

Systematic review with meta-analysis: impact of one-handed vs. two-handed technique on quality outcomes of colonoscopy

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Abstract. – OBJECTIVE: Colonoscopy is usually performed with the one-handed technique (1HT), although several countries and operators still adopt the two-handed technique (2HT). It is still uncertain whether the 1HT can improve the quality outcomes of colonoscopy. We performed a systematic review with meta-analysis to explore the quality outcomes in patients undergoing 1HT or 2HT colonoscopy.

MATERIALS AND METHODS: We performed a systematic review with meta-analysis to compare the pooled rates of adenoma detection rate (ADR), cecal intubation rate (CIR), cecal intubation time (CIT), and withdrawal time (WT), in patients undergoing 1HT or 2HT colonoscopy via PubMed/EMBASE, SCOPUS, and Cochrane databases. The primary outcome was the pooled rate of ADR and CIR. CIT and WT were also assessed. Pooled odds ratio (OR), standard mean differences (SMD), and 95% confidence intervals (CI) were calculated using fixed or random-effect models.

RESULTS: Five studies (15,763 patients) met the inclusion criteria. The pooled ADR was not significantly different between the two techniques (OR 1.10; 95% CI 0.88-1.39; $p=0.16$), and CIR was not significantly different in 1HT from 2HT (OR 0.757; 95% CI 0.55-1.02; $p=0.07$), with no significant heterogeneity. Furthermore, no significant differences were seen for CIT (SMD 0.95; $p=0.62$) and WT (SMD 0.58; $p=0.74$).

CONCLUSIONS: The 1HT colonoscopy does not add relevant improvement in the quality and efficacy of colonoscopy.

Key Words:

Colonoscopy, One-handed colonoscopy, Adenoma detection rate, Cecal intubation rate, Quality outcomes.

Abbreviations

1HT: one-handed technique; 2HT: two-handed technique; ADR: adenoma detection rate; CIR: cecal intubation rate; CIT: cecal insertion time; WT: withdrawal time; SMD: standard mean differences; CI: confidence intervals; OR: odd ratio; CRC: colorectal cancer; BMI: body mass index; PRISMA: preferred reporting items for systematic reviews and meta-analyses; RCT: randomized clinical trial.

Introduction

Colonoscopy is considered the gold standard procedure for the exploration of the colon and for colorectal cancer (CRC) screening programs worldwide, as it has been shown to have the ability to reduce the incidence or the mortality of CRC through polyps and adenomas detection and removal of precancerous lesions^{1,2}. However, in order to diagnose polyps or adenomas and reduce subsequent CRC-related mortality, several quality indicators of colonoscopy are required.

In the last few years, Gastroenterology Societies have identified the most important quality indicators in colonoscopy^{3,4}. First of all, the adenoma detection rate (ADR), which indicates the rate of patients with, at least, one adenoma detected during colonoscopy, represents the strongest quality metric of colonoscopy. It has been shown that ADR significantly correlates with the risk of interval cancer⁵⁻⁷, even in the presence of great variability among endoscopists⁶.

Secondly, cecal intubation rate (CIR) – defined as passage of the colonoscope tip to a point proximal to the ileocecal valve, so that the entire cecal caput, including the medial wall of the cecum between the ileocecal valve and appendiceal orifice, is visible – is considered another important indicator of the quality of a colonoscopy³. According to American³ and European⁴ recommendations, the rates above 90% for all colonoscopies, and

above 95% for screening colonoscopies should be achieved. Low CIR has been associated with higher rates of interval proximal colon cancer⁸.

Moreover, withdrawal time (WT) is considered a quality indicator able to affect ADR^{3,9}. WT should be measured in all colonoscopy examinations, with the performance target being a \geq 6-minute average withdrawal time in negative-result screening colonoscopies³.

However, all the abovementioned quality indicators depend on patient-related factors (age, gender, body mass index, bowel habits, colonic diverticular disease, prior abdominal and pelvic surgery, and colon preparation quality), endoscopist-related factors (experience and procedure volume of endoscopists) and technique-related factors (use of medications for sedation and the selection of instruments for the colonoscopy)¹⁰.

In the setting of endoscopist-related and technique-related factors, the active manipulation of the scope during the procedure is still a little-explored field. Colonoscopy is usually performed with the one-handed technique (IHT); through this method, the endoscopist's right hand persists on the tube, and the steering is accomplished primarily with the use of the up-down knob alone, accompanied with a right-left torque of the colonoscope. Another option is the two-handed technique (2HT), where the assistant (usually endoscopic nurse) actively handles the scope during the insertion and withdrawal phases, and both the endoscopist's hands are used to move the knobs to direct the scope.

Even though the IHT is recommended by the American Gastroenterological Societies and represents the standard practice in the USA¹¹, the 2HT is still commonly adopted in some European and Eastern Countries. It is still uncertain whether the IHT can really improve the quality outcomes of colonoscopy.

Starting from these assumptions, we performed a systematic review of the existing literature and conducted a meta-analysis of eligible studies to compare the pooled rates of ADR, CIR, CIT, and WT in patients undergoing IHT or 2HT colonoscopy.

Materials and Methods

Literature Search and Selection of Primary Studies

The strategy for building the evidence base for the comparison between IHT and 2HT was performed with a systematic review of the avail-

able evidence in the literature, conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines¹².

The systematic literature review was performed in PubMed/MEDLINE, EMBASE, SCOPUS, and Cochrane databases to identify the reports that assessed IHT for quality outcomes compared with 2HT from the beginning of indexing for each database till May 1, 2017. The bibliographic review of the selected articles was examined as secondary sources for full-length articles of investigations of IHT colonoscopy compared with 2HT colonoscopy. A literature search was performed and verified by 2 independent reviewers (N.I. and A.R.) using the following index terms: "colonoscopy or endoscopy" AND "one-handed technique or single-handed technique or one person technique" AND "adenoma, ADR, adenoma detection" OR "cecal intubation rate" OR "cecal insertion time" OR "withdrawal time". Figure 1 presents the PRISMA flow diagram for the selection of studies.

