Safety and efficacy of underwater versus conventional endoscopic mucosal resection for colorectal polyps: Systematic review and meta-analysis of RCTs

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ABSTRACT

Background and study aims Conventional endoscopic mucosal resection (C-EMR) is limited by low en-bloc resection rates, especially for large (> 20 mm) lesions. Underwater EMR (U-EMR) has emerged as an alternative for colorectal polyps and is being shown to improve en-bloc resection rates. We conducted a systematic review and meta-analysis comparing the two techniques.

Methods Multiple databases were searched through November 2022 for randomized controlled trials (RCTs) comparing outcomes of U-EMR and C-EMR for colorectal polyps. Meta-analysis was performed to determine pooled proportions and relative risks (RRs) of R0 and en-bloc resection, polyp recurrence, resection time, and adverse events.

Results Seven RCTs with 1458 patients (U-EMR: 739, C-EMR: 719) were included. The pooled rate of en-bloc resection was significantly higher with U-EMR vs C-EMR, 70.17% (confidence interval [CI] 46.68–86.34) vs 58.14% (CI 31.59–80.68), respectively, RR 1.21 (CI 1.01–1.44). R0 resection rates were higher with U-EMR vs C-EMR, 58.1% (CI 29.75–81.9) vs 44.6% (CI 17.4–75.4), RR 1.25 (CI 0.99–1.6). For large polyps (> 20 mm), en-bloc resection rates were comparable between the two techniques, RR 1.24 (CI 0.83–1.84). Resection times were comparable between U-EMR and C-EMR, standardized mean difference −1.21 min (CI −2.57 to −0.16). Overall pooled rates of perforation, and immediate and delayed bleeding were comparable between U-EMR and C-EMR. Pooled rate of polyp recurrence at surveillance colonoscopy was significantly lower with U-EMR than with C-EMR, RR 0.62 (CI 0.41–0.94).

Conclusions Colorectal U-EMR results in higher en-bloc resection and lower recurrence rates when compared to C-EMR. Both techniques have comparable resection times and safety profiles.

Introduction

Colorectal cancer (CRC) is the third most common cause of cancer worldwide and the third leading cause of cancer deaths in Western countries. [1] Colonoscopy remains a commonly performed screening test for CRC as it has both diagnostic and therapeutic capabilities. Studies have shown a strong association between screening colonoscopy and a reduced risk of death from colorectal cancers [2]. Endoscopic mucosal resection (EMR) is the standard method for removing sessile colorectal polyps larger than 10 mm [3, 4]. Conventional EMR (C-EMR) involves filling the colonic lumen with air or CO_2 followed by submucosal injection of fluid underneath the polyp to decrease the risk of causing accidental transmural thermal injury leading to perforation [5]. It has been shown to have high therapeutic success rates and allows for a 90% reduction in the need for long-term surgery [6]. However, with piecemeal C-EMR, local recurrence rates of > 30% have been described, which is a clear disadvantage of the procedure, forcing the use of alternative techniques to reduce these figures [7, 8]. Furthermore, high recurrence rates have prompted the application of thermal ablation to the EMR defect which adds both time and cost to the procedure [9].

Underwater EMR (U-EMR) is a technique, described a decade ago, in which the colon is filled with water instead of air/CO_2, decreasing colonic wall tension and resulting in potential benefits that may improve the opportunity for safe and complete en-bloc resection of mucosal lesions [10]. The technique eliminates the need for submucosal injection, because of the "floating" effect of water submersion on the mucosa and submucosa, resulting in separation from the muscularis propria [11, 12]. Several systematic reviews and meta-analysis have attempted to compare outcomes of U-EMR with C-EMR, however the strength of evidence remains low, as most of these include observational, retrospective cohort studies [13, 14, 15, 16].

Given these limitations of existing literature, we conducted an updated systematic review and meta-analysis to evaluate the efficacy and safety of U-EMR in comparison to C-EMR for colorectal lesions, assessing data only from published randomized controlled trials (RCTs).

