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Efficacy and Safety of Full-Thickness Resection Device (FTRD) for Colorectal Lesions Endoscopic Full- Thickness Resection: A Systematic Review and Meta-Analysis

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Abstract

Background and Aims: Endoscopic full thickness resection (eFTR) is a field of increasing interest that offers a minimally invasive resection modality for lesions that are not amenable for resection by conventional methods. Full-thickness resection device (FTRD) is a new device that was developed for a single-step eFTR using an over-the scope-clip (OTSC). In this meta-analysis, we aim to assess the efficacy and safety of FTRD for eFTR of colorectal lesions.

Methods: A Comprehensive literature review of different databases to identify studies reporting FTRD with outcomes of interest was performed. Studies with <10 cases were excluded. Rates of histologic complete resection (R0), technical success, and complications were extracted. Efficacy was assessed by using the technical and the R0 rates whereas safety was assessed by using the complications rates. Weighted pooled rates (WPR) and the 95% confidence interval (CI) were calculated depending on the heterogeneity (I^2 statistics).

Results: Nine studies including 551 patients with 555 lesions were included in this study. The WPR for overall R0 was 82.4% (95% CI: 79.0–85.5%),with moderate heterogeneity (I^2 = 34.8%). The WPR rate for technical success was 89.25% (95% CI: 86.4–91.7%), with low heterogeneity (I^2 = 23.7%). The WPR for total complications rate was 10.2% (7.8,12.8%) with no heterogeneity. The pooled rate for minor bleeding, major bleeding, postpolypectomy syndrome, and perforation were 3.2%, 0.97%, 2.2%, and 1.2%, respectively. Of 44 peri-appendicular lesions, the pooled rate for acute appendicitis was 19.7%.

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AUTHORS CONTRIBUTIONS

Conception and design: Yazan Fahmawi and Meir Mizrahi. Analysis and interpretation of the data: Yazan Fahmawi, Abrahim Hanjar, Madhuri S. Mulekar, and Meir Mizrahi. Drafting of the article: All authors. Final approval of the article: Meir Mizrahi.

COFLICT OF INTEREST:

All authors have no conflict of interest to disclose.

Conclusion: FTRD seems to be effective and safe for eFTR of difficult colorectal lesions. Large prospective studies comparing FTRD with conventional resection techniques are warranted.

Keywords

Endoscopic full-thickness resection; endoscopic full-thickness resection device; colorectal lesions

Introduction:

While conventional endoscopic resection methods such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are highly effective techniques for colorectal lesions resection, those techniques harbor high perforation and incomplete resection rates in cases of non-lifting adenomas such as recurrent/residual adenomas; adenomas in difficult locations such as peri-appendicular and peri-diverticular lesions, and in cases of subepithelial lesions due to the presence of submucosal fibrosis [1–4]. Endoscopic full-thickness resection (eFTR) is an emerging field that offers a minimally invasive modality for resection of gastrointestinal (GI) lesions that are not amenable to conventional methods [5,6]. Two eFTR techniques; exposed (free-hand eFTR) and non-exposed (Device-assisted eFTR), have been described in term of managing the GI wall defect that results from eFTR [7,8]. In the exposed or free-hand technique, ESD full-thickness resection is done first followed by wall defect closure with clips, endoloop, and/or endoscopic suturing. This technique has been widely used for gastric submucosal lesions resection especially in Asian countries with good clinical outcomes [9–11]. The non-exposed or device-assisted technique consists of securing the GI wall patency first with a clip followed by full-thickness resection [7,8]. Over-the-scope clip (OTSC, Ovesco Endoscopy GmbH, Tübingen, Germany) is an example of clips that can be used either to secure the wall patency or to close the iatrogenic wall defect [7]. Full thickness resection device (FTRD) is a device that was developed for one-step eFTR using a 14mm OTSC mounted over an elongated cap (21mm) as well as with an integrated snare system [12]. Two FTRD systems have been manufactured; colonic FTRD and gastroduodenal FTRD [13]. Colonic FTRD is commercially available, U.S. Food and Drug Administration (FDA) approved for lower GI lesions, as well as with an increasingly experience using it in clinical settings compared to gastroduodenal FTRD which is still not commercially available and with very limited clinical experience [13]. In this meta-analysis study, our aim was to assess safety and efficacy of FTRD for colorectal lesions eFTR.

Methods

Study Selection, Data Extraction, and Quality Assessment

This meta-analysis study was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines (PRISMA guideline) [14]. A comprehensive literature search from the inception until April 2019 of MEDLINE, Cochrane library, and Scopus databases was done using the same search strategy; (endoscopic full thickness resection) And ((FTRD) OR (full thickness resection device) OR (over the scope) OR (OTS)). To increase the yield of our search strategy; references of the included studies as well as the last two issues of Gastrointestinal Endoscopy Journal were reviewed to identify any relevant study that was missed during the initial search strategy. Eligibility criteria were

pre-determined by two authors (Y.F and M.M). Only studies in English reporting technical success, complete resection (R0), and complication rates of FTRD for colorectal lesions were included. As well as, only studies with 10 or more patients were included to reduce bias associated with case reports and small number of case studies. Animal and experimental studies, FTRD for upper GI lesions, and reviews and commentaries, were excluded. In addition to that, studies were excluded if their data were included in a more recent or a larger study which was already included in our study. All results were downloaded into EndNote X9 (Thompson ISI ResearchSoft, Philadelphia, Pennsylvania, USA). Any duplication was identified and removed. Two reviewers (Y.F and A.H) screened the titles and abstracts of the initially extracted studies. Both reviewers reviewed the full text of the potentially eligible studies. Any disagreement was resolved by consensus or by consulting a third author (M.M).

Two reviewers (Y.F and A.H) extracted the data of interest from the included studies independently using a standardized Excel sheet data. The extracted data include; Study authors, publication year, study design, patients demographics, lesions size and location, indications of the eFTR by FTRD, procedure time, complete resection, technical success, full-thickness resection rates, snare malfunction incidence, complication rates, OSTC fate, duration of hospital stay, and Follow-up period. After data extraction, data sheets from both the reviewers were compared. Any disagreement was resolved by consensus or by consulting a third author (M.M).

The quality of all of the included studies were assessed independently by two reviewers (Y.F and A.H) using the Newcastle-Ottawa Scale (NOS) [15]. A score > 7 was considered high quality, 4–6 was considered moderate quality, and <4 was considered low quality. Disagreements between the two reviewers were resolved by consensus or by consulting a third investigator (M.M).

Definitions:

Difficult Adenomas: non-lifting recurrent, non-lifting residual, non-lifting primary, peri-appendicular, and peri-diverticular adenomas.

Complete resection (R0): Histologically tumor-free margins (Lateral and deep) resection

Technical success: reaching the lesion, then deploying the clip successfully, followed by macroscopically full resection using the integrated snare.

Full-thickness Resection (FTR) rate: Histologically confirmed full-thickness resection (mucosa, submucosa, and muscle layers).

