and lower gastrointestinal tract [3]. These techniques require resection of the target lesion as well as reliable closure of the wall defect. The best-studied device for EFTR is the FTRD (Ovesco Endoscopy, Tübingen, Germany). This device is an over-the-scope system based upon an over-the-scope clip combined with a preloaded electrocautery resection snare, and, thus, it incorporates resection and defect closure in a single device [4, 5]. Even though there is increasing evidence for use of FTRD in the upper gastrointestinal tract as well [6, 7], mainstay of the device remains the lower gastrointestinal tract, particularly resection of so-called "difficult adenomas". These include "non-lifting" lesions, either due to submucosal scarring after previous treatment, due to adenoma recurrence, or submucosal tumor invasion, as well as lesions at anatomically difficult locations such as a diverticulum or appendiceal orifice [1, 8]. Current knowledge on FTRD in the colon was mostly based on retrospective or single-center studies until a prospective multi-center study (WALLRESECT) was published recently [9]. The study was conducted in 9 German hospitals and included 181 patients. It reported technical success in 89.5 % and a histological complete resection in 76.9 % of procedures. Adverse events occurred in 9.9 %.

In this analysis, we aimed to summarize current knowledge on effectiveness and safety of EFTR with FTRD in the colon. Therefore, a systematic review and meta-analysis of studies reporting on use of FTRD in the colon was done.

Methods

The study is reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. A completed PRISMA statement checklist can be found as Supplementary Material.

Outcome parameters

The aim of this meta-analysis was to assess effectiveness and safety of colonic EFTR with FTRD. Therefore, the following outcome parameters were calculated: 1) rate of target lesions that were reached with FTRD mounted on top of the endoscope; 2) rate of primary technical successful resection; 3) rate of histological confirmed R0 resection; 4) rate of difficulties during resection; 5) rate of overall adverse events; 6) rate of bleeding; 7) rate of perforation; and 8) rate of need for emergency surgery due to an adverse event.

Primary technical successful resection was defined as successful incorporation of the lesion into the device's cap, clip deployment, and snare resection. Completeness of resection or achievement of full-thickness resection was not considered in defining technical success.

Eligibility criteria

Studies were eligible for inclusion in this meta-analysis if they reported at least on one of the below-mentioned outcome parameters for EFTR with FTRD in the colon and included at least 10 FTRD procedures in the colon. Studies published as full-text articles as well as meeting abstracts were included. Studies conducted in humans only were eligible for inclusion.

Information sources and search

The following databases were searched to identify eligible studies: PubMed, Science Citation Index Expanded, BIOSIS Previews, and Cochrane Library. Search was conducted using the combination of the following search terms: "FTRD" OR "full-thickness resection device" OR "EFTR" OR "endoscopic full-thickness resection." In addition to these databases, the following journals were searched using the same search string in order to identify meeting abstracts: Gastroenterology, Gut, Gastrointestinal Endoscopy, Endoscopy, United European Gastroenterology Journal, and German Journal of Gastroenterology. Database searches were last updated on 14th February 2020, and all search results were screened for inclusion into the analysis.

Study selection

First, titles and abstracts were screened. Potentially eligible studies were then reviewed in full text. Studies that met the above-mentioned in- and exclusion criteria after full-text review were included in the meta-analysis. Review was done by 2 authors (AW, BM).

Reducing the risk of bias

Based upon the search strategy and decision to include full-text articles and meeting abstracts, an important cause of bias was believed to be double publication bias. Thus, if studies were published as meeting abstract and full-text articles, full-text articles were included in the analysis. Further, if results from a single center were reported as meeting abstract or full-text and the results from this center were as well included in larger multi-center study, only the latter was included. If results were presented at several meetings, only the most recent meeting abstract was included. To identify potential double publications, we retrieved information on the participating authors, their affiliations, and participating centers as well as periods of study performance for all screened studies.

There were no restrictions in the eligibility criteria with regard to study design or indication for EFTR. Even though a minimum study size of 10 FTRD procedures was required for studies to be eligible, there still was a risk of differences in size of included stud-

ies, and experience with the procedure might vary between studies. A random-effects model was thus used.

Data extraction

From all eligible studies, we included information on study type, numbers of participating centers, and time of study performance. Further, characteristics of included patients (i. e., age and sex) as well as indication for EFTR, size, and location of the target lesion were retrieved. If available, the following outcome variables were included: 1) number of procedures in which the target lesion was reached with FTRD and reasons for not reaching the target lesion; 2) number of technically successful procedures; 3) number of histologically confirmed complete resection (R0 resection); 4) number of difficulties during FTRD and underlying cause; 5) number and causes of adverse events; and 6) need for emergency surgery due to an adverse event.