Eligibility Criteria

Two reviewers (N.I. and A.R.) independently evaluated all the reports retrieved according to the eligibility criteria and any differences between the data sets were resolved by discussion. The researches were included if they met all of the following criteria: (1) randomized controlled trial (RCT) or prospective studies or retrospective studies with control group comparing IHT vs. 2HT; (2) quality indicators (ADR, CIR, CIT, WT) as primary or secondary endpoints; (3) endoscopy procedures performed by experienced endoscopists (not trainees). We excluded the articles if there was no sufficient documentation on ADR or CIR or CIT or WT, if they were in languages other than English, and if they did not separately report the outcome data for IHT and 2HT. Narrative reviews, duplicate publications, and editorial were also excluded.

Data Extraction and Management

The data were independently extracted and entered into standardized Excel spreadsheets (Microsoft Inc., Redmond, Washington, USA). Any disagreements were resolved through discussion. The following data were extracted from each study: first author, year of publication, study design, country, number of participants, age, gender, indication for colonoscopy, rate of adenoma detected, rate of cecal intubation, time of cecal

insertion, withdrawal time, procedure-related complications.

Study outcomes included adenoma detection rate (ADR), cecal intubation rate (CIR), cecal insertion time (CIT), and withdrawal time (WT).

Statistical Analysis

Comprehensive Meta-analysis Software version 3.0 (Biostat, Englewood, NJ, USA) was used to perform statistical analyses. Odds ratio (OR) was calculated for categorical outcomes including ADR, CIR, and tolerability. The standard mean differences (SMD) were calculated for continuous variables, including CIT and WT. These were pooled, and meta-analysis was conducted using a fixed-effect model in the case of non-significant heterogeneity ($p > 0.1$), and a random effect model when significant heterogeneity was present ($p < 0.1$). $p < 0.05$ was considered statistically significant for all outcomes. The corresponding forest plots were constructed for the pooled estimates of these outcomes, and the weight of indi-

vidual analyses are represented by the size of the individual squares. Heterogeneity was assessed by using Chi-squared statistics and I2 measure of inconsistency. Publication bias was evaluated by use of a funnel plot in which the OR was plotted against the inverse standard error for each study. This was tested with the Egger linear regression test. A p -value < 0.05 represented a significant publication bias. The quality of the analyzed investigations was evaluated by two reviewers (N.I and A.R.) in consensus using a quality assessment tool for diagnostic accuracy studies (QUADAS-2). The risk of publication bias and concerns regarding the applicability of studies were then assessed by visually inspecting QUADAS-2 plots.

Results

Figure 1 shows the PRISMA flow diagram of the literature selection process. The search strategy identified a total of 426 publications on the

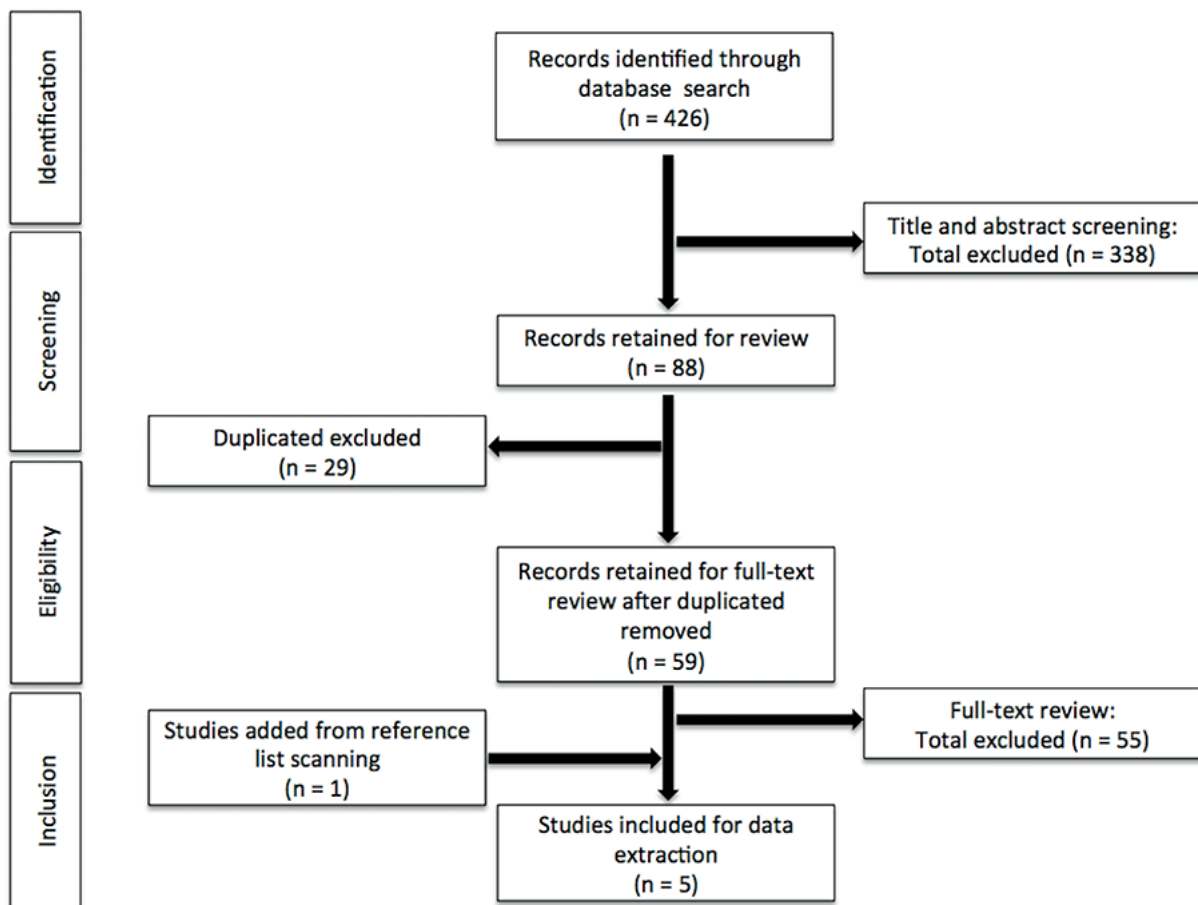


Figure 1. PRISMA flow diagram of the search strategy and selection of studies included in the meta-analysis.