Proximal Colon: Lesions that were in cecum, ascending colon, or transverse colon.

Distal Colon: Lesions that were in descending colon, sigmoid, or rectosigmoid areas.

Major bleeding: bleeding that required intervention or blood transfusion.

Minor bleeding: bleeding that did not require intervention or blood transfusion.

Statistical Analysis:

We evaluated safety and efficacy of eFTR of colorectal lesions using FTRD. Efficacy was assessed as technical and R0 rates whereas safety was assessed by post-procedural complication rates. Weighted pooled rate (WPR) with 95% confidence interval (CI) were calculated for the primary outcomes of interest; technical success, R0, and total complications rate. I^2 statistics and Cochrane Q test were used to assess the presence of heterogeneity. A P value <0.1 resulting from Cochrane Q test was considered as an indication of the presence of heterogeneity. A significant heterogeneity was considered to be present if the I^2 value was more than 50% [16]. Depending on the heterogeneity, random or fixed effects model was chosen. If the heterogeneity was substantial (>50%), a random effect model was selected otherwise a fixed effects model was used. Only if it was reported, subgroup analysis was conducted to assess R0 rate according to the indications and site of lesions. For secondary outcomes; FTR rate, snare malfunction rate, and surgical intervention rate, only WPR was conducted. Publication bias was assessed using the funnel plots for technical success, R0 rates, and total complications rate. Quantifying the publication bias if present was not done given the small number of the included studies. The statistical analysis in this meta-analysis was performed using MetCalc by an expert statistician (M.S.M).

Results:

Study Characteristics and Quality Assessment

Figure 1 shows the study selection process and study characteristics. Three hundred and eighty-one studies were identified from the search strategy and from manual search, of which 130 were duplicates. Of the remaining 251 studies, 199 were excluded after screening titles and reviewing abstracts. Full-text review was performed on the remaining 52 studies. 9 cohort studies (6 retrospective and 3 prospective) were retained and included in this meta-analysis[5,6,17–23]. Two of the included studies were abstracts[21,22]. All the studies were conducted in Europe and were published between 2016–2019 except for one study that was conducted in the United States. Three studies were excluded for possible overlapping with larger multicenter studies[12,24,25]. A study by Kuellmer et al. evaluating FTRD only in early colorectal cancer resection was also excluded for probable data overlapping with larger included studies [26]. eFTR using FTRD were planned to be done on 555 lesions in 551 patients. All nine included studies reported the primary outcomes of interest: complete resection (R0), technical success rate, and complication rates. Of these nine studies, six studies also reported subgroup analysis for R0 according to the indication [5,6,18–20,23]and four reported the R0 according to the site of lesions [5,18,19,23].

The quality of the included studies was assessed using the Newcastle-Ottawa score scale. All the included studies were moderate in the methodological quality.

Meta-Analysis Results:

Difficult adenomas resection using FTRD was the most frequent indication (68.7%) followed by early carcinoma resection (17.5%), and then subepithelial lesions (10.7%). 47.3% of the lesions were in the proximal colon, 28.9% in the rectum, and 22.8% in the distal colon. Table 1, Table 2, and Table 3 show the indications, site of lesions, and the

clinical outcomes. All the included studies reported the technical success rate, which was defined as reaching the lesion and successfully deploying the clip followed by macroscopically fully resecting the lesion with the integrated snare system. Failure to do any of these steps were considered as a technical failure. Pooled WPR for technical success of FTRD was 89.25% (95% CI: 86.4–91.7%), Cochran Q test P = 0.23, I^2 = 23.7% (Figure 2). Funnel plot was fairly symmetrical (Figure 3). Technical failure due to snare malfunction were reported in 32 cases out of 420 cases (7.6%). The other main cause of the technical failure was non-reachable lesions as reported in 10 out of 420 cases. R0 rate which defined as histologically tumor-free margins of the resected lesion, was also reported in all included studies. Pooled WPR for R0 rate of FTRD was 82.4% (95% CI: 79.0– 85.5%), with moderate heterogeneity; Cochran Q test P = 0.14, I^2 = 34.8% (Figure 4). Funnel plot was symmetrical (Figure 5). Subgroup analysis of the R0 rate according to the indications and site of lesions were conducted. Six studies reported the R0 rate according to the indication. From those six studies, 297 difficult adenomas were reported with R0 WPR of 82.7% (95% CI: 74.7–89.5%). Peri-appendicular and peri-diverticular lesions were considered as difficult adenomas. Six studies reported specifically the R0 for peri-appendicular lesions with WPR of 82.8%. The WPR for R0 rate for early carcinoma was 81.3% (95% CI: 70.3–89.6%). For subepithelial lesions, the WPR was 81.9% (95% CI: 68.8–91.2%). According to locations, the WPR for R0 rate for lesions located in proximal colon was 76.6% (95% CI: 68.9–83.3%). For lesions located in the distal colon, the WPR for R0 rate was 78.6% (95% CI: 65.8–88.4%). Finally, the WPR for R0 rate for rectal lesions was 78.5% (95% CI: 65.1–88.5%). From the nine included studies, six studies reported the FTR rate. The WPR for FTR was 88.6%. Out of the six studies, three studies reported FTR according to the lesion site. For lesions located in the proximal colon, the WPR for FTR was 77.6% whereas the WPR for lesions located in the distal colon and rectum were 72.8% and 71.9%, respectively.

Complications:

Table 4 summarizes the complication rates. The WPR for total complication rate was 10.2% (95% CI: 7.8–12.8%), Cochran Q test P = 0.51, I^2 = 0% (Figure 6). Funnel plot for total complication rate was fairly symmetrical (Figure 7). The most common complication reported in the included studies was minor bleeding (3.2%). The WPR for major bleeding, postpolypectomy syndrome, perforation, and traumatic bowel wall injury, were 0.97%, 2.2%, 1.2%, and 0.78%, respectively. Of 44 patients with peri-appendicular lesions, the pooled rate of appendicitis was 19.7%. Following eFTR, 38 patients underwent surgery for any reason with WPR of 6.7%. For complications-related surgery, the WPR was 2.2%.

Discussion:

FTRD is a newly emerging over-the scope-clip device that is developed for single-step eFTR for colorectal lesions that are not amenable for resection by conventional methods. FTRD has been increasingly used for colorectal lesions resection with variations in its efficacy and safety profiles among the studies. Thereby, we aimed in this study to evaluate the cumulative efficacy and safety of this new device.