Statistical analysis

Pooled estimates were calculated for all of the above-mentioned outcome parameters. They are reported with corresponding 95 % confidence interval (CI) and prediction interval (PI). The meta-analysis was conducted using a random effects model. A logit transformation was used in case of the outcome parameters "reaching of target lesion," "technical success," and "R0 resection." In case of the outcome parameters "technical difficulties," "adverse events" (including "bleeding" and "perforation"), and "emergency surgery," a double arcsine transformation was used. Heterogeneity was assessed calculating I^2 and a chi-squared test with corresponding p-value. Statistical analysis was performed using R (version 4.0.0, https://www.r-project.org) [10] and the R packages "meta" and "metaphor" [11, 12].

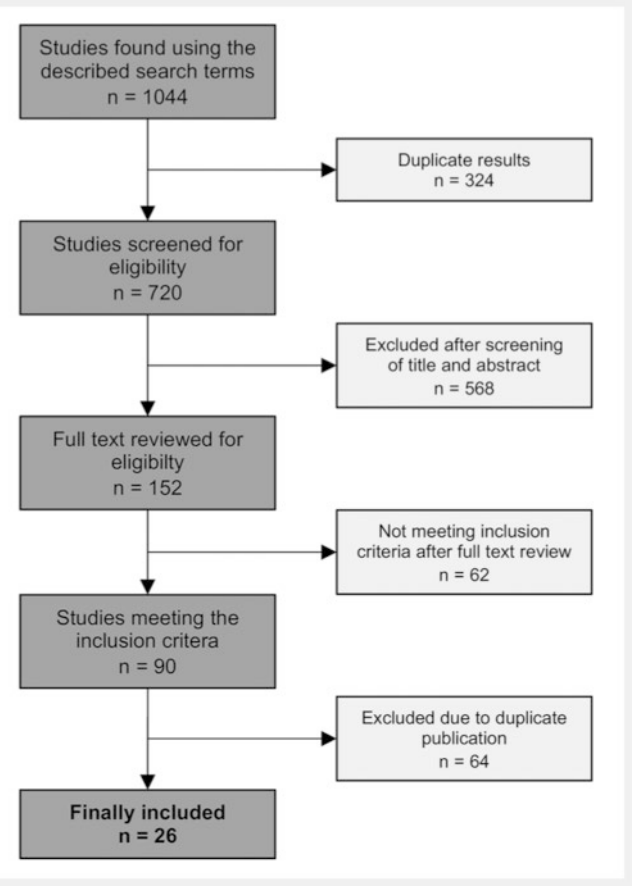
Sensitivity and subgroup analyses

Outliers and potentially influential studies were identified in further sensitivity analyses, and, if identified, the pooled estimate was calculated leaving out those influential studies. Subgroup analyses were performed for the following pre-defined subgroups: Publication type ("full text publication" versus "meeting abstract"), study design ("prospective" versus "retrospective"), and study size ("less than 25 FTRD procedure" versus "25 or more FTRD procedures").

Results

Overview of included studies

Finally, 26 studies were included in the analysis, among which 12 were published as full-text articles and 14 as conference abstracts. The process of identifying and selecting the final studies is depicted in ▶ **Fig. 1**, and an overview of included studies is presented in ▶ **Table 1**. The 26 included studies reported on a total of 1565 FTRD procedures (▶ **Table 2, 3**).



▶ **Fig. 1** Identification of eligible studies. Flowchart resembling how studies were identified and screened for this analysis, including numbers and reasons for exclusion.

Effectiveness of FTRD in the colon

Pooled rate for reaching the target lesion with FTRD mounted on the endoscope was 96.1 % (95 % CI: 94.6–97.1, PI: 94.5–97.2; ▶ **Fig. 2A**). Information on reaching the target lesion was available in all but 1 study. The main reasons for not reaching the target lesion were unsuccessful passage of the sigma (n = 11) and difficulties advancing the endoscope with mounted FTRD to the target lesion (n = 11), while the cause was not further specified in the remaining cases (n = 5). There was no indication of heterogeneity (I^2 = 0 %, p = 0.99); however, the study by Krutzenbichler et al. [13] was identified as influential study. Leaving this study out led to a pooled estimate of 96.3 % (95 % CI: 94.7–97.4).

Primary technical successful resection of the target lesion was achieved with a pooled rate of 90.0 % (95 % CI: 87.0–92.3, PI: 76.5–96.1; ▶ **Fig. 2B**). However, a moderate level of heterogeneity was present (I^2 = 50 %, p < 0.01). Excluding the study by Zwager et al. [14], which was identified as an influential outlier, resulted in a pooled rate of 88.9 (95 % CI: 86.0–91.3).