Methods

Search strategy

The literature was searched by a medical librarian for the concepts of RCTs, underwater EMR and colorectal polyps. Search strategies were created using a combination of keywords and standardized index terms. Keywords included “endoscopic mucosal resection,” “EMR,” “colorectal lesions” and “underwater EMR” along with phrases associated with the procedure such as “colonoscopy”. Searches were run on November 25, 2022 in Ovid Cochrane Central Register of Controlled Trials (1991 +), Ovid Embase (1974 +), Ovid Medline (1946 + including epub ahead of print, in-process & other non-indexed citations), Scopus (1823 +), and Web of Science Core Collection (Science Citation Index Expanded 1975 + & Emerging Sources Citation Index 2015 +). After limiting results to English language with some pediatric and animal studies removed, a total of 178 citations were retrieved. Deduplication was performed in EndNote following the Bramer method [17] leaving 85 citations. Manual search for studies of interest was performed in google scholar by two authors (SC, DSD). Details of study selection are provided in PRISMA Flow Chart – **Supplementary Fig. 1**. [18] The full search strategy is available in Supplementary Appendix-1. The PRISMA checklist was followed and is provided as Supplementary Appendix-2. Reference lists of evaluated studies were examined to identify other studies of interest.

Study selection

In this meta-analysis, we included only RCTs where outcomes of C-EMR and U-EMR were provided. Studies were included irrespective of inpatient/outpatient setting, follow-up time, geography and whether published as full manuscripts or abstracts, as long as they provided the clinical outcomes data needed for the analysis.

Our exclusion criteria were as follows: 1) cohort studies reporting outcomes of U-EMR only, C-EMR only and/or U-EMR vs C-EMR; 2) studies that included less than 25 patients; 3) studies performed in the pediatric population (age < 18 years); and 4) studies not published in English language. In cases of multiple publications from a single research group reporting on the same patient, same cohort and/or overlapping cohorts, data from the most recent and/or most appropriate comprehensive report were retained. The retained studies were decided by two authors (SC, BPM) based on the publication timing (most recent) and/or the sample size of the study (largest).

Data abstraction and quality assessment

Data on study-related outcomes from the individual studies were abstracted independently onto a standardized form by at least two authors (SC, DR). Author DSD cross-verified the collected data for possible errors and two authors (SC, JB) did the quality scoring independently. The Cochrane Collaboration tool to assess risk of bias (Supplementary Appendix-3) [19]. The quality of evidence presented in the RCTs was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (**Supplementary Fig. 2**) [20].

Outcomes assessed

Patients were classified into two cohorts based on the technique used – underwater EMR (U-EMR) and conventional EMR (C-EMR).

The primary outcomes were: 1) pooled risk ratio and proportions of R0 resection, defined as a complete en-bloc resection of a lesion with tumor-free lateral and vertical margins [21]; 2) pooled risk ratio and proportions of en-bloc resection; and 3) pooled risk ratio and proportions of lesion recurrence, defined as an adenoma or cancer at the resection site on follow-up colonoscopy.

The secondary outcomes were: 1) pooled risk ratio and proportions of piecemeal resection; 2) pooled risk ratio and proportions of incomplete resection, defined as at least one neoplastic tissue retrieved from the resection edge after polypectomy, presence of any adenomatous or serrated pathology in the biopsy specimen or polyps requiring complementation with thermal ablation after resection attempt; 3) mean difference in resection time, defined as period between the start of submucosal injection (in the C-EMR group) or intra-intestinal water injection (in the U-EMR group) and completion of the colonoscopic resection; and 4) pooled risk ratio and proportions of adverse events including perforation, immediate and delayed bleeding.

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates and 95% CIs (confidence intervals) in each case following the methods suggested by DerSimonian and Laird using the random-effects model [22]. When the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis [23]. The Mantel-Haenszel-type method was used to estimate the pooled odds ratio for all outcomes. [24] Heterogeneity between studies was assessed by means of a χ^2 test (Cochran Q statistic) and quantified with the I^2 statistics. In this, values of < 30%, 30% to 60%, 61% to 75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively. Publication bias was ascertained, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test [25]. When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie's 'Trim and Fill' test was used to ascertain the impact of the bias [26]. $P < 0.05$ was considered statistically significant while comparing the two groups.

All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 3 (BioStat, Englewood, New Jersey, United States).

Results

Search results and population characteristics

From an initial pool of 468 studies, 257 records were screened after reduplication, 81 full-length articles were assessed. A total of seven RCTs with 1458 patients (U-EMR: 739, C-EMR: 719) were included in the final analysis. Overall, 865 (177, > 20 mm) and 826 (192, > 20 mm) polyps were resected using U-EMR and C-EMR, respectively. Mean age ranged from 55.1 to 70 years. Further details along with the population characteristics are described in ▶ **Table 1** and ▶ **Table 2**.