We found that FTRD had excellent efficacy for managing difficult colorectal lesions with technical success rate of 89.2% with low heterogeneity and R0 rate of 82.2% with moderate heterogeneity. In addition to its high technical success and R0 rates, FTRD has shown to have high FTR rate (88.6%). In two meta analyses investigating the clinical outcomes of ESD in colorectal lesions resection, the R0 rates were 80.3% and 82.9% with FTR of 91% in the two studies [27,28]. These numbers seem to be similar to the numbers found in this study. However, certain points should be addressed. First, the study population is different in our study as FTRD was mainly used for non-lifting adenomas and adenomas in difficult locations. Given the presence of fibrosis and scar tissue, these non-lifting adenomas harbor high perforation and incomplete resection rates if they were resected by ESD even by expert hands [29,30]. Second, in fact, the R0 rate for ESD in Western countries is significantly lower than in Eastern countries. In two meta-analyses, the R0 rates for ESD in Western countries were 74% and 71.3% compared to 89% and 85.6%, respectively [27,31]. This difference between Western and Eastern R0 rates for ESD is most likely multifactorial as it could be due to long learning curve, long procedure times, differences in incidences of diseases, etc. On the other hand, in our study, all FTRD procedures were done in Western countries and the R0 rate was 82.2%. Third, further modification and development of the FTRD would increase the technical success rate thereby leading to increase in the R0 rate. As an example, in the current study, 7.6% of the technical failure was due to malfunction of the integrated snare. This technical failure would result in more cases with incomplete resection. According to Schmidt el al. [5], the integrated snare was modified by the company which could lead to an increase in the technical success and R0 rates in the future studies. Furthermore, evaluating the incorporation of the lesions prior to resection by using a novel ‘test-cap’ (prOVE CAP, Ovesco Endoscopy) could also increase the R0 rates. FTRD may not be attempted and another resection modality should be considered if the lesion cannot be fitted and pulled into this ‘test-cap’. Ultimately, given the different population, different ESD experience between Western and Eastern countries, and the room for further development and modification for FTRD, FTRD seems to be more effective than the conventional resection methods in selected patient population.

The most frequent indication for FTRD was difficult adenomas followed by early carcinoma resection, then by subepithelial lesions resection. Although not reported in all included studies, a subgroup analysis was conducted to evaluate the R0 rate for different indications and site of the lesion. The pooled R0 rate for difficult adenomas was 82.7%. For early carcinoma resection and subepithelial, the pooled R0 rates were 82.3% and 81.9%, respectively. The R0 rates for the different three indications were almost the same which indicate that FTRD has the same efficiency regardless of the indication. Similarly, R0 resection rates were almost similar for lesions located in the proximal colon, distal colon, or in the rectum (76.6%, 78.6%, and 78.5%, respectively). Therefore, indicating that FTRD is again efficient regardless of the site of the lesion in the colorectum.

In addition to its efficacy, we found that FTRD is safe with low complication and surgery requirements rates. The pooled total complication rate was 10.2% with no heterogeneity. Minor bleeding that was managed either endoscopically during the procedure or conservatively was the most common complication encountered (3.2%) followed by perforation (2.2%). The perforation rate for colorectal ESD has been reported in two

different meta analyses to be near 5% [27,28]. The perforation rate is higher in ESD as this technique becomes more difficult with extensive scar tissue and fibrosis which is expected to be seen in recurrent or residual adenomas. Usually, lesions involving or around the appendiceal orifices are managed surgically. From the included studies, 44 peri-appendicular lesions were resected using FTRD with pooled R0 of 82.8%. Despite its feasibility and efficacy to resect peri-appendicular lesions, closure of the appendiceal orifice during the procedure with the FTRD will increase the risk of acute appendicitis. In this meta-analysis, 19.7% of the peri-appendicular lesions that were resected using FTRD were complicated with acute appendicitis. In addition to the previous complications, the rates for other complications were low as well. The occurrence rates of major bleeding, postpolypectomy syndrome, traumatic injury, and other complications were 0.97%, 1.2%, 0.8%, and 1.9%, respectively. Finally, the pooled rate of surgical intervention regardless of the etiology was 6.7%. Nevertheless, surgical intervention secondary to post-FTRD complications was required only in 2.2% of cases. On the other hand, the rate of post-ESD surgical intervention was reported to be up to 9.9% [27,28]. Again, extensive submucosal fibrosis and scar tissue could be the main cause of the high post-ESD surgical intervention rate.

One of the main limitations of this analysis is that all the included studies were non controlled cohort studies because no randomized clinical trials have been published. As well as, the variations in the endoscopists expertise could be a source of bias. In addition to these limitations, not all included studies stratified the R0 rates according to the site of the lesions or by the indications of the FTRD, which resulted in inadequately investigating the observed moderate heterogeneity for R0 (I^2 =34.8%).

In conclusion, FTRD seems to be effective and safe in managing difficult colorectal lesions. However, the evidence presented in this study is derived from observational studies. Larger randomized controlled trials comparing FTRD with conventional resection methods are warranted.

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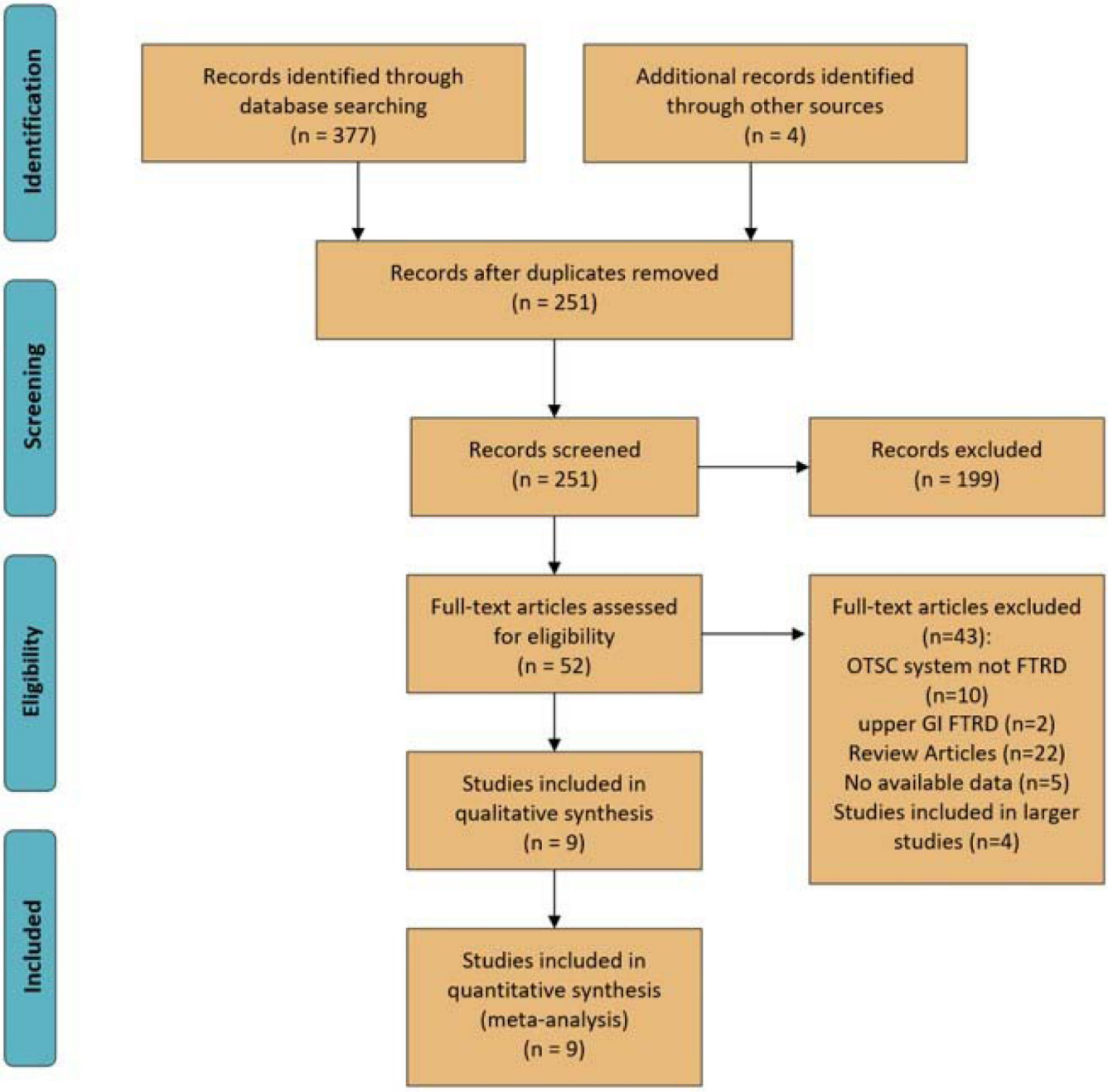