Pooled estimate of histologically complete (R0) resection was 77.8 % (95 % CI: 74.7–80.6, PI: 68.3–85.0) in the included studies (▶ **Fig. 2C**), and there was no evidence of substantial heterogeneity (I^2 = 30 %, p = 0.07). In further analysis, the study by Andrisani

▶ **Table 1** Summary of included studies with information on number of FTRD procedures performed as well as the study design.

study	procedures, n	centers, n	design	country	time of study	comment	ref.
Schmidt 2015	25	2	retrospective cohort study	DE, CH	07/2012–07/2014		[5]
Richter-Schrag 2016	20	1	retrospective cohort study	DE	11/2014–06/2015		[23]
Thomsen 2016[a]	15	2	retrospective cohort study	DE	01/2015–N/A		[34]
Altmann 2017[a]	11	1	retrospective cohort study	DE	08/2015–01/2017		[35]
Meier 2017	10	1	retrospective cohort study	DE	06/2016–08/2016	only hybrid EMR-FTRD	[32]
Pickartz 2017[a]	17	1	retrospective cohort study	DE	10/2016–04/2017		[36]
Aepli 2018	33	2	retrospective cohort study	CH	05/2016–11/2016		[18]
LaBaleur 2018[a]	60	11	retrospective cohort study	FR	N/A	includes one gastric FTRD	[24]
Braun 2018[a]	12	1	retrospective cohort study	CH	2015–2017	only diagnostic EFTR (amyloidosis)	[37]
Falt 2018[a]	24	1	retrospective cohort study	CZ	06/2016–09/2017		[38]
Hu 2018[a]	38	8	retrospective cohort study	UK	04/2015–01/2018		[19]
Schmidt 2018	188	9	prospective observational cohort study	DE	02/2015–04/2016		[9]
Valli 2018	60	1	retrospective cohort study	CH	04/2012–10/2016	includes five gastric FTRDs	[20]
Vitali 2018	13	1	prospective observational cohort study	DE	06/2015–06/2016		[25]
Albrecht 2019	67	3	retrospective cohort study	DE	11/2014–12/2017		[26]
Andrisani 2019	114	12	retrospective cohort study	IT	01/2015–03/2018		[15]
de-Ferro 2018	10	1	retrospective cohort study	PT	03/2017–02/2018		[39]
von Helden 2019	30	1	retrospective cohort study	DE	01/2016–11/2018		[21]
Ichkhanian 2019[a]	79	24	retrospective cohort study	US	10/2017–10/2018		[27]
Krutzenbichler 2019[a]	164	5	retrospective cohort study	DE	2015–2018	includes one gastric FTRD	[13]
Sferrazza 2019[a]	11	2	prospective observational cohort study	IT	N/A		[40]
Stathopoulos 2019[a]	38	1	retrospective cohort study	DE	11/2016–04/2019		[41]
Uchima 2019[a]	71	10	retrospective cohort study	ES	06/2015–07/2018		[22]
Velegraki 2019	17	2	retrospective cohort study	GR	10/2015–12/2018		[42]
Yuen 2019	37	1	retrospective cohort study	US	N/A		[33]
Zwager 2020[a]	401	22	prospective	NL	09/2015–1072018		[14]

N/A: not available. DE: Germany, CH: Switzerland, FR: France, CZ: Czech Republic, PT: Portugal, UK: United Kingdom, US: United States of America, IT: Italy, ES: Spain, GR: Greece, NL: The Netherlands.
[a] Published as meeting abstract.

et al. [15] was identified as influential outlier. The pooled estimate was 76.9 (95 % CI: 73.9–79.6) excluding this study.

Technical difficulties

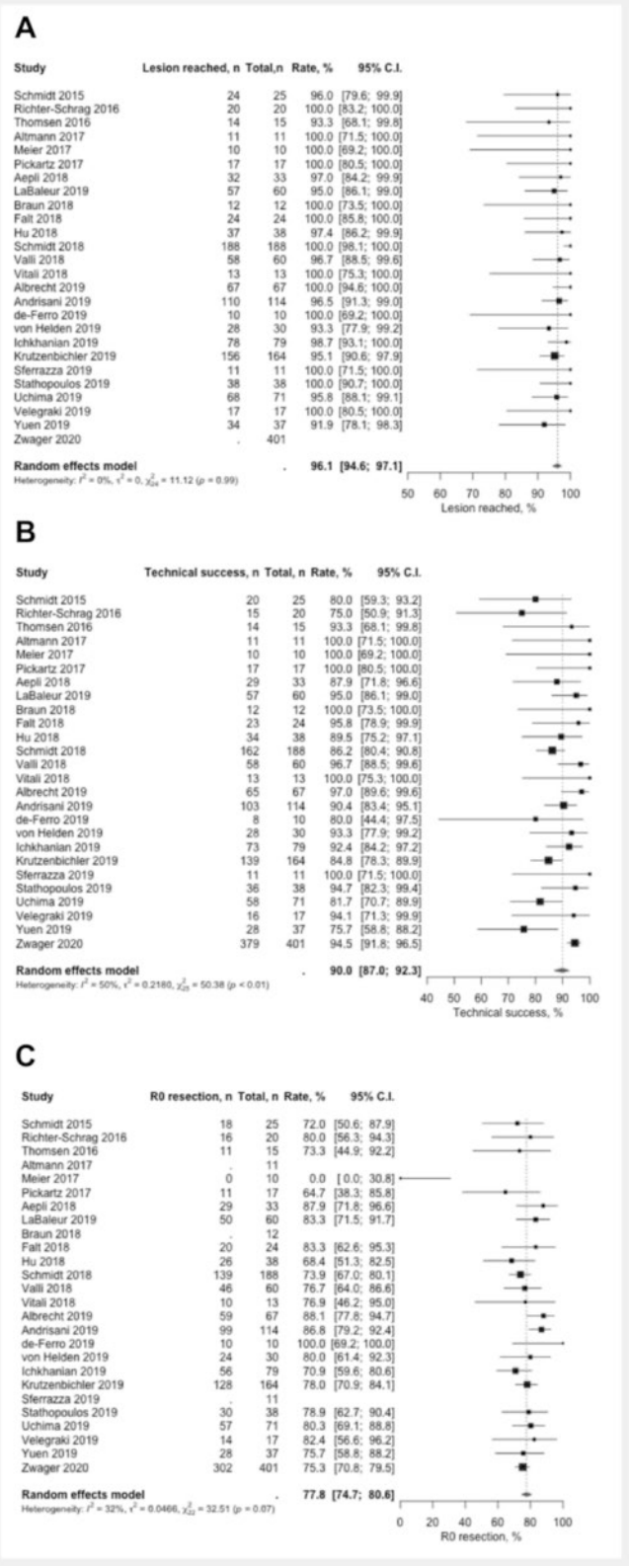
Difficulties occurred with a pooled estimate rate of 6.1 % (95 % CI: 3.6–9.0; PI: 0.0–19.6; ▶ **Fig. 3**). Snare-resection associated problems were the most commonly reported cause of technically difficult resection and occurred in 51 cases. However, in 33 cases, resection could successfully be completed using a conventional resection snare thereafter. Difficulties incorporating the lesion into the cap were reported in 32 cases, and malfunction of the preloaded clip in 8 procedures.