Characteristics and quality of included studies

All included trials in our analysis were prospective with two single-center [27, 28] and five multicenter trials [29, 30, 31, 32, 33]. All trials originated from different geographical regions including Asia, North America, and Europe.

Meta-analysis outcomes

Primary outcomes

Overall pooled rate of R0 resection was higher with U-EMR, 58.05% (CI 29.75–81.89, I^2 96%) vs 44.57% (CI 17.38–75.45, I^2 96%) with C-EMR. The difference between the two was found to be approaching statistical significance, RR 1.25 (CI 0.99–1.59, I^2 68%), $P = 0.07$ (▶ **Fig. 1**).

Overall pooled rate of successful en-bloc resection was significantly higher with U-EMR than C-EMR, 70.17% (CI 46.68–86.34, I^2 97%) vs 58.14% (CI 31.59–80.68, I2 97%), respectively, RR 1.21 (CI 1.01–1.44, I^2 77%), $P = 0.02$ (▶ **Fig. 2**). Based on three trials, for polyps > 20 mm in size, we found no statistically significant difference in rates of en-bloc resection between the two techniques, 37.8% (CI 29.77–46.63, I^2 65%) vs 29.14% (CI 24.29–34.51, I^2 0%), RR 1.24 (CI 0.83–1.84, I^2 57%), $P = 0.3$ (▶ **Table 3**).

Overall pooled rate of polyp recurrence at surveillance colonoscopy was significantly lower with U-EMR, 7.88% (CI 5.16–11.85, I^2 51%) as compared to C-EMR, 15.95% (CI 12.48–20.17, I^2 14%), RR 0.62 (CI 0.41–0.94, I^2 0%), $P = 0.005$ (▶ **Fig. 3**).

Secondary outcomes

Overall pooled rate of piecemeal resection was significantly lower with U-EMR than C-EMR, 19.16% (CI 4.35–56.65, I^2 97%) vs 33.8% (CI 7.62–75.97, I^2 97%), respectively, RR 0.66 (CI 0.43-1.02, I^2 36%), $P = 0.05$ (**Supplementary Fig. 3**).

While the overall pooled rate of incomplete resection was lower with U-EMR, 5.12% (CI 1.98–12.60, I^2 83%) than 6.15% (CI 1.79–19.1, I^2 90%) with C-EMR, the difference between the two was found to be approaching statistical significance, RR 0.67 (CI 0.41- 1.08, I^2 0%), $P = 0.07$ (**Supplementary Fig. 4**).

▶ **Table 1** Study details and population characteristics.

Study	Design	Total patients		Gender		Mean age		Polyp morphology	
		U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR
Zhang, 2020	Prospective, parallel-group, open-label, randomized controlled trial (RCT), May 2019 to November 2019, multicenter, China	66	64	40/26	35/29	55.1 (11.2)	57.6 (9.8)	0-Is (50), 0-Ip (0), 0-IIa (21)	0-Is (54), 0-Ip (1), 0-IIa (16)
Yen, 2020	Prospective, randomized controlled trial (RCT), October 2016 to September 2018, single-center, United States	128	127	123/5	125/2	64.4 (8.3)	64.6 (8.3)	Is 126, IIa 107, IIb 11	Is 115, IIa 88, IIb 4
Yamashina, 2019	Prospective, randomized controlled trial (RCT), multicenter, Japan	108	102	64/44	75/27	70 (43–86)	68 (42–95)	Ip 2, Is 41, IIa 64, IIc 1	Ip 0, Is 44, IIa 58, IIc 0
Nagl, 2021	Prospective, randomized controlled trial (RCT), August 2017 to October 2020, single-center, Germany	81	76	51/30	52/24	68.1 (9.6)	66.3 (11.9)	Is 14, IIa 54, IIb 3, IIc 0, 0-IIa/0-IIc 0, 0-IIa/0-Is 10	Is 20, IIa 49, IIb 2, IIc 1, 0-IIa/0-IIc 1, 0-IIa/0-Is 3
Lenz, 2022	Prospective, randomized controlled trial (RCT), April 2017 to March 2022, multicenter, Brazil	53	52	25/28	22/30	64.4	64	–	–
Hamerski, 2019 (Abs)	Prospective, randomized controlled trial (RCT), multicenter, United States and Italy	158	145	NR	NR	NR	NR	NR	NR
Rodríguez Sánchez, 2022	Prospective, randomized controlled trial, multicenter February 2018 to February 2020, Spain	145	153	87/58	96/57	67.5 (10.4)	67.2 (9.8)	Is 74, IIa 65, IIc 10	Is 66, IIa 80, IIc 16

NR, not reported; IQR, interquartile range; U-EMR, underwater endoscopic mucosal resection; C-EMR, conventional endoscopic mucosal resection.