Figure 1:
Study selection process using PRISMA flow diagram[14]

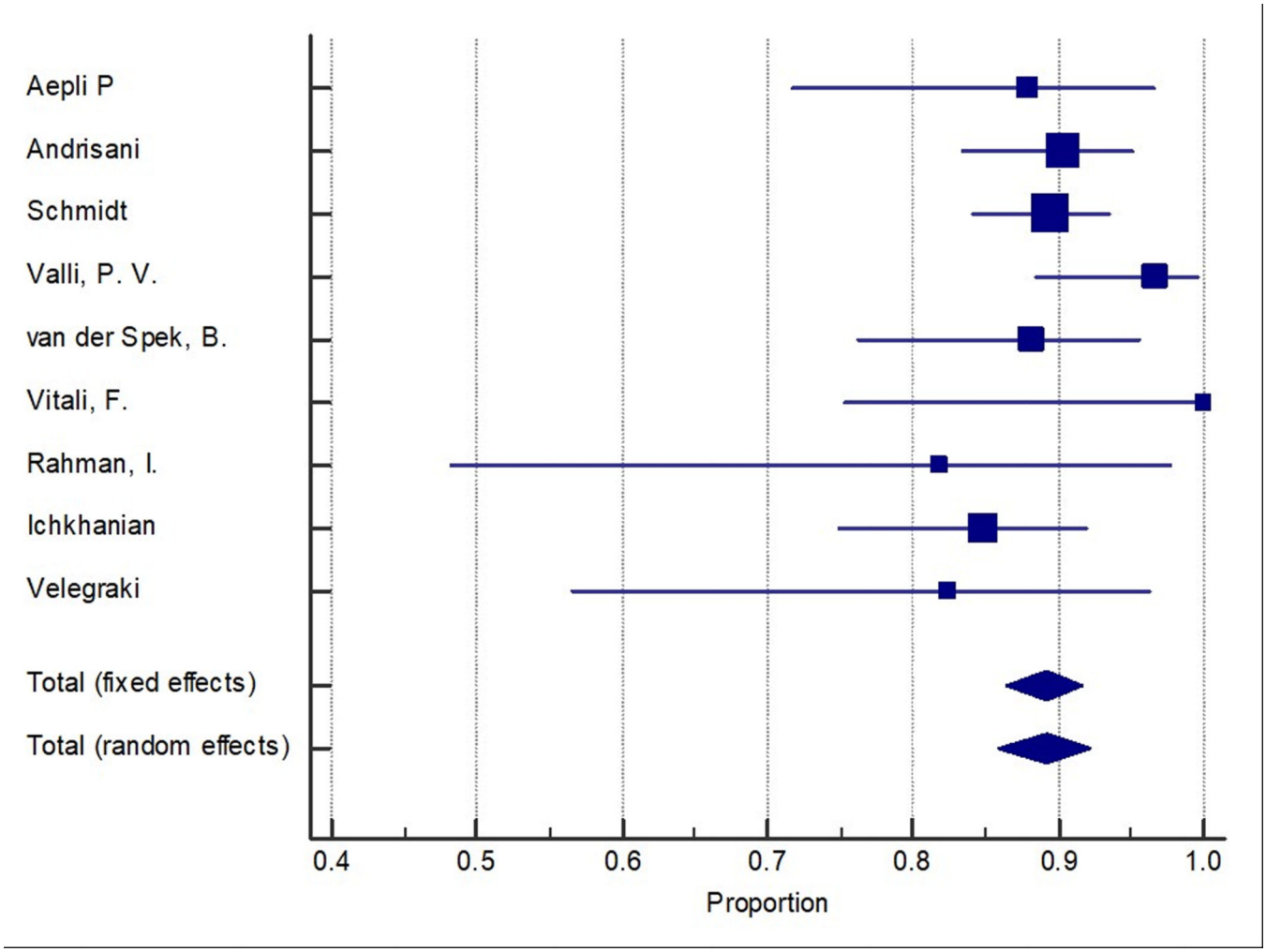

Figure 2:
Forest plot for technical success of Full thickness resection device (FTRD). Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% (Confidence Interval) CIs. The diamond is placed on the summary correlation coefficient of the observational studies, and the width indicates the corresponding 95% CI.

