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MINIREVIEWS

Water-assisted colonoscopy in inflammatory bowel diseases: From technical implications to diagnostic and therapeutic potentials

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Abstract

Water-assisted colonoscopy (WAC) application in inflammatory bowel diseases (IBD) endoscopy offers significant technical opportunities. Traditional gas-aided insufflation colonoscopy increases patient discomfort, presenting challenges in the frequent and detailed mucosal assessments required for IBD endoscopy. WAC techniques, including water immersion and exchange, provide superior patient comfort and enhanced endoscopic visualisation. WAC effectively reduces procedural pain, enhances bowel cleanliness, and increases adenoma detection rates, which is crucial for colorectal cancer screening and disease-related evaluations in IBD patients. Additionally, underwater techniques facilitate basic and advanced endoscopic resections, such as polypectomy and endoscopic mucosal and submucosal resections, often required for resecting IBD-associated neoplasia.

Key Words: Colonoscopy; Water-immersion; Water-exchange; Water-aided; Water-assisted; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Endoscopy; Underwater

Core Tip: Water-assisted colonoscopy (WAC) offers significant advantages over traditional gas-aided colonoscopy, particularly for patients with inflammatory bowel diseases (IBD). WAC enhances patient comfort, reduces procedural pain, and improves bowel cleanliness and mucosal visualisation. These improvements increased adenoma detection rates, enhanced diagnostic accuracy, and facilitated resective endoscopy. Given the elevated risk of colorectal cancer in IBD patients and, consequently, the increased frequency of endoscopic examinations in this population, WAC may prove beneficial for routine IBD endoscopies, ultimately improving the quality of care and patient outcomes.

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INTRODUCTION

Colonoscopy is a digestive endoscopy technique that allows for the endoscopic exploration of the rectum, colon, and terminal ileum through intubation of the ileocecal valve and retrograde ileoscopy. It forms the basis for diagnosing major lower gastrointestinal tract diseases and is a cornerstone for colorectal cancer (CRC) screening[1]. This technique requires adequate visualisation of the intestinal lumen to appreciate the endoluminal and mucosal characteristics, intending to identify qualitative and quantitative alterations.

Nonetheless, in the contemporary era, endoscopy has achieved technical advancements paving the way to the concept of optical diagnosis through advanced imaging strategies (*e.g.*, narrow band imaging[2], i-Scan digital contrast[3], or flexible spectral imaging colour enhancement[4]) based on high-quality white light and virtual chromoendoscopy techniques[5]. Endoscopic magnification has allowed for the detailed study of the endoluminal tissue pit pattern[6], achieving a level of detail reaching a peak in the confocal laser endomicroscopy[7].

All of this requires an optimal lumen distension. Traditionally and historically, gas insufflation (usually carbon dioxide, CO_2 or air) was the reference technique. Nonetheless, compared to more modern water-based techniques, these gas-based luminal visualisation techniques demonstrate inferior performance in patient-reported pain[8]. Furthermore, they also show reduced effectiveness in polyp detection, as evidenced by a Bayesian network meta-analysis[8].

The greater potential for pain with gas insufflation is attributable to the fact that when the examination begins in the standard left lateral decubitus position, the caecal fundus of the colon represents the highest point in terms of altitude[9]. Air, tending to reach this highest point, elongates the colonic segments, making the flexures more angular, rendering the procedure technically more complex and promoting the formation of scope loops[9,10]. This issue can be mitigated because a significant proportion of endoscopic procedures today are performed under sedation, which can ensure a certain degree of patient comfort during the procedure[11]. However, water-assisted techniques have also shown benefits in this area, providing an advantage in reducing the sedation rate during colonoscopy[12,13].

The use of techniques enabling a faster, more effective, and less painful colonoscopy procedure is undoubtedly desirable when the patient already has gastrointestinal damage, as in the case of inflammatory bowel disease (IBD). These conditions cause chronic, self-sustaining, relapsing-remitting inflammation of the gastrointestinal tract[14].

Indeed, it is well known that patients with IBD (especially if on steroid therapy and experiencing severe endoscopic disease activity) who require frequent endoscopic monitoring are at a higher risk of intraprocedural complications during colonoscopy compared to the healthy population. These complications include iatrogenic intestinal perforation[15,16]. For this reason, in cases of acute severe ulcerative colitis (UC), it is advisable to proceed with a simple flexible sigmoidoscopy rather than a complete colonoscopy to avoid iatrogenic complications[17].

Furthermore, in the case of IBD, there are specific considerations to consider even before colonoscopy, such as those related to bowel preparation. It is essential to avoid preparations with extreme osmotic power that could cause mucosal damage, favouring preparations based on isosmotic polyethene glycol rather than low-volume preparations with osmotic agents[18]. Lately, the role of low-volume preparations has also increasingly emerged in this setting[19].

Consequently, this review aims to assess the current evidence, considering all previously mentioned considerations surrounding the use of water-assisted colonoscopy techniques in IBD.

NARRATIVE REVIEW RESEARCH STRATEGY

The search for studies aligned with the objectives of this review was conducted across three primary databases: PubMed MEDLINE, EMBASE, and Web of Science. The search criteria employed for each database were as follows:

PubMed MEDLINE: (water-assisted OR water assisted OR water-immersion OR water immersion OR water-exchange OR water exchange OR underwater) AND (colonoscopy) AND (inflammatory bowel disease OR IBD OR Crohn’s OR ulcerative colitis).