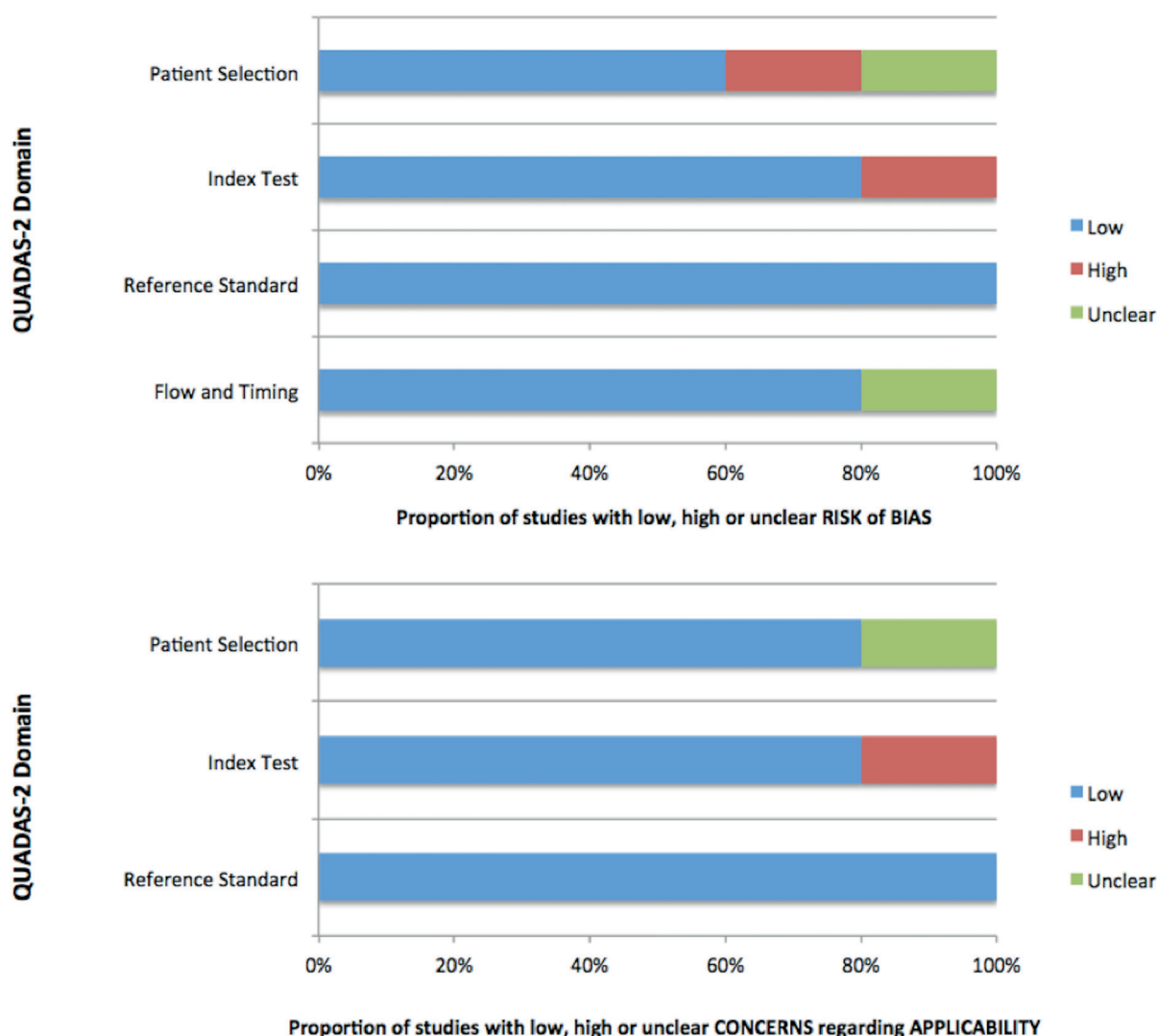


Figure 2. Results of QUADAS-2 quality assessment of selected studies. *A*, Risk of bias. *B*, Concerns regarding applicability.

initial search. After screening the title and abstract and removal of duplicates, 59 articles were selected for further review. After exclusion of 55 articles based on exclusion criteria, 5 studies were included in the meta-analysis¹³⁻¹⁷. Of the 5 selected works, 2 were clinical trials^{13,16} and 3 were real-life investigations with a prospective^{14,15} or a retrospective¹⁷ design. The selected investigations were conducted in Italy (n = 2)^{13,14}, Norway (n = 1)¹⁵, and Taiwan (n = 2)^{16,17}. All were performed in tertiary care settings.

Finally, a total of 15,763 patients (males 50.3%, mean age 55 years) were included in these works out of which 12,610 underwent colonoscopy with 1HT and 3153 with 2HT. Table I shows the characteristics of the included studies.

Quality of Studies and Risk of Bias

Scores of QUADAS-2 evaluation are presented in Figure 2. Overall, the reports showed a low-to-moderate risk of bias and a few concerns about applicability. Three investigations scored a low risk of bias in all domains of the QUADAS-2 system. The highest risk of bias was associated with patient selection. Considering concerns regarding the applicability, all works but one presented a low risk.

Adenoma Detection Rate (ADR)

Adenoma detection rate was reported in 3 studies^{13,14,15}, which included 10,351 subjects. The pooled ADR was 25.2% and 29.3% in patients undergoing 1HT (7654 patients) and 2HT (2697 pa-

Table I. Details of studies selected for meta-analysis.