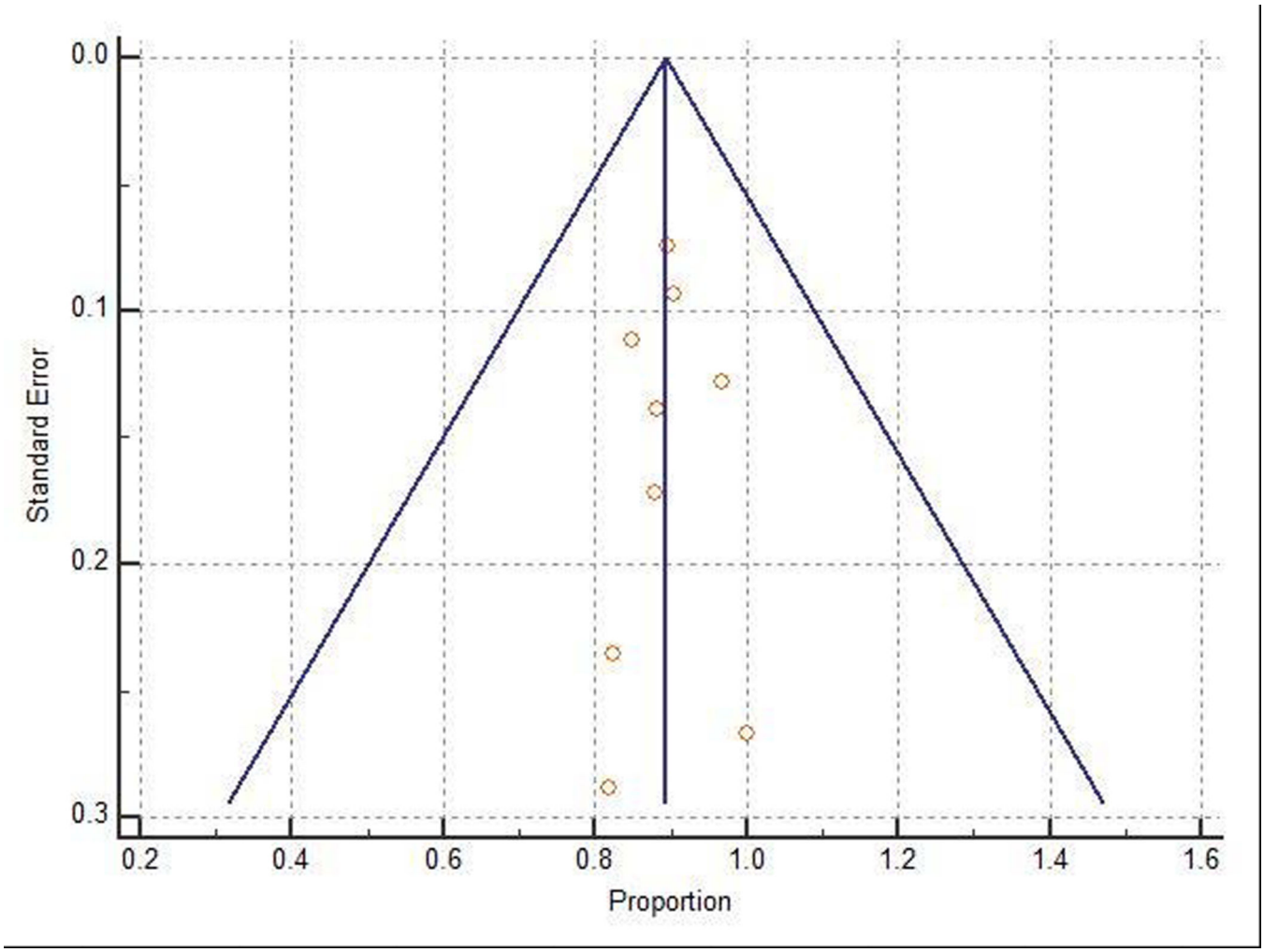

Figure 3:
Funnel plot for technical success

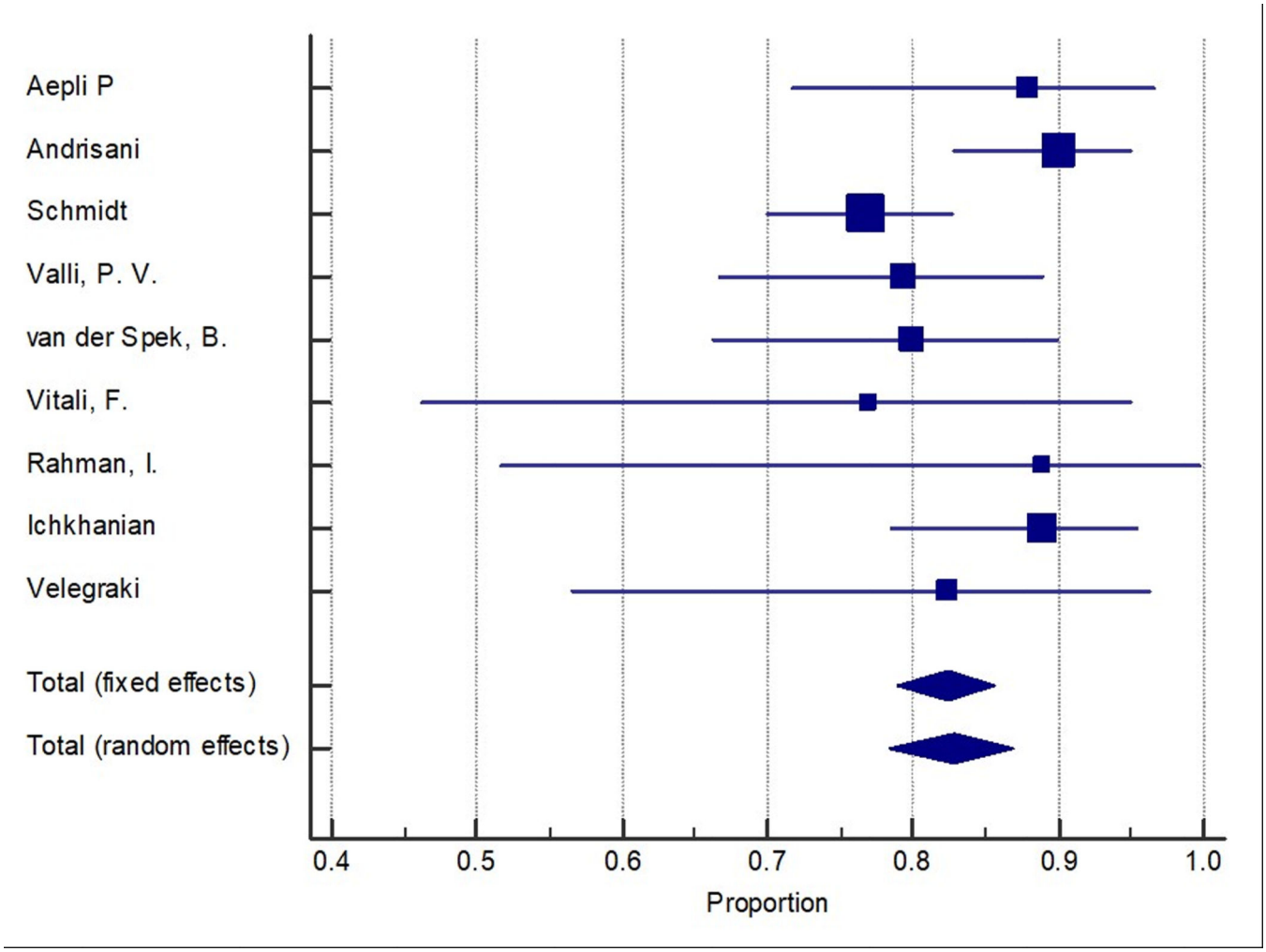

Figure 4:

Forest plot for complete resection (R0) of Full thickness resection device (FTRD). Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% (Confidence Interval) CIs. The diamond is placed on the summary correlation coefficient of the observational studies, and the width indicates the corresponding 95% CI.