Overall resection times were not significantly different comparing U-EMR and C-EMR, standardized mean difference −1.21 min (−2.57, 0.16, I2 99%), P = 0.08 (**Supplementary Fig. 5**).

Overall adverse events

Pooled rates of perforation, immediate and delayed bleeding with U-EMR vs C-EMR were, 0.2% (CI 0.01–2.74, I^2 0%) vs 0.26% (CI 0.02–3.89, I^2 0%), 3.54% (CI 0.89–13.1, I^2 87%) vs 3.95% (CI 1.22–12.06, I^2 78%), and 1.14% (CI 0.28–4.61, I^2 0%) vs 2.05% (CI 0.72–5.66, I^2 6%), respectively. These events were comparable between U-EMR and C-EMR, RR 0.75 (CI 0.24–2.35, I^2 0%), P = 0.6, RR 1.16 (CI 0.80–1.69, I^2 0%), P = 0.4 and RR 0.73 (CI 0.41–1.29, I^2 0%), P = 0.3, respectively (**Supplementary Fig. 6**, **Supplementary Fig. 7**, **Supplementary Fig. 8**).

Validation of meta-analysis results

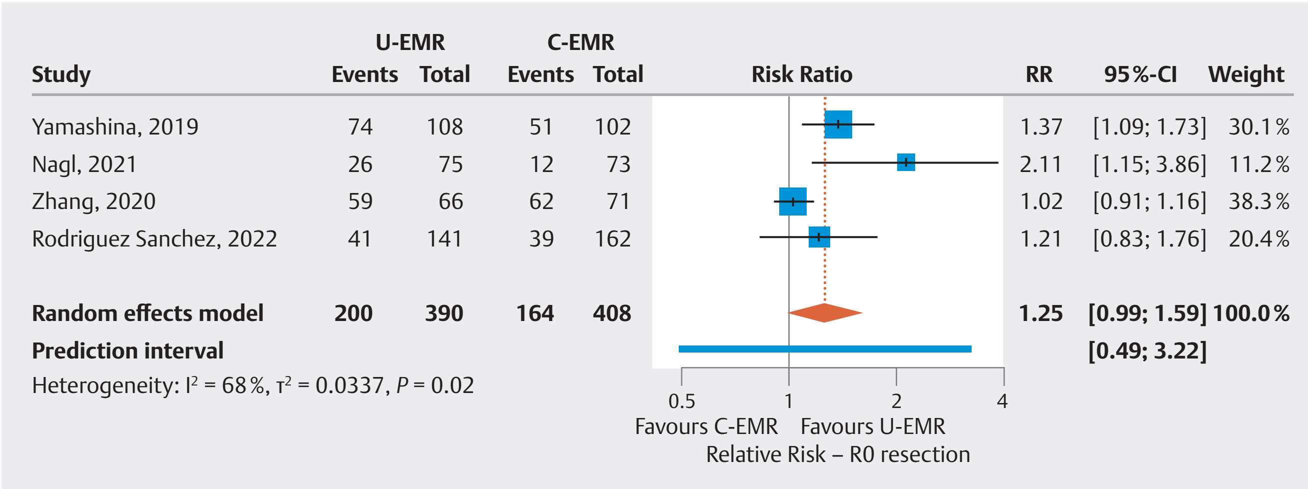
Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. Sensitivity analysis revealed no significant difference in the pooled outcomes for polyp recurrence. Upon exclusion of the study by Zhang et al, we found that the pooled RR for R0 resection was statistically significant in favor of U-EMR, RR 1.39 (CI 1.11–1.75), P = 0.005. This can likely be explained by the fact that that this study only included colorectal polyps less than 10 mm in size and reported that the rate of R0 resection was comparable between U-EMR and C-EMR, P = 0.706. As a result, its exclusion