Reference	Design	Country	Sample size	Gender		Mean age (SD)	Technique		ADR n (%)		CIR n (%)		CIT min		WT min	
				Male	Female		1HT	2HT	1HT	2HT	1HT	2HT	1HT	2HT	1HT	2HT
Paggi 2014 ¹³	RCT	Italy	352	174	178	60.4 (12.6)	176	176	58 (33)	54 (30.7)	172 (97.7)	172 (97.7)	8	8.13	7.6	8.9
Ricci 2013 ¹⁴	P	Italy	3150	1651	1499	60 (14)	1553	1597	537 (34)	568 (35.5)	-	-	-	-	-	-
Hoff 2011 ¹⁵	P	Norway	6849	3111	3738	62.5	5925	924	1336 (23)	170 (18)	5460 (92)	889 (96)	13.6	9.5	7.7	5.39
Lee 2006 ¹⁶	RCT	Taiwan	80	40	40	55	40	40	-	-	40 (100)	39 (97.5)	6.8	8	-	-
Hsu 2011 ¹⁷	R	Taiwan	5332	2966	2366	49.5 (11.4)	4916	416	-	-	4822 (98.1)	402 (96.6)	-	-	-	-

RCT: randomized controlled trial; P: prospective study; R: retrospective study; SD: standard deviation; 1HT: one-handed technique; 2HT: two-handed technique; ADR: adenoma detection rate; CIR: cecal intubation rate; CIT: cecal intubation time; WT: withdrawal time

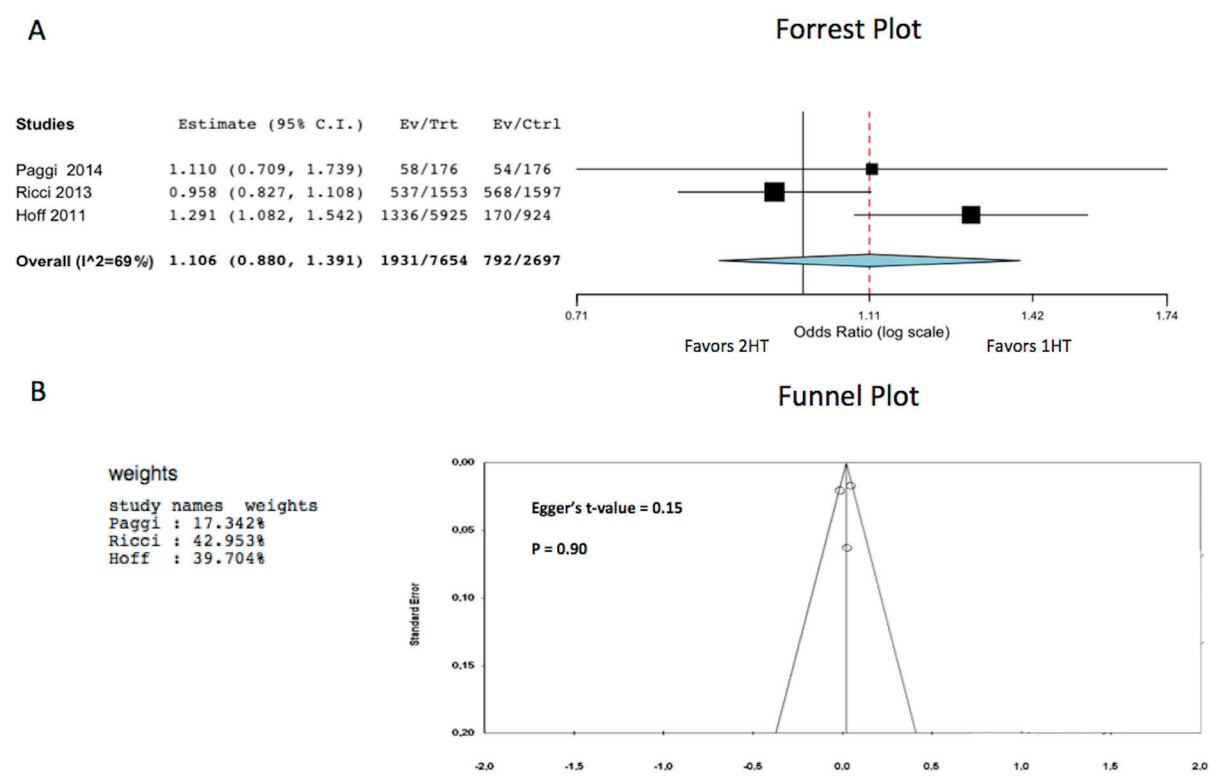


Figure 3. *A*, Forest plot comparing the adenoma detection rate of 1HT vs. 2HT. *B*, Funnel plot to detect publication bias.

tients) procedure, respectively, and the result was not significantly different (OR 1.10; 95% CI 0.88-1.39; $p = 0.16$) (Figure 3A). However, there was considerable heterogeneity in this estimate ($I^2 = 69\%$; $p = 0.039$). On the other hand, Egger's test showed no evidence of publication bias (Egger's t -value = 0.15; $p = 0.90$) (Figure 3B).

Cecal Intubation Rate (CIR)

All selected reports but one^{13,15-17} reported the rate of cecal intubation. CIR was evaluated in 12,513 patients. The overall CIR was 95.7% and 96.8% in patients undergoing 1HT (10,962 patients) and 2HT (1551 patients), respectively, but did not appear statistically significant (OR 0.757; 95% CI 0.55-1.02; $p = 0.07$), with little or no heterogeneity ($I^2 = 0\%$) (Figure 4A). Furthermore, no evidence of publication bias was observed, as assessed by Egger's test (Egger's t -value = 0.86; $p = 0.47$) (Figure 4B).

Cecal Intubation Time (CIT)

Cecal intubation time was an endpoint of 3 studies involving a total of 7821 subjects^{13,15,16}. Pooled SMD for CIT was 0.95 (95% CI 2.86-4.77), with no statistically significant difference

between 1HT and 2HT colonoscopy ($p = 0.62$). There was significant heterogeneity among investigations ($I^2 = 97\%$; $p < 0.001$) (Figure 5A), but no selection bias (Egger's t -value = 0.27; $p = 0.83$) (Figure 5B).

Withdrawal Time (WT)

Only 2 studies^{13,15} enrolling a total of 7201 patients reported the mean withdrawal time for both 1HT and 2HT colonoscopy examination. Pooled SMD for WT was 0.58 (95% CI 2.94-4.12), without statistically significant differences between the two techniques ($p = 0.74$). However, the results were characterized by significant heterogeneity among studies ($I^2 = 95\%$; $p < 0.001$). Furthermore, Egger's test could not be calculated because of the presence of only 2 studies.