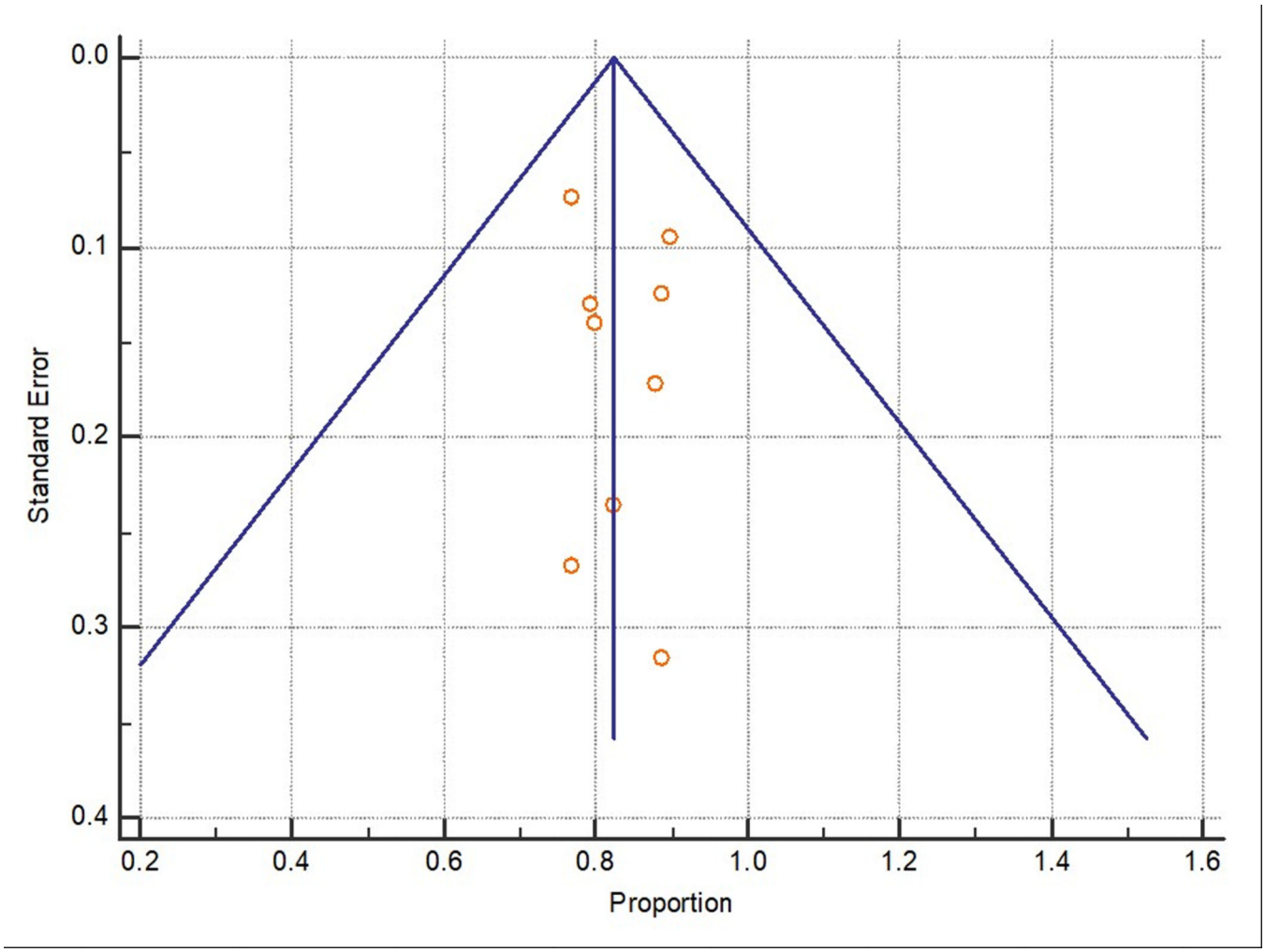

Figure 5:
Funnel plot for complete resection (R0) of Full thickness resection device (FTRD).