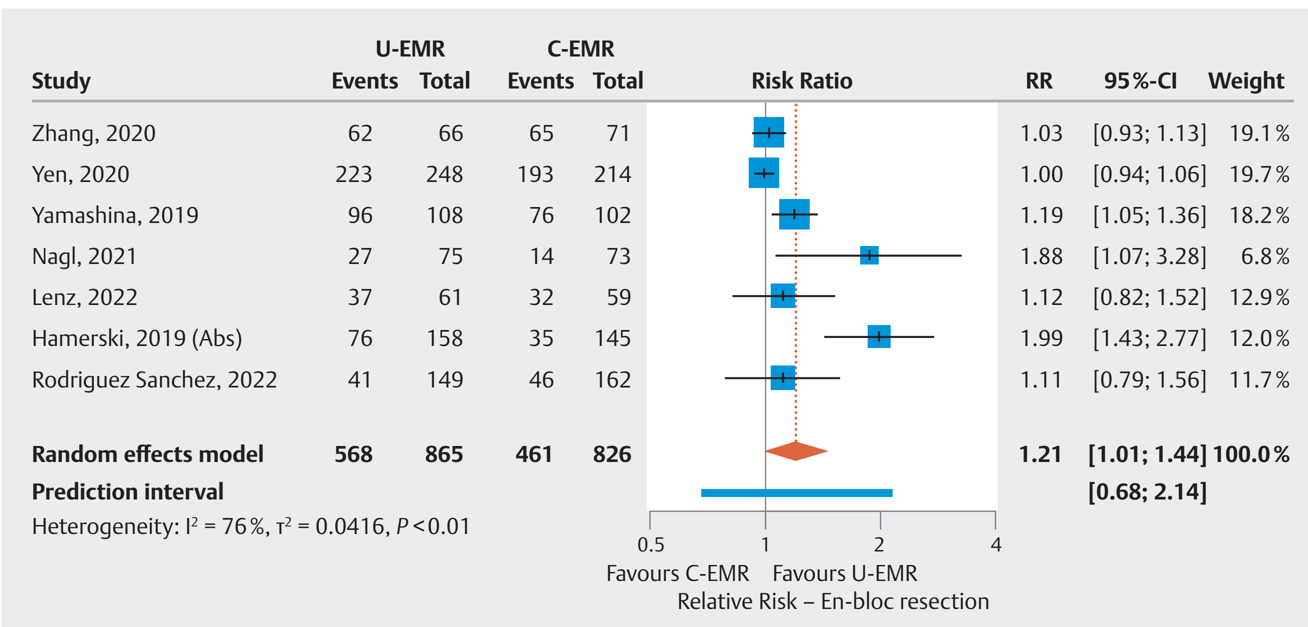
▶ **Table 2** Study outcomes.

Study	Total polyps		Polyp size (mm)		Outcomes																	
					R0 resection		Incomplete resection		En-bloc resection		Resection time		Perforation		Immediate bleeding		Delayed bleeding		Piecemeal resection		Recurrence	
	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR
Zhang, 2020	66	71	6.0 (IQR 5.0–8.0) [median]	5.0 (IQR 4.0–7.0) [median]	59/66	62/71	7/66	9/71	62/66	65/71	1.2 (IQR 0.8–1.4) [minute]	1.35 (IQR 0.9–1.8) [minute]	0/71	0/71	1/71	1/71	0/71	2/71	4/66	6/71	NR	NR
Yen, 2020	248	214	9.9 (6–40) [mean]	9.9 (6–45) [mean]	NR	NR	5/248	4/214	223/248	193/214	3.8 (+/-0.34) [minute]	5.4 (+/-0.35) [minute]	0/248	0/214	5/248	4/214	0/248	0/214	NR	NR	NR	NR
Yamashina, 2019	108	102	14 (IQR 7–25) [median]	13.5 (IQR 7–25) [median]	74/108	51/102	NR	NR	96/108	76/102	2.75 (IQR 1.95–4.6) [minute] {median}	2.91 (IQR 2.2–4.4) [minute] {median}	0/108	0/102	0/108	0/102	3/108	2/102	12/108	26/102	NR	NR
Nagl, 2021	75	73	25 (IQR 20–40) [median]	30 (IQR 20–40) [median]	26/75	12/73	NR	NR	27/75	14/73	7 (IQR 3–13) [minute] {median}	13 (IQR 7–25) [minute] {median}	0/81	0/76	19/76	11/76	1/81	2/76	48/75	59/73	8/50	15/64
Lenz, 2022	61	59	17.4 (IQR 8) [median]	17.5 (IQR 8) [median]	NR	NR	1/61	1/59	37/61	32/59	NR	NR	0/61	0/59	2/61	5/59	0/61	0/59	NR	NR	1/50	8/53
Hamerski, 2019 (Abs)	158	145	NR	NR	NR	NR	NR	NR	76/158	35/145	10.8 (+/- 10.2)	16.9 (+/- 13.2)	1/158	2/145	NR	NR	9/158	9/145	NR	NR	10/124	16/103
Rodríguez Sánchez, 2022	149	162	30 (IQR 25–40) [median]	30 (IQR 25 – 38.8) [median]	41/149	39/162	12/131	26/148	47/149	46/162	14 (IQR 6–30) [minutes]	23 (IQR 9.2–45) [minutes]	4/149	5/162	24/149	25/162	7/149	13/162	NR	NR	24/149	25/162