Some heterogeneity was present ($I^2 = 59\,\%$, $p < 0.01$), yet analysis did not identify any outlying studies.

▶ **Table 2** Baseline demographic characteristics of patients who underwent treatment with FTRD in the included studies.

study	patients, n	age, years	sex, n (male/female)
Schmidt 2015	25	mean: 70 (range: 43–84)	N/A
Richter-Schrag 2016	20	median: 65 (range: 19–85)	11/9
Thomsen 2016	15	mean: 65.5 (range: 47–79)	12/3
Altmann 2017	11	N/A	9/2
Meier 2017	10	mean: 72.5 (range: 53–82)	N/A
Pickartz 2017	17	N/A	N/A
Aepli 2018	33	mean: 65.9 (range: 44–85)	23/10
LaBaleur 2018	60	mean: 70 (range: 41–87)	40/20
Braun 2018	12	median: 73 (range: 29–81)	7/5
Falt 2018	24	mean: 68.8 (SD: 12.3)	21/3
Hu 2018	38	mean: 70 (range: 39–93)	N/A
Schmidt 2018	181	median: 65 (range: 29–88)	99/82
Valli 2018	60	mean: 68 (range: 38–88)	N/A
Vitali 2018	12	mean: 64.3 (SD: 6.3)	7/5
Albrecht 2019	70	mean: 79.5 (range: 25–89)[a]	42/25[a]
Andrisani 2019	114	mean: 68 (range: 20–90)[a]	61/49[a]
de-Ferro 2018	9	mean: 69 (range: 51–92)	6/3
von Helden 2019	30	median: 72.7 (range: 21.5–81.6)	19/10
Ichkhanian 2019	79	mean: 65	48/31
Krutzenbichler 2019	164	N/A	102/62
Sferrazza 2019	11	median: 68.4 (IQR: 63.9–74.1)	9/2
Stathopoulos 2019	38	median: 69	25/13
Uchima 2019	71	N/A	N/A
Velegraki 2019	17	mean: 59.7	10/7
Yuen 2019	37	mean: 71 (range: 50–89)	19/18
Zwager 2020	401	mean: 69 (SD: 8.6)	251/150

IAR: interquartile range. N/A: not available. SD: standard deviation.
[a] Based upon patients who finally underwent FTRD resection.



▶ **Fig. 2** Effectiveness of colonic EFTR with FTRD. Forest plots of effectiveness endpoints for colonic FTRD: **A** rate of target lesions reached, **B** rate of technical successful resection, and (C) rate of R0 resection.