Other outcomes

In one study¹³, all procedures were performed under conscious sedation (intravenous midazolam plus meperidine), while in another¹⁴ about 74% of patients in both 1HT and 2HT procedures underwent colonoscopy with conscious sedation. Again, while a study¹⁷ was conducted in deeply sedated patients (propofol), another one¹⁶ only enrolled

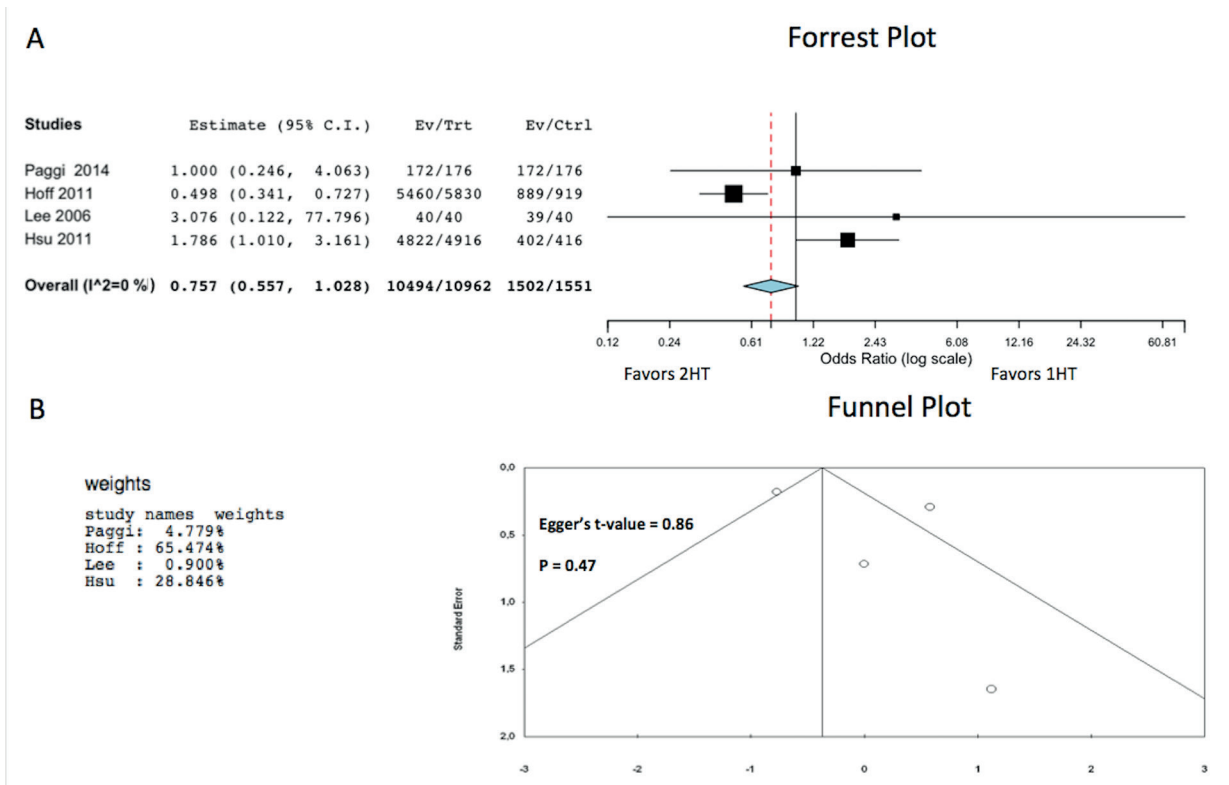


Figure 4. *A*, Forest plot comparing the cecal intubation rate of 1HT vs. 2HT. *B*, Funnel plot to detect publication bias.

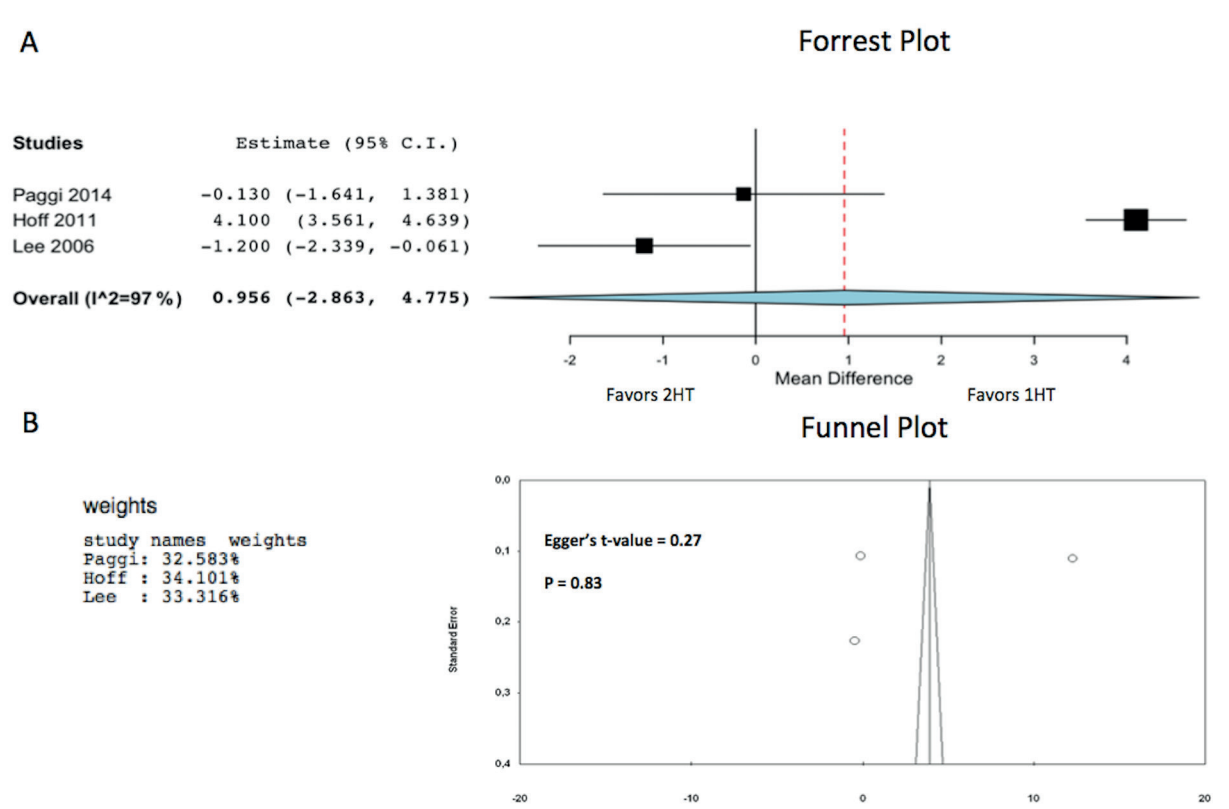


Figure 5. *A*, Forest plot comparing the cecal intubation time of 1HT vs. 2HT. *B*, Funnel plot to detect publication bias.