NR, not reported; IQR, interquartile range; U-EMR, underwater endoscopic mucosal resection; C-EMR, conventional endoscopic mucosal resection.



▶ **Fig. 1** Forest plot, RR, R0 resection.



▶ **Fig. 2** Forest plot, RR, en-bloc resection.

most likely resulted in favorable outcomes for U-EMR during our sensitivity analysis.

Heterogeneity

We assessed dispersion of the calculated rates using the CI and I^2 percentage values. The CI gives an idea of the range of the dispersion and I^2 tells us what proportion of the dispersion is true vs chance [34]. Overall, low to moderate heterogeneity was noted in the pooled risk ratios of adverse events as well as incomplete and piecemeal resection. Considerable to substantial heterogeneity was noted in pooled risk ratios of R0 and en-bloc resection. This is likely due to the inclusion of polyps in different locations and of variable sizes.

Bias assessment

Based on GRADE assessment of bias, overall quality of evidence was graded as moderate (Grade B). This was primarily because due to the inherent design of the trials, the performing endoscopist could not be blinded to the resection technique. Additionally, publication bias was not ascertained as the number of studies included in our analysis were less than 10.

Discussion

Our analysis, based on data from RCTs, shows that U-EMR achieves a higher rate of successful en-bloc and R0 resections as well as lower rates of incomplete resection for colorectal polyps compared to C-EMR. We found that for polyps greater

▶Table 3 Study outcomes for polyps > 20 mm in size.

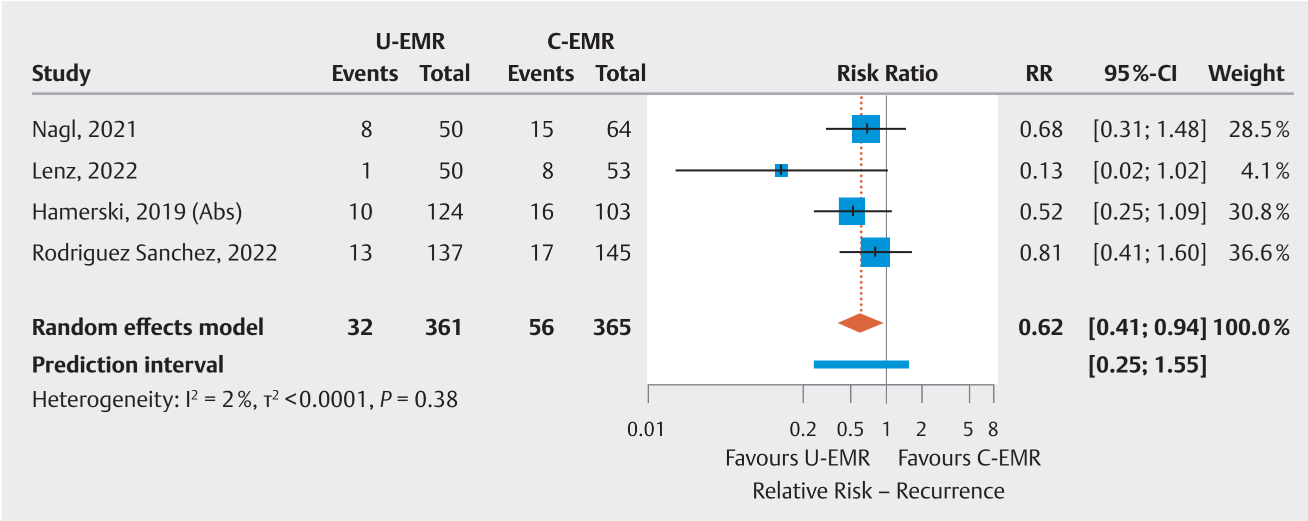
Study	Polyps > 20 mm in size		Incomplete resection		En-bloc resection		Resection time (minutes) (SD)		Perforation		Immediate bleeding		Delayed bleeding		Piecemeal resection		Recurrence	
	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR	U-EMR	C-EMR
Yen, 2020	16/248	16/214	1/16	0/16	4/16	7/16	7.3 (0.62)	9.5 (0.66)	0/16	0/16	3/16	2/16	0/16	0/16	12/16	9/16	NR	NR
Lenz, 2022	12/61	14/59	NR	NR	NR	NR	NR	NR	0/12	0/14	NR	NR	0/12	0/14	NR	NR	0/11	5/14
Hamerski, 2019 (Abs)	NR	NR	NR	NR	68/150	39/139	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rodríguez Sánchez, 2022	149/149	162/162	12/131	26/148	47/149	46/162	14 (IQR 6–30)	23 (IQR 9.2–45)	4/149	5/162	24/149	25/162	7/149	13/162	NR	NR	24/149	25/162