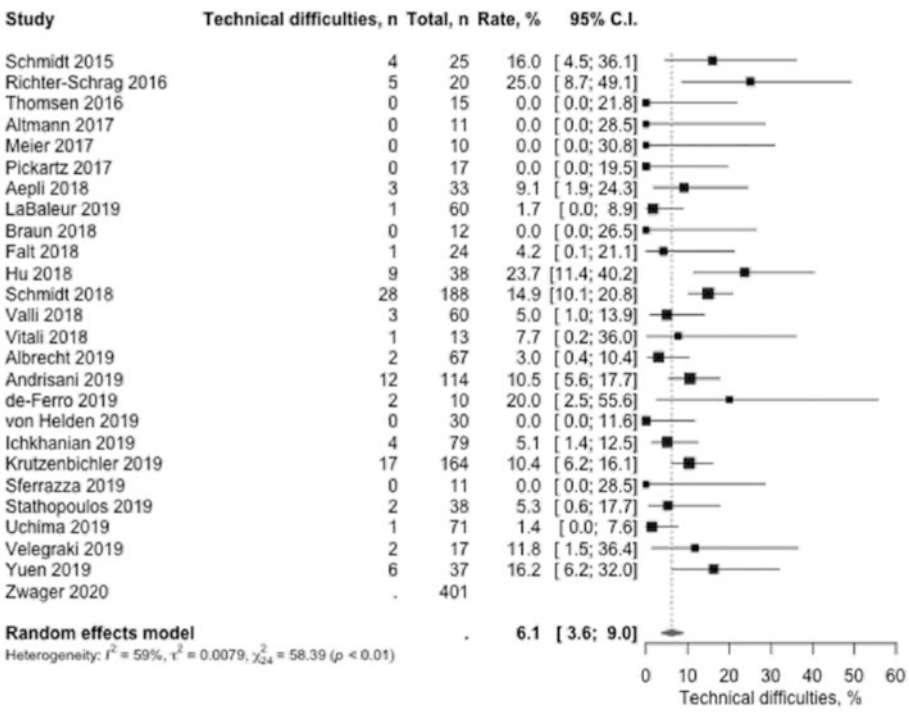
▶ **Table 3** Summary of the indications for endoscopic full-thickness resection with FTRD in the different studies and the size and location of the target lesion.

study	indication							size, mm[b]	location					
	non-lifting, residual, or recurrent adenoma	appendix	diverti-culum	carcinoma	SET	diagnostic EFTR	other		coecum	ascending colon	trans-verse colon	descending colon	sigmoid	rectum
Schmidt 2015	13	5	1	2	2	1	1	mean: 24 (range: 12–40)	5	5	3	4	5	2
Richter-Schrag 2016	12	0	0	6	2	0	0	median: 25 (range: 16–54)	2	2	1	1	3	11
Thomsen 2016	N/A							N/A	12					2
Altmann 2017	5	0	0	4	0	2	0	N/A	6					5
Meier 2017	10	0	0	0	0	0	0	median: 35 (range: 30–50)	4	4	0	0	2	0
Pickartz 2017	13	0	0	2	1	1		N/A	N/A					
Aepli 2018	23	2	1	4	1	0	2	mean: 13.5 (range: 1–25)	9	9	0	2	1	12
LaBaleur 2018	48	4	2	0	0	0	1	mean: 17 (range: 3–30)	8	8	11	5	17	10
Braun 2018	0	0	0	0	0	12	0	N/A	0	0	0	0	0	12
Falt 2018	20	2	0	0	1	1	0	N/A	N/A					
Hu 2018	18	3	0	10	7	0	0	median: 22 (range: 10–30)[c]	N/A					
Schmidt 2018	104	34	5	15	23	0	0	mean: 15 (range: 2–30)	55	35	22	8	30	30
Valli 2018	29	4	1	10	5	0	11	mean: 24 (range: 10–35)	5	15	1	16		14
Vitali 2018	11	0	1	0	1	0	0	mean: 17 (SD: 4)[c]	2	4	0	1	0	6
Albrecht 2019	50	2	0	10	5	0	0	mean: 23 (range: 9–37)	6	18	4	6	14	19
Andrisani 2019	77	4		16	10	3	0	mean: 18 (range: 5–40)	7	11	6	10	10	59
de-Ferro 2019	9	0	0	0	1	0	0	median: 15 (range: 12–20)	1	3	2	1	1	2

▶ **Table 3** (Continuation)

study	indication							size, mm[b]	location					
	non-lifting, residual, or recurrent adenoma	appendix	diverti-culum	carcinoma	SET	diagnostic EFTR	other		coecum	ascending colon	trans-verse colon	descending colon	sigmoid	rectum
von Helden 2019	29	0	0	0	0	0	0	median 25 (range: 14–33)[c]	0	18		9		3
Ichkhanian 2019	48			17	10	0	0	mean: 15.3 (SD: 6.5)	46			17		16
Krutzenbichler 2019	110	0	0	38	13	0	3	mean: 16 (range: 4–50)	20	41	22	13	24	38[d]
Sferrazza 2019	5	0	1	5	0	0	0	mean 18 (range: 10–25)	1	3	0	1	2	3[d]
Stathopoulos 2019	21	0	0	11[a]	5	1	0	median: 18 (range: 3–50)	N/A					
Uchima 2019	58	2	0	5	3	0	3	mean 21.53 (95% CI: 19.87–23.2)[c]	N/A					
Velegraki 2019	6	2	0	3	6	0	0	mean: 12.7 (Range: 5–30)	3	0	1	0	11	2
Yuen 2019	26	4	1	4[a]	2	0	0	mean: 16 (FTRD group) mean: 34 (Hybrid EMR-FTRD group)	8	10	9	9		1
Zwager 2020	146			238	15	2	0	median: 23.4 (range: 5–45)[c]	N/A					

N/A: not available. SD: standard deviation.
[b] If not otherwise specified as estimated in situ prior to resection.
[c] Measured on the resection specimen.
[d] Including one or more not further specified location.
[a] Carcinoma or adenoma with high-grade intraepithelial neoplasia.