non-sedated patients. Instead, a study¹⁵ reported a rate of conscious sedation in 26.7% of subjects, with less frequent use of sedation in the 2HT group than 1HT (17% vs. 28%, $p < 0.001$). For these reasons, the data about technique tolerability were not evaluated due to high differences in the sedative drugs administration in the analyses.

Regarding complications, there were no major complications reported in a study¹⁶, while no data were available for two other studies^{14,15}. Three complications were observed (one immediate post-polypectomy bleeding in the 1HT group and two respiratory adverse events, one in each group) in a study¹³, while hypoxemia and transient hypotension were reported in 0.6% and 14%, respectively, from another study¹⁷. Except for post-polypectomy bleeding, all the above mentioned complications appeared to be linked to sedation rather than the colonoscopy technique used.

Discussion

Adenoma detection rate and cecal intubation rate are validated measures of the performance quality of colonoscopy^{7,8,18,19}. The present meta-analysis showed that the 1HT colonoscopy does not improve the detection of adenoma, cecal intubation rate, as well as the mean time for cecal intubation and for withdrawal, compared to the 2HT.

American Gastroenterological Societies¹¹ recommend the 1HT, while the 2HT is still commonly adopted in some European and Eastern countries. As a matter of fact, few reports compared the 1HT vs. 2HT procedures in terms of quality outcomes of colonoscopy, with contrasting results.

After a systematic review of the literature, we found five studies¹³⁻¹⁷ enrolling a total of 15,763 patients. The small number of works testifies that the evidence-based medicine on this topic is still sparse. Among these, three studies¹³⁻¹⁵ reported ADR as a primary endpoint.

In a multicentric Norwegian prospective study, Hoff et al¹⁵ enrolled 6849 patients who underwent colonoscopy for CCR screening or because of symptoms. They found that ADR was significantly higher in the 1HT group than that found in the 2HT group (23% vs. 18%, $p = 0.005$).

On the other hand, in a multicentric Italian prospective study Ricci et al¹⁴, performed 3150 colonoscopies and found that ADR was not significantly different between 1HT and 2HT procedures (34.5% vs. 35.5%, $p = \text{NS}$).

More recently, Paggi et al¹³ performed an RCT including 352 subjects. The authors found 33% of ADR in the 1HT group vs. 30.7% in the 2HT group ($p = 0.65$). Furthermore, their subgroup analysis strengthens this finding, as the endoscopists achieved comparable results when performing colonoscopy by one method or the other one, independently from the technique they adopted in their routine clinical practice.

Our meta-analysis on 10,351 subjects concluded that the pooled ADR was 25.2% and 29.3% in patients undergoing 1HT and 2HT procedure, respectively, and the result was not significantly different (OR 1.10; $p = 0.16$), although there was considerable heterogeneity in this estimate ($I^2 = 69\%$; $p = 0.039$). Probably, if colonoscopy is complete, neither the 2HT, nor the 1HT will influence the ADR outcome. In our mind, endoscopists should perform colonoscopy by using the technique they feel more comfortable with.

Moreover, CIR was evaluated as the endpoint in four studies^{13,15-17}. In 2006, an RCT by Lee et al¹⁶ found that CIR was achieved in all 40 patients that underwent 1HT colonoscopy while it was reached in 39 out of 40 subjects who experienced 2HT. Hsu et al¹⁷ found that, among experienced colonoscopists, the 1HT method was associated with a higher completion rate of colonoscopy than the 2HT (98.1% vs. 96.6%, respectively, $p = 0.006$). By contrast, Hoff et al¹⁵ reported a lower CIR in 1HT than that found in the 2HT group (92% vs. 96%, $p < 0.001$). Paggi et al¹³ found that CIR was the same in the two groups (97.7% for both). Interestingly, our meta-analysis on 12,513 patients showed that CIR was not significantly higher in 2HT when compared with 1HT (OR 0.757; $p = 0.07$), with no heterogeneity and no publication bias. Unfortunately, none of the included investigations reported the length of colonoscope used. Furthermore, no reports reported the differences in the length of colonoscope between endoscopists performing the 1HT and those performing the 2HT. Consequently, it could be difficult to compare CIR if the same device was not used in the two groups.

In an era where the rush to new technologies to improve endoscopic outcomes is based on the use of sophisticated instruments and new colonoscope accessories, we believe that education and proper examination techniques are the pivotal keys. In this setting, endoscopists should choose a technique able to optimize the colonoscopy outcomes at "baseline level"; we were not able to demonstrate any significant advantage by adopting the 1HT rather than

the 2HT. Performing the 1HT means having full control and continuous feel of resistance to optimize combined rotation, angulation, straightening, and advancement of the endoscope. Furthermore, the application of the 1HT could release the nurse for other relevant tasks (e.g., patient's monitoring, selective abdominal compression, use of accessories, etc.). Several expert endoscopists criticize the 2HT because of an increased – but not demonstrated – the risk of perforation due to the loops and the absence of sensitiveness by the physician. However, this data is very hard to prove from a statistical point of view, because of the enormous sample size needed to obtain a statistically significant difference between the two groups. Furthermore, it is thought that the 1HT is more effective to perform efficient therapeutic procedures as polypectomy and endoscopic mucosal resection compared to the 2HT, but scientific data are also lacking about this topic.