U-EMR, underwater endoscopic mucosal resection; C-EMR, conventional endoscopic mucosal resection; IQR, interquartile range.

than 20 mm in size, both techniques are able to achieve similar rates of en-bloc resection. While U-EMR and C-EMR appear to have a similar safety profile in terms of immediate and delayed bleeding as well as perforation, U-EMR is also associated with comparable resection time and lower rates of polyp recurrence at surveillance colonoscopy.

U-EMR, described in 2012, has been well described by experts for lesions ≥ 20 mm [35]. It is easily learned does not require additional or new equipment [36]. Visualization of a polyp is enhanced underwater due to the "magnification" effect that occurs owing to the higher index of refraction of water compared with air. Water immersion also minimizes luminal distension, flexure angulation, and loop formation, allowing for better maneuverability of the endoscope [37]. Compared to C-EMR, with U-EMR, larger mucosal surface area can be captured in a snare as the colon is not distended or stretched. This feature could provide the possibility to increase en-bloc resection rates, even for lesions larger than 20 mm [38]. In our analysis, we included a total of 369 polyps > 20 mm in size. In this group, while U-EMR had a higher rate of successful en-bloc resection, it did not reach statistical significance, U-EMR 38% vs C-EMR 29%, $P = 0.3$. This is likely due to the fact that only three of the included trials reported outcomes for polyps greater than 20 mm size. We believe that for polyps between 20 mm and 30 mm in size, both EMR and endoscopic submucosal dissection (ESD) can be considered. While EMR is acceptable if en-bloc resection is feasible, ESD could be a better alternative if endoscopic appearance of the polyp i. e., pit pattern, is worrisome for high-grade dysplasia or submucosal invasion. Furthermore, ESD may also be the preferred method of resection if the anatomic location of the lesion is the rectum or morphologically it has large nodules or depressed areas [39, 40, 41].

Interval cancer after colonoscopy can occur due to several reasons including adenoma miss rate, which is about 17% for larger polyps (≥ 10 mm) [42, 43]. An additional risk for development of interval CRC is incomplete resection rate (IRR) of polyps at index colonoscopy. Malignant lesions have been shown to arise in prior polypectomy sites in as many as 19% to 27% cases [44]. Furthermore, IRR is known to be significantly higher for sessile serrated adenomas/polyps particularly those between 10 mm and 20 mm in size [45]. It is believed that R0 resection of colon polyps should be a key performance indicator for endoscopists performing polypectomy [46]. In our analysis, outcomes of R0 resection were only reported in four trials. We found that U-EMR resulted in higher rates of successful R0 resection and lower IRR. Additionally, polyp recurrence at surveillance colonoscopy, as reported in four trials, was seen in up to 15.9% patients with C-EMR as opposed to 7.9% in patients with U-EMR. The statistically significant lower rate of recurrence with U-EMR may eventually lead to lower rates of post colonoscopy CRC. There was insufficient data for us to calculate the pooled rates of incomplete resection and recurrence for polyps > 20 mm in size. However, based on two studies [31, 47], a total of 18 of 148 polyps (12.2%) with U-EMR and 32 out of 157 (20.4%) with C-EMR were incompletely resected. Additionally, nine of 140 patients (6.4%) undergoing U-EMR and 22 of 145 patients (15.2%) undergoing C-EMR had recurrence at