▶ **Fig. 3** Technical difficulties. Forest plot summarizing the rate of difficulties during colonic FTRD resection.

Adverse events

Overall adverse events occurred with a pooled rate of 8.0 % (95 % CI: 5.8–10.4, PI: 1.9–16.7). Pooled estimates for bleeding and perforation were 1.5 % (95 % CI: 0.3–3.3, PI: 0.0–10.6) and 0.3 % (95 % CI: 0.0–0.9, PI: 0.0–1.8), respectively (▶ **Fig. 4A–C**). With regard to adverse events and bleeding, moderate heterogeneity was present, but statistical analysis failed to identify outlying and influential studies. In case of perforation, the study by Zwager was identified as outlier in sensitivity analysis; omitting that study led to a pooled estimated of 0.7 % (95 % CI: 0.0–1.3).

All adverse events are summarized in ▶ **Table 4**. In most cases adverse events could successfully be managed conservatively or endoscopically; surgical therapy as consequence of an adverse event was necessary with a pooled rate of 1.0 % (95 % CI: 0.4–1.8, PI: 0.4–1.9; ▶ **Fig. 4D**). No evidence of heterogeneity was present as assessed by I^2 (I^2 = 0 %, p = 1.00). Omitting the 2 outliers (Schmidt et al. [9], Zwager et al. [14]) identified in sensitivity analysis resulted in a pooled estimate of 0.9 (95 % CI: 0.2–2.0).

Subgroup analysis

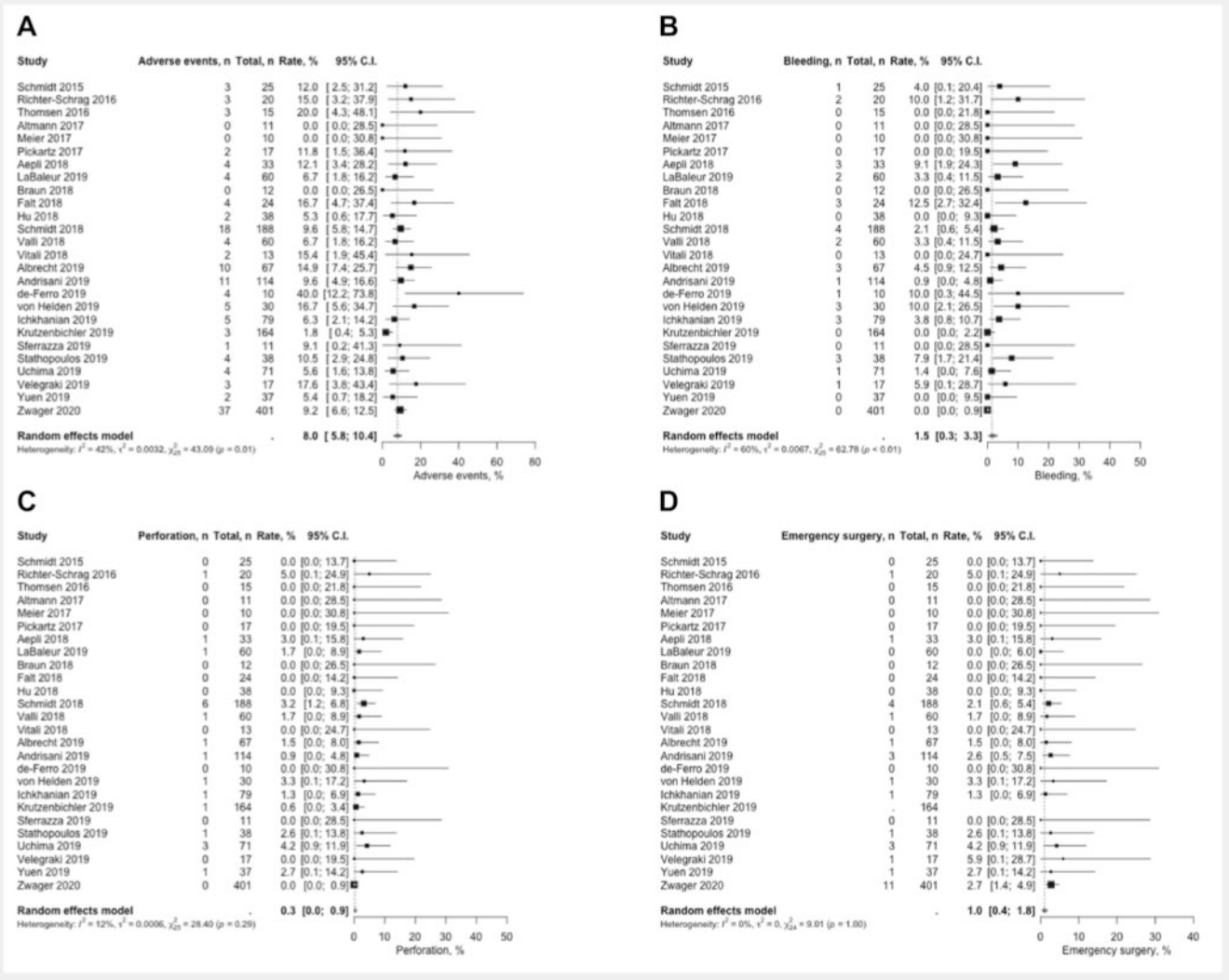
Subgroup analysis revealed a significantly higher (p = 0.02) adverse event rate reported in studies published as full text articles (pooled estimate: 10.5 %, 95 % CI: 7.6–13.8) compared to results published as meeting abstracts (pooled estimate: 5.7 %, 95 % CI: 3.3–8.6). There was no further significant difference between these 2 subgroups with regard to remaining outcome parameters. No differences were observed for any of the analyzed outcome parameters between prospective and retrospective studies and between studies including at least 25 FTRD procedures and those with less than 25 FTRD procedures (▶ **Table 5**).