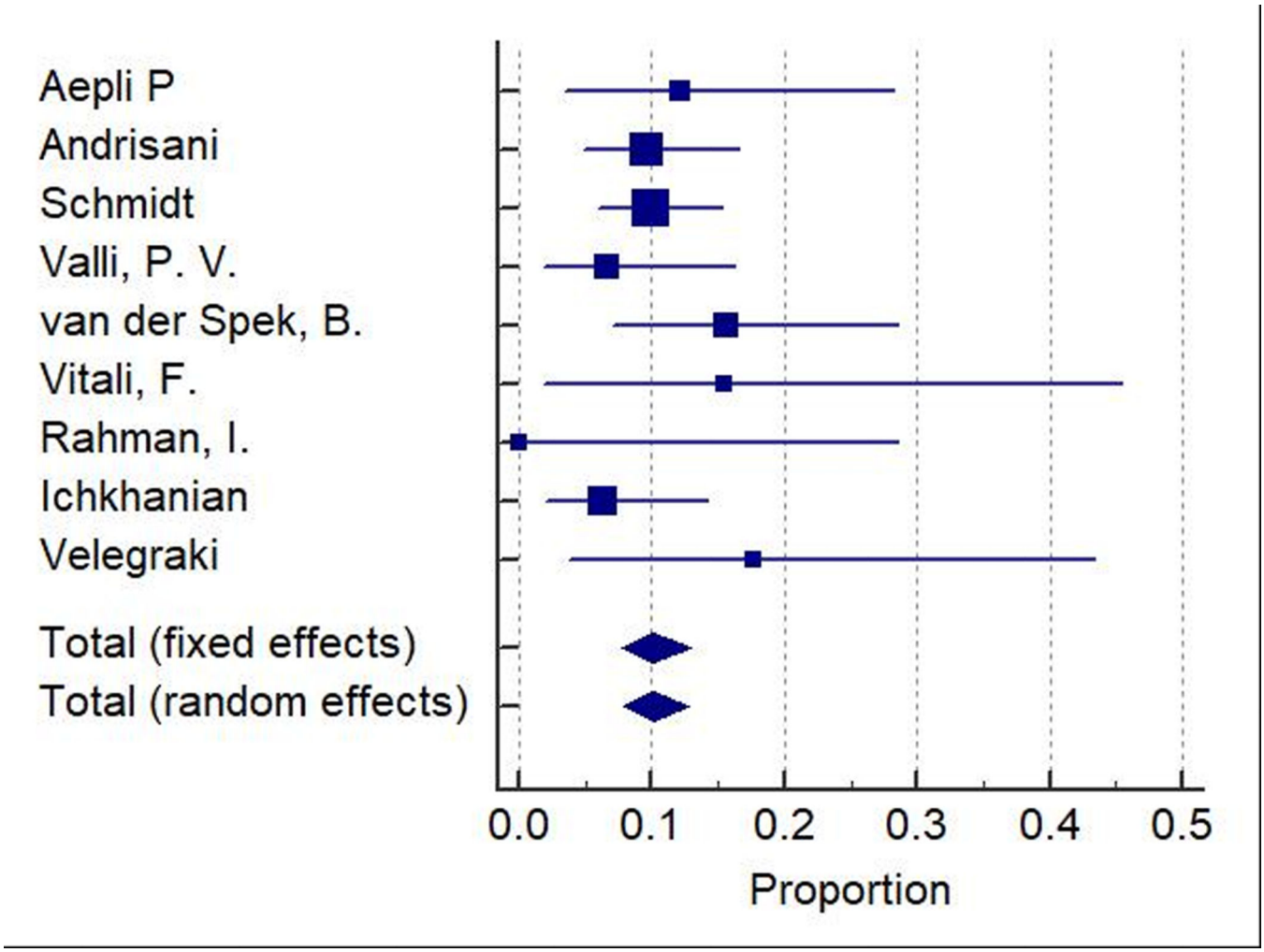

Figure 6:
Forest plot for total complications rate. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% (Confidence Interval) CIs. The diamond is placed on the summary correlation coefficient of the observational studies, and the width indicates the corresponding 95% CI.

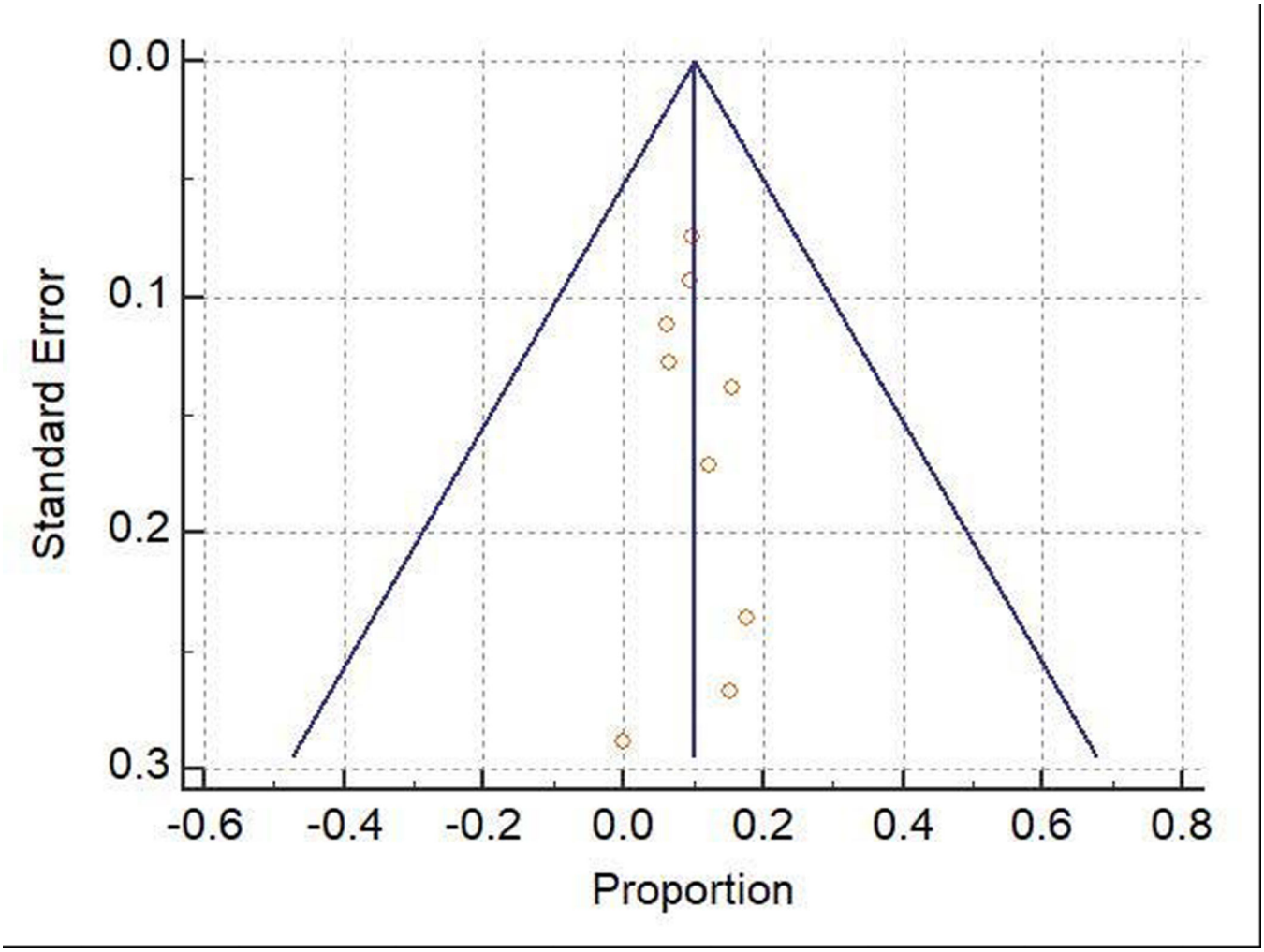

Figure 7:
Funnel plot for total complications rate

Table 1

Studies characteristics. eFTR: Endscopic full-thickness resection

Study	Country	Study Design	Patient number	Age	Gender (M/F)	Number of lesions	Lesion Size before resection (mm)	Indications	Study quality Using NOS
Aepli P et al., 2017 [18]	Switzerland	Retrospective	33	65.9 (mean)	(23/10)	33	13.5	Recurrent adenoma (18) Staging after resection of a malignant polyp (4), Primary non-lifting adenoma (2), Peri-appendicular adenomas (2), Primary eFTR of polyps suspected to be malignant (2), Non-lifting malignancy recurrence after eFTR (1), Incomplete resection of neuroendocrine tumor (1).	Moderate
Andrisani et al.,2019[6]	Italy	Retrospective	110	68 (mean)	(61/49)	114	17.8	Residual/recurrent adenoma (39), Histologic R1 resection (26), Non-lifting sign adenoma (12), Para-diverticular and para appendicular adenoma (4), Submucosal lesion (10), suspected T1 carcinoma (16), Diagnostic resection of the colo-rectal wall (3).	Moderate
Schmidt et al., 2018[5]	Germany	Prospective	181	65 (median)	(99/82)	181	15.0	Difficult adenoma (143) (Adenoma with negative lifting sign – 104/143, adenoma involving the appendiceal orifice 34/143 and adenoma involving diverticulum 5/143) T1 carcinoma (15), Subepithelial tumor (23)	Moderate
Valli et al., 2018[19]	Germany	Retrospective	60	68 (mean)	N/A	60	N/A	Recurrent adenomas (22), primary nonlifting adenoma (2), eFTR in addition to piecemeal resection (10), para-diverticular (2), peri-	Moderate