▶ **Fig. 3** Forest Plot, RR, polyp recurrence.

follow. Importantly, post resection thermal ablation was not applied in any of the trials, to avoid bias in the outcomes.

One of the concerns with U-EMR technique is possibly a higher risk of perforation or deep muscle injury, as reported in a few cases. Contrary to C-EMR, in U-EMR, a submucosal lifting agent separating the muscle layer from the mucosal layer is not employed [35, 48]. In our analysis, the pooled rates of perforations were comparable between the two techniques. With C-EMR, while the use of electrocautery is thought to minimize intraprocedural bleeding, higher rates of delayed bleeding have been reported in up to 5.1% patients. [49] We found that the cumulative rates of delayed bleeding were comparable between U-EMR and C-EMR, 1.14% vs 2.05%. Overall, our analysis confirms our previously reported findings that U-EMR outperforms C-EMR in terms efficacy with comparable safety profile.

There are several strengths to our review including systematic literature search with well-defined inclusion criteria, careful exclusion of redundant studies, inclusion of good quality studies with detailed extraction of data, rigorous evaluation of study quality, and statistics to establish and/or refute the validity of the results of our meta-analysis. The study outcomes and definitions were uniform across all the trials. We analyzed efficacy outcomes for all colorectal lesions and en-bloc resection rates separately for polyps > 20 mm in size, and found that in the latter case, the two techniques have comparable outcomes. Polyp recurrence was clearly defined as histologically proven adenomas taken from biopsy samples of the resection scar at surveillance colonoscopy, rather than visual appearance of the post-polypectomy site only. Only one of the trials included in our analysis was published in abstract form [32]. We included updated data from one trial [47] while all others were published as full-length manuscripts. Finally, the majority of RCTs included in our meta-analysis were multicenter experiences, performed at different geographic locations around the world – Europe, the United States, and Asia — thus making our results more generalizable.

There are also several limitations to this study, most of which are inherent to any meta-analysis. First and foremost, one of the included studies in our analysis was only published as a conference abstract [32]. Second, in two of the included trials, the mean/median polyp size was < 10 mm [27, 29], which could have influenced our overall pooled rates of resection. Third, we found that while pooled rates of R0 resection were higher with U-EMR, those of en-bloc resection were comparable. This may be due to the fact that R0 resection rates were assessed from only four trials. Fourth, we included colorectal lesions of different sizes and morphology and were unable to characterize our outcomes based on these variables. In two of the included trials, information regarding blinding of participants and outcome assessment was not reported [31, 32]. In all other trials, while the pathologist was blinded to the resection technique, the performing endoscopists were not blinded, which likely resulted in risk of bias in outcomes assessment. Finally, due to the inherent design of the included trials, the performing endoscopists were not blinded to the resection technique, which could have influenced the outcomes. Additionally, while in most studies, a group of experienced endoscopists performed the procedures, in the study by Yen et al [27], all resections were performed by a single endoscopist, which may have resulted in bias. Nevertheless, our study is the most up-to-date review, based on well-designed RCTs across various geographical locations, comparing the efficacy and safety of U-EMR and C-EMR.

Conclusions

Based on our results, we conclude that in terms of successful R0 and en-bloc resection, U-EMR outperformed C-EMR. Lower rates of polyp recurrence, piecemeal and incomplete resection, further validate the efficacy of U-EMR for colorectal lesions. We found that rates of en-bloc resection for lesions > 20 mm size as well as adverse events are similar between the two techniques.

Conflict of Interest

Dr. Othman – Consultant for Abbvie, BSC, Olympus, Lumedni and ConMed Dr. Rodríguez – Consultant for Microtech Endoscopy. Dr. Draganov – Consultant for Olympus, Boston Scientific, Cook, Fujifilm, Medtronic, Merit, Lumendi, Steris, Microtech. The remaining authors have no conflict of interest to declare.

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