Discussion

In this meta-analysis, we investigated the effectiveness and safety of EFTR with the FTRD system in the colon. Results confirm a high technical success rate and a good rate of histologically complete resections, while harboring a low rate of adverse events.

This is largest meta-analysis on EFTR in the colon and the first to exclusively focus on the FTRD system. A currently published meta-analysis by Li et al. included only approximately one-third of studies and patients (9 studies, 469 patients) and analyzed studies using the FTRD system and, in one case, the Padlock Clip (STERIS plc., Mentor, Ohio, U.S.A) in combination with subsequent conventional snare resection [16, 17]. In contrast, we included 26 studies and 1565 EFTR procedures, all performed with FTRD. The larger number of studies included in our analysis is mainly due to inclusion of published meeting abstracts in addition to full text publications, which is a further strength of this analysis. With regard to results for effectiveness of colonic EFTR, the study by Li et al. reported slightly higher rates for technical success (94.0 %) and R0 resection (84.9 %) [16].

To summarize findings of this analysis, the target lesion can be reached in the majority of cases with the FTRD mounted on the endoscope. Based on the data provided here and upon our own experience, the most challenging part is passage of the sigmoid colon, especially in cases of diverticulosis [5, 18–22]. In these cases, placement of a guidewire might help to safely pass the sig-



▶ **Fig. 4** Adverse events after FTRD resection in the colon. Shown is the forest plot for the overall adverse event rate **A** for bleeding **B** and perforations **C** after colonic FTRD as well as the need for emergency surgery due to an FTRD-related complication **D**.

▶ **Table 4** Summary of adverse events after use of the FTRD in the colon. Absolute numbers of adverse events reported in the 26 analyzed studies reporting on 1538 FTRD procedures in the colon.

adverse events	n
bleeding	33
perforation	20
postpolypectomy syndrome or pain	24
appendicitis[a]	12
others, including not specified	49

[a] After FTRD resection of adenomas involving appendiceal orifice.

ma. One study also suggested use of the prOVE Cap (Ovesco Endoscopy, Tübingen, Germany), a distal attachment cap similar in size to the FTRD, to facilitate passage of the sigmoid colon prior to mounting FTRD [15]. Once the target lesion is reached, it can successfully be resected in a high number of cases. One of the major causes for technical failure and non-successful resection were related to snare problems, such as breakage under high-frequency current [5, 9, 14, 15, 18–20, 23–27]. These were reported in 35 resections, of which 29 could be removed in a second step using a conventional resection snare. In this case, attention should be paid not to entrap the clip in the snare, as this might cause thermal injury and perforation [9].

Regarding the safety of FTRD resections, overall adverse event rate was 8.0 %. This rate was not calculated in the analysis by Li et al. [16] but is similar to the prospective study by Schmidt et al. (adverse event rate: 9.9.%) [9]. The most common adverse events were bleeding, of which most could be handled by conservative or endoscopic treatment, followed by pain or postpolypectomy syndrome. Pooled estimate for bleeding was 1.5 %, while rate for per-

▶ **Table 5** Pooled estimates of all outcome parameters for the 3 pre-defined subgroup analyses. With exception of the adverse event rate, which was significantly different between studies published as full text articles and those published as meeting abstracts, there was no significant influence of any of the subgroups on the outcome parameters.