Study	Country	Study Design	Patient number	Age	Gender (M/F)	Number of lesions	Lesion Size before resection (mm)	Indications	Study quality Using NOS
								appendicular (4), Submucosal lesions (5), early carcinoma (7), follow-up resection of a malignant polyp (6), eFTR over endoloop (2).	
Vitali et al., 2018[20]	Germany	Prospective	12	64.3 (mean)	(7/5)	13	N/A	Primary non-lifting adenomas (6), Recurrent/ residual adenomas (5), Para-diverticular adenoma (1), Subepithelial lesion (1).	Moderate
van der Spek et al., 2018[17]	Netherland	Retrospective	48	67 (mean)	(30/18)	51	12.2	Non-lifting Adenoma (19) T1 carcinoma (28), Adenoma involving a diverticulum (2), Neuroendocrine tumor (2)	Moderate
Rahman et al., 2016[22]	United Kingdom	Prospective	11	76 (Median)	N/A	11	N/A	Non-lifting adenomas (5), T1 polyps (4),and Subepithelial lesion (2).	Moderate
Ichkhanian et al., 2019[21]	USA	Retrospective	79	65 (mean)	(48/31)	79	15.3	Difficult adenoma (48), Subepithelial lesion (10), Early carcinoma (17)	Moderate
Velegraki et al., 2019[23]	Greece	Retrospective	17	59.7 (mean)	(10/7)	17	12.7	Recurrent/residual (5), Primary non-lifting adenomas (1), Peri-appendicular (2), T1 carcinoma (3), Subepithelial tumor (6)	Moderate

Table 2:

Indications and site of lesions

	Indications								Locations		
	Difficult Adenomas					Early Carcinoma	Subepithelial	Others	Proximal Colon		
Study	Recurrent nonlifitng adenomas	Resiudal nonlifitng adenomas	Primary nonlifting adenomas	Peri-appendicular adenomas	Peri-diverticular adenomas				Cecum	Ascending Colon	Transve
Aepli P et al., 2017[18]	19	0	4	2	1	2	1	4 (staging)	9	9	0
Andrisani et al.,2018[6]	39	26	12	2	2	16	10	3 (Diagnostic resection)	7	11	17
Schmidt et al., 2018[5]	53	19	32	34	5	15	23	N/A	55	35	22
Valli et al., 2018[19]	22	10	2	4	2	13	5	2 (Over endoloop)	9	15	1
Vitali et al., 2018[20]	2	3	6	N/A	1	N/A	1	N/A	2	4	0
Van der Spek et al., 2018[17]	3	12	4	N/A	2	28	2	N/A	1	8	2
Velegraki et al., 2019[23]	0	5	1	2	0	3	6	N/A	3	0	1
Rahman et al., 2016[22]	5					4	2	N/A	Not reported	Not reported	Not reporte
Ichkhanian et al., 2019[21]	48					17	10	N/A	46		
Total	384 (68.7%)					98 (17.5%)	60 (10.7%)		257 (47.3%)		

Table 3:

Studies clinical outcomes. eFTR: Endoscopic full-thickness resection, N/A: Not Applicable.

Study	Procedure Time (Minutes)	Complete Resection (R0) Rate	Technical Success Rate	eFTR Resection Rate	Mean Diameter of Resected Specimen (mm)	Complications	Surgery secondary to complication	Technical failure	OTSC Fate	Hospital Stay (Days)
Aepli P et al., 2017[18]	63 (mean)	29/33 (87.9%)	29/33 (87.9%)	25/31 (80.6%)	27.0	Minor bleeding (2), Major bleeding (1), Perforation (1)	N/A	Not reachable lesions (1), Snare malfunction (3)	Not reported	3.1 (mean)
Andrisani et al.,2018[6]	45 (mean)	99/110 (90%)	103/114 (90.3%)	100/110 (90.9%)	20.0	Traumatic wall injury (4), Stenosis after the deployment of the clip (1), Appendicitis (1), Perforation (1), Postpolypectomy syndrome (1), Tenesmus and perineal pain (2), Major bleeding (1)	2	Snare malfunction (12), Not reachable lesions (4)	Spontaneously fallen off (100), In place (10), Removed Endoscopically (2)	91/110 (82.7%) stayed one day, 19/110 (17.3%) as outpatient
Schmidt et al., 2018[5]	50 (median)	139/181 (76.8%)	162/181 (89.5%)	162/181 (89.5%)	Not reported	Minor bleeding (4),Appendicitis (3), Postpolypectomy (3), Recurrent Abdominal pain (1), Perforation (6), Enterocolonic fistula (1)	4	Snare malfunction (13)	Spontaneously fallen off (106/154), In place (48), Enodscopically removed (10)	4 (median)
Valli et al., 2018[19]	60 (Median)	46/58 (79.3%)	58/60 (96.7%)	51/58 (87.9%)	24.0	Minor bleeding (2), Appendicitis (1), Incomplete OTSC deployment (1).	N/A	Not reachable lesions (2), Snare malfunction (4)	Spont. Fallen off (26), In place (4), Removed endoscopically (3), unknown (24)	Not reported
Vitali et al., 2018[20]	68 (mean)	10/13 (76.9%)	13/13 (100%)	Not reported	17.0	Postpolypectomy (2)	N/A	Snare malfunction (1)	N/A	2.5 (mean)
Van der Spek et al., 2018[17]	Not reported	40/50 (80%)	45/51 (88.2%)	43/50 (86%)	21.0	Minor bleeding (4), Major bleeding (1), Perforation (1), Postprocedural cardiac event (1), urinary retention (1)	N/A	N/A	N/A	N/A
Rahman et al., 2016[22]	40 (Median)	8/9 (88.9%)	9/11 (81.8%)	9/9 (100%)	22.0	N/A	N/A	N/A	N/A	N/A
Ichkhanian et al., 2019[21]	63 (mean)	56/63 (88.9%)	67/79 (84.8%)	N/A	N/A	Appendicitis (1), Perforation (1), Minor bleeding (3)	2	Snare malfunction (3), clip closure (1),, Not reachable lesion (1)	N/A	0.4
Velegraki el al., 2019[23]	36.9 (mean)	14/17 (82.3%)	14/17 (82.3%)	N/A	N/A	Minor bleeding (1), Appendicitis (1), Recurrent	1	Not reachable lesion (2), Macroscopically	N/A	1–3 days

Study	Procedure Time (Minutes)	Complete Resection (R0) Rate	Technical Success Rate	eFTR Resection Rate	Mean Diameter of Resected Specimen (mm)	Complications	Surgery secondary to complication	Technical failure	OTSC Fate	Hospital Stay (Days)
						abdominal pain of unknown cause (1)		incomplete resection (1)		

Table 4:

Complication rates. WPR: Weighted pooled rate

Complications	WPR
Total	10.2%
Minor bleeding	3.2%
Major bleeding	0.97%
Perforation	1.2%
Postpolypectomy syndrome	2.2%
Traumatic injury	0.78%
Acute appendicitis: Rate out of total lesions Rate out of peri-appendicular lesions	1.7% 19.7%
Surgery for any reason	6.7%
Surgery secondary to complications	2.2%