EMBASE: ('water-assisted' OR 'water assisted' OR 'water-immersion' OR 'water immersion' OR 'water-exchange' OR 'water exchange' OR 'underwater') AND ('colonoscopy') AND ('inflammatory bowel disease' OR 'IBD' OR 'Crohn's' OR 'ulcerative colitis').

Web of Science: (((ALL = (water-assisted) OR ALL = (water assisted) OR ALL = (water-immersion) OR ALL = (water immersion) OR ALL = (water-exchange) OR ALL = (water exchange) OR ALL = (underwater)) AND (ALL = (colonoscopy)) AND ((ALL = (inflammatory bowel disease) OR ALL = (IBD) OR ALL = (Crohn's) OR ALL = (ulcerative colitis))).

No specific filters were applied in these search engines to select particular study types or language preferences. Due to this review's narrative and non-systematic approach, specific inclusion or exclusion criteria for the studies included in this work were not predefined. Furthermore, we did not limit the search to a specific timeframe up to the most recent update available as of July 15, 2024.

WATER-AIDED COLONOSCOPY IN IBD: PRELIMINARY CONSIDERATIONS: TECHNICAL PRINCIPLES AND CLASSIFICATION OF WATER-ASSISTED COLONOSCOPY TECHNIQUES

Colonoscopy with water assistance (also often referred to as water-aided) utilises a luminal distension technique during the insertion and advancement of the endoscope primarily based on water instead of gas (air or CO_2), with the use of gas during the withdrawal phase of the scope[20]. This technique was initially proposed in 1984 as a strategic tool for traversing the sigmoid colon, facilitating its opening and reducing colonic spasms[21].

Over time, indeed, there has been a gradual paradigm shift, examining more advantageous alternatives to simple air as the insufflation technique in colonoscopy. In the 1950s, CO_2 had been proposed as an alternative to air due to several advantageous characteristics, including being a non-flammable gas, easily absorbable by the intestinal wall compared to air (over a hundred times compared to nitrogen and over ten times oxygen)[21]. Even in studies specifically focused on IBD, CO_2 has significantly reduced post-colonoscopy abdominal symptoms compared to air, making it the preferred choice in gas-based colonoscopy over plain air[22].

However, water-assisted colonoscopy techniques have evolved over the years and have been classified into different types, each retaining specific characteristics. To date, the following distinctions are recognised[23]:

Water-immersion colonoscopy: In this technique, water is introduced to facilitate the progression of the endoscope more efficiently and promote the intubation of the cecum, using gas insufflation as needed. Most of the introduced water is aspirated during the withdrawal of the endoscope[24].

Water-exchange colonoscopy: Unlike the water-immersion colonoscopy (WIC), the water-exchange colonoscopy (WEC) introduces water, which is aspirated as the scope progresses through the colon to promote cleaning of intraluminal fluids without using gas for insufflation[24]. This eliminates excess gas and faecal residues during progression, promoting a higher degree of bowel cleanliness. Due to its characteristics, WEC generally requires a few extra minutes (estimated at around 2 minutes) compared to standard techniques to complete the procedure[23]. Additionally, WEC may be a rescue technique in difficult-to-perform colonoscopies where caecal intubation proves particularly challenging[25].

WIC and WEC can provide advantages in sedation-free colonoscopy compared to gas-based colonoscopy and promote a higher caecal intubation rate and adenoma detection rate (ADR)[23]. Finally, applying water-assisted techniques for operative endoscopic procedures introduces the concept of underwater resective endoscopy, which allows for procedures such as polypectomies or endoscopic mucosal resections (EMR)[23].

Head-to-head comparisons between WIC and WEC, as revealed by meta-analyses involving over two thousand patients, suggest that WEC benefits from a higher ADR and reduced intraprocedural pain during the insertion phase[26]. However, these advantages come at the cost of increased water infusion and a longer overall procedure duration[26]. The differences and basic principles of the techniques are summarised in Figure 1.

Lastly, predictably, WIC and WEC require a certain level of operator experience to achieve better performance and a higher likelihood of technical success in the procedures, as demonstrated by a recent survey among professionals[27]. Generally, it seems that for WEC, it is recommended to learn it through hands-on sessions initially; however, it can also be learned after receiving instructions from expert mentors, with a learning curve of approximately fifty cases for experienced endoscopists[28].

WATER-AIDED COLONOSCOPY IN IBD AS A STRATEGY TO REDUCE PROCEDURAL PAIN

Patient-reported pain, particularly during the insertion phase of colonoscopy, is a critical target in research settings aimed at ensuring the highest possible comfort for patients undergoing the procedure. This target becomes even more significant for patients with IBD, who, for various reasons, are required to undergo multiple colonoscopies throughout their lives[18].

Indeed, patients with IBD experience chronic abdominal pain due to their condition, resulting in a heightened sensitivity to pain[29]. This makes the pain management target extremely relevant when these patients need to undergo inherently invasive and painful examinations. In other terms, IBD patients may exhibit heightened sensitivity to pain, thereby complicating the colonoscopy procedure. In the context of IBD, the mucosal and systemic concentrations of numerous inflammatory mediators, including cytokines, chemokines, and other substances released during the inflammatory process, are markedly elevated. This elevation directly and indirectly affects visceral afferent function, sensitising