outcome	publication type			study design			study size		
	full text	meeting abstract	P	prospective	retrospective	P	25 or more FTRD procedures	less than 25 FTRD procedures	P
effectiveness									
target lesion reached	96.7 (94.5–98.1)	95.6 (93.4–97.0)	0.36	98.4 (91.3–99.7)	95.9 (94.3–97.0)	0.29	96.0 (94.4–97.2)	96.2 (91.9–98.3)	0.89
technical success	89.1 (84.6–92.4)	90.7 (86.3–93.8)	0.55	92.2 (83.6–96.5)	89.3 (85.9–91.9)	0.45	89.8 (86.2–92.5)	89.6 (82.6–94.0)	0.95
R0 resection	80.2 (73.8–85.3)	76.0 (73.1–78.6)	0.22	74.9 (71.3–78.2)	78.7 (74.8–82.1)	0.15	77.9 (74.9–80.6)	75.2 (61.7–85.1)	0.66
safety									
technical difficulties	8.2 (4.4–12.8)	4.4 (1.5–8.2)	0.16	10.0 (3.0–19.6)	5.7 (3.2–8.7)	0.31	6.5 (3.5–10.1)	5.1 (1.2–10.6)	0.63
adverse events	10.5 (7.6–13.8)	5.7 (3.3–8.6)	0.02	8.1 (5.8–10.6)	8.1 (5.3–11.2)	1.00	6.9 (4.8–9.2)	12.4 (6.7–19.4)	0.08
bleeding	2.7 (1.0–4.9)	0.5 (0.0–2.3)	0.08	0.0 (0.0–2.1)	2.1 (0.7–4.0)	0.08	1.1 (0.0–3.0)	3.5 (0.8–7.5)	0.17
perforation	1.0 (0.1–2.4)	0.1 (0.0–0.9)	0.12	0.0 (0.0–3.6)	0.5 (0.0–1.4)	0.62	0.4 (0.0–1.4)	0.6 (0.0–3.2)	0.84
emergency surgery	1.2 (0.2–2.6)	0.8 (0.2–1.9)	0.64	1.1 (0.2–2.4)	0.9 (0.2–2.1)	0.88	1.0 (0.3–1.9)	1.1 (0.0–4.0)	0.94

foration was 0.3 %. Surgery as consequence of an adverse event was necessary only in 1.0 %. Most common causes for surgery were perforations and appendicitis after EFTR of polyps at the appendiceal orifice. Number of FTRD resections at the appendiceal orifice could be retrieved from all but 4 studies. The remaining 22 studies reported 10 cases of appendicitis after 64 FTRD resections for this indication. This is in line with first small studies on this particular matter that indicate need for surgery after appendiceal EFTR in approximately 15–20 % of cases [28, 29].

In particular in the colorectum, use of EFTR and FTRD is mostly limited to situations where EMR has already failed or is not feasible. Thus, comparison of EFTR to EMR is difficult. The more likely alternative treatment options would be ESD, surgery, or EMR in combination with hot avulsion in most cases. Yet, use of ESD for resection of colorectal lesions, especially in the Western world, is controversial [30]. The potential benefits have to be weighed against the risks while the procedure itself requires a high level of experience. The fact that size of the study did not affect effectiveness of FTRD resection, might possibly indicate a faster learning curve for FTRD. Further, ESD for early colorectal cancer in Western studies was curative only in single cases. Surgical resection was necessary in the other cases due to a high-risk situation [30]. Given these limitations, easier use of FTRD, results from this meta-analysis, and data by Küllmer et al. [31] on colonic EFTR for polyps with malignant histology, full-thickness resection with FTRD would be the primary choice for difficult adenomas. The role of a hybrid-technique combining EFTR and EMR for lager lesions seems promising [32, 33] but yet needs to be further evaluated.

Even though this study provides good evidence on the use of the FTRD in the colon, there are some limitations that have to be considered. First, the included studies were heterogeneous with regard to design and indications for FTRD resection as well as patient numbers. We address this point by applying a random-effects model and performed sensitivity and subgroup analyses. Interestingly, rate of adverse events was significantly higher in studies published as full text publications compared to meeting abstracts. Whether or not a reporting bias is responsible for that finding remains hypothetical. Further, this meta-analysis does not allow us to draw any conclusions on the different indications for FTRD resection. This especially holds true for outcome after resection of difficult adenomas or for lesions with incidental finding of an adenocarcinoma. With regard to difficult adenomas, R0 resection rate was 77.7 %, and a residual lesion was found in 15.3 % in the prospective study by Schmidt et al. [9] Outcome in the subgroup of patients with malignant histology was recently reported by Küllmer at al. [31]. That study included 156 patients, of whom 64 underwent repeat resection of a malignant polyp and 92 who underwent EFTR for a non-lifting lesion with subsequently malignant histology. EFTR allowed for discrimination between low- and high-risk situation in > 99 % and achieved a R0 resection rate of 71.8 % throughout the study. That particular study was not included in the current meta-analysis as it summarized data from multiple German hospitals, many of which had already published results on more than the subgroup of patients with malignant polyps.

To summarize, the use of the FTRD system in the colon is highly feasible, efficient, and safe. It allows for endoscopic treatment of difficult adenomas and should be considered as the primary alternative to ESD or surgical resection in case of non-lifting adenomas.

Conflict of interest

AW declares that there is no potential conflict of interest.
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KC received grants and speecher fees from Ovesco Endoscopy.
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