Recently, Holme et al²⁰ underlined the importance of endoscopy assistants in improving the performance indicators, in line with the results of our meta-analysis. Quero et al²¹ underlined the importance of quality indicators of colonoscopy as the key factors capable of avoiding the incorrect tumour localization and subsequent changes in surgical management.

Other quality outcomes, which have been evaluated in our study, are recommended by the American and European societies^{3,4}.

We found no statistically significant differences between the 1HT and the 2HT in terms of CIT (pooled SMD for CIT was 0.95, $p = 0.62$), even though there was significant heterogeneity among studies ($I^2 = 97\%$; $p < 0.001$). These results are in accordance with those found by Paggi et al¹³ and Lee et al¹⁶, while Hoff et al¹⁵ reported a significantly longer intubation time in the 1HT procedure than in the 2HT. In our mind, our results mean that the 1HT procedure does not require an “extra-time”; thus it is not a time-consuming technique in the daily endoscopic list.

In this meta-analysis, the choice of 1HT or 2HT seemed not to affect the WT. However, only two studies enrolling a total of 7201 patients^{13,15} reported the data on WT. Paggi et al¹³ found no statistically significant differences in the two groups in terms of WT (7.2 min vs. 8.9 min for 1HT and 2HT, respectively, $p = 0.25$), while Hoff et al¹⁵ reported a higher WT in the 1HT group (7.70 min vs. 5.39 min, $p < 0.001$). Probably, the lower WT found in the study by Hoff et al¹⁵ also explained the lower ADR they found.

Regarding the procedure tolerability, Lee et al¹⁶ demonstrated that patients receiving the 1HT colonoscopy experienced less discomfort compared with those receiving a 2HT colonoscopy, and this was associated with less sedation request. Both Paggi et al¹³ and Hoff et al¹⁵ found no differences in terms of tolerability between the two procedures, although patients receiving the 1HT needed more sedation ($p < 0.001$) in the study by Hoff et al¹⁵. However, we cannot exclude different effects of sedation used in the investigations on this result: therefore, the data about procedure tolerability could not be accurately evaluated.

There are several strengths to our study. First and foremost is the large sample size of the patients included in this meta-analysis, notwithstanding the fact that only five studies were included. This is the first meta-analysis conducted at such a large scale, which focused exclusively on the quality outcomes of colonoscopy in both the 1HT and the 2HT procedures. Secondly, we decided to include only studies whose endoscopy procedures were performed by experienced endoscopists at tertiary centers.

There are, of course, limitations to this meta-analysis. Firstly, not all the included reports had the same endpoints, so that some pooled analyses were performed only on the part of selected works. However, we believed that this might not be clinically relevant as the sample size for each analysis was wide (although only two RCT were included). Secondly, the pooled estimate for ADR, CIT, and WT was limited by considerable heterogeneity among studies; thus, our results should be interpreted with caution. Thirdly, there was a possibility of operator bias, even though patients were kept blind to their assignment to either group and even though it would not have been possible to keep endoscopists blind to the intervention. Moreover, all reports were performed in large, tertiary care settings, which might limit their generalizability. Finally, it is important to consider that we included only five studies (2 RCT, two prospective studies and one retrospective study), and despite the large sample size, this could be a limitation and the results of such a meta-analysis need to be considered with caution.

Conclusions

In summary, we found no differences between the 1HT and 2HT procedures in terms of quality outcomes of colonoscopy. Despite the

potential advantages of the IHT (full control and continuous feel of resistance to optimize combined rotation, angulation, straightening and advancement of the endoscope, extra-time not required), the present meta-analysis does not suggest any advantage in the use of the IHT compared to the 2HT.

Conflict of Interests

The Authors declare that they have no conflict of interests.

Authorship statement

Guarantor of the article: Dr. Nicola Imperatore.

Authorship statement

Nicola Imperatore: planning the study, drafting the article, analysis and interpretation of data; Giovanni Domenico De Palma: critical revision of the article for important intellectual content, final approval of the article; Pasquale Dolce: analysis and interpretation of data; Alessandra Grassano: interpretation of data; Nicola Caporaso: critical revision of the article for important intellectual content; Antonio Rispo: planning the study, drafting the article, analysis and interpretation of data, final approval of the article. All authors approved the final version of the article, including the authorship list. The manuscript is submitted on behalf of all authors, and they have all participated in the work to be published in *Endoscopy*. The manuscript, including related data, figures, and tables has not been previously published, and the manuscript is not under consideration elsewhere.

References

- 1) ZAUBER AG, WINAWER SJ, O'BRIEN MJ, LANSDORP-VOGELAAR I, VAN BALLEGOOIJEN M, HANKEY BF, SHI W, BOND JH, SCHAPIRO M, PANISH JF, STEWART ET, WAYE JD. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med* 2012; 366: 687-696.
- 2) BRENNER H, CHANG-CLAUDE J, SEILER CM, RICKERT A, HOFFMEISTER M. Protection from colorectal cancer after colonoscopy: a population-based, case-control study. *Ann Intern Med* 2011; 154: 22-30.
- 3) REX DK, SCHOENFELD PS, COHEN J, PIKE IM, ADLER DG, FENNERTY MB, LIEB JG 2ND, PARK WG, RIZK MK, SAWHNEY MS, SHAHEEN NJ, WANI S, WEINBERG DS. Quality indicators for colonoscopy. *Gastrointest Endosc* 2015; 81: 31-53.
- 4) REMBACKEN B, HASSAN C, RIEMANN JF, CHILTON A, RUTTER M, DUMONCEAU JM, OMAR M, PONCHON T. Quality in screening colonoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE). *Endoscopy* 2012; 44: 957-968.
- 5) KAMINSKI MF, REGULA J, KRASZEWSKA E, POLKOWSKI M, WOJCIECHOWSKA U, DIDKOWSKA J, ZWIERKO M, RUPINSKI M, NOWACKI MP, BUTRUK E. Quality indicators for colonoscopy and the risk of interval cancer. *N Engl J Med* 2010; 362: 1795-1803.
- 6) ZORZI M, SENORE C, DA RE F, BARCA A, BONELLI LA, CANNIZZARO R, FASOLI R, DI FURIA L, DI GIULIO E, MANTELLINI P, NALDONI C, SASSATELLI R, REX D, HASSAN C, ZAPPA M; Equipe Working Group. Quality of colonoscopy in an organised colorectal cancer screening programme with immunochemical faecal occult blood test: the EQUiPE study (Evaluating Quality Indicators of the Performance of Endoscopy). *Gut* 2015; 64: 1389-1396.
- 7) CORLEY DA, JENSEN CD, MARKS AR, ZHAO WK, LEE JK, DOUBENI CA, ZAUBER AG, DE BOER J, FIREMAN BH, SCHOTTINGER JE, QUINN VP, GHAI NR, LEVIN TR, QUESENBERY CP. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med* 2014; 370: 1298-1306.
- 8) BAXTER NN, SUTRADHAR R, FORBES SS, PASZAT LF, SASKIN R, RABENECK L. Analysis of administrative data finds endoscopists quality measures associated with postcolonoscopy colorectal cancer. *Gastroenterology* 2011; 140: 65-72.
- 9) BARCLAY RL, VICARI JJ, GREENLAW RL. Effect of a time-dependent colonoscopic withdrawal protocol on adenoma detection during screening colonoscopy. *Clin Gastroenterol Hepatol* 2008; 6: 1091-1098.
- 10) ASLINIA F, URADOMO L, STEELE A, GREENWALD BD, RAUFMAN JP. Quality assessment of colonoscopic cecal intubation: an analysis of 6 years of continuous practice at a university hospital. *Am J Gastroenterol* 2006; 101: 721-731.
- 11) SEDLACK RE, SHAMI VM, ADLER DG, COYLE WJ, DEGRECORIO B, DUA KS, DIMAIO CJ, LEE LS, MCHENRY L JR, PAIS SA, RAJAN E, FAULX AL. Colonoscopy core curriculum. *Gastrointest Endosc* 2012; 76: 482-490.
- 12) MOHER D, SHAMSEER L, CLARKE M, GHERSI D, LIBERATI A, PETTICREW M, SHEKELLE P, STEWART LA; PRISMA-P Group. Preferred reporting items for systematic reviews and meta-analysis protocols (PRISMA-P) 2015 statements. *Syst Rev* 2015; 4: 1.
- 13) PAGGI S, RONDONOTTI E, AMATO A, BACCARIN A, SPINZI G, RADAELLI F. One or two operator technique and quality performance of colonoscopy: a randomised controlled trial. *Dig Liver Dis* 2014; 46: 616-620.
- 14) RICCI E, HASSAN C, PETRUZZIELLO L, BAZZOLI F, REPICI A, DI GIULIO E. Inter-centre variability of the adenoma detection rate: a prospective, multicentre study. *Dig Liver Dis* 2013; 45: 1022-1027.
- 15) HOFF G, VOLKER M, BRETTHAUER M, AABAKKEN L, HØIE O, DELANGE T, BERSET I, KJELLEVOLD Ø, GLOMSAKER T, HUPPERTZ-HAUSS G, LANGE O, SANDVEI P. Gastronet survey on the use of one- or two-person technique for colonoscopy insertion. *BMC Gastroenterol* 2011; 11: 73.

- 16) LEE IL, WU CS. Less patient discomfort by one-man colonoscopy examination. *Int J Clin Pract* 2006; 6: 635-638.
- 17) HSU CM1, LIN WP, SU MY, CHIU CT, HO YP, CHEN PC. Factors that influence cecal intubation rate during colonoscopy in deeply sedated patients. *J Gastroenterol Hepatol* 2012; 27: 76-80.
- 18) ROTONDANO G, RISPO A, BOTTIGLIERI ME, DE LUCA L, LAMANDA R, ORSINI L, BRUZZESE D, GALLORO G; SIED CAMPANIA PISCOPO STUDY GROUP INVESTIGATORS, ROMANO M, MIRANDA A, LOGUERCIO C, ESPOSITO P, NARDONE G, COMPARE D, MAGNO L, RUGGIERO S, IMPERATORE N, DE PALMA GD, GENNARELLI N, CUOMO R, PASSANANTI V, CIRILLO M, CATTANEO D, BOZZI RM, D'ANGELO V, MARONE P, RICCIO E, DE NUCCI C, MONASTRA S, CARAVELLI G, VERDE C, DI GIORGIO P, GIANNATTASIO F, CAPECE G, TARANTO D, DE SETA M, SPINOSA G, DE STEFANO S, FAMILIARI V, CIPOLLETTA L, BIANCO MA, SANSONE S, GALASSO G, DE COLIBUS P, ROMANO M, BORGHERESI P, RICCO G, MARTORANO M, GRAVINA AG, MARMO R, REA M, MAURANO A, LABIANCA O, COLANTUONI E, IULIANO D, TROVATO C, FONTANA A, PASQUALE L, MORANTE A, PERUGINI B, SCAGLIONE G, MAURO B. Quality of bowel cleansing in hospitalized patients undergoing colonoscopy: a multicentre prospective regional study. *Dig Liver Dis* 2015; 47: 669-674.
- 19) DE PALMA GD, GIGLIO MC, BRUZZESE D, GENNARELLI N, MAIONE F, SICILIANO S, MANZO B, CASSESE G, LUGLIO G. Cap cuff-assisted colonoscopy versus standard colonoscopy for adenoma detection: a randomized back-to-back study. *Gastrointest Endosc* 2018; 87: 232-240.
- 20) HOLME Ø, PEDERSEN IB, MEDHUS AW, AABAKKEN L, GLOMSAKER T, KVAMME JM, LØBERG M, BRETTHAUER M, SEIP B, KJELLEVOLD Ø, JØRGENSEN A, FURHOLM S, HOFF G, DE LANGE T. Endoscopy assistants influence the quality of colonoscopy. *Endoscopy* 2018; 50: 871-877.
- 21) QUERO G, GALIANDRO F, HASSAN C, FIORILLO C, MENGHI R, ROSA F, CINA C, LATERZA V, ALFIERI S. Colonoscopy quality assessment and accuracy: analysis of the influencing factors and surgical sequelae on 216 colonoscopies. *Eur Rev Med Pharmacol Sci* 2019; 23: 2532-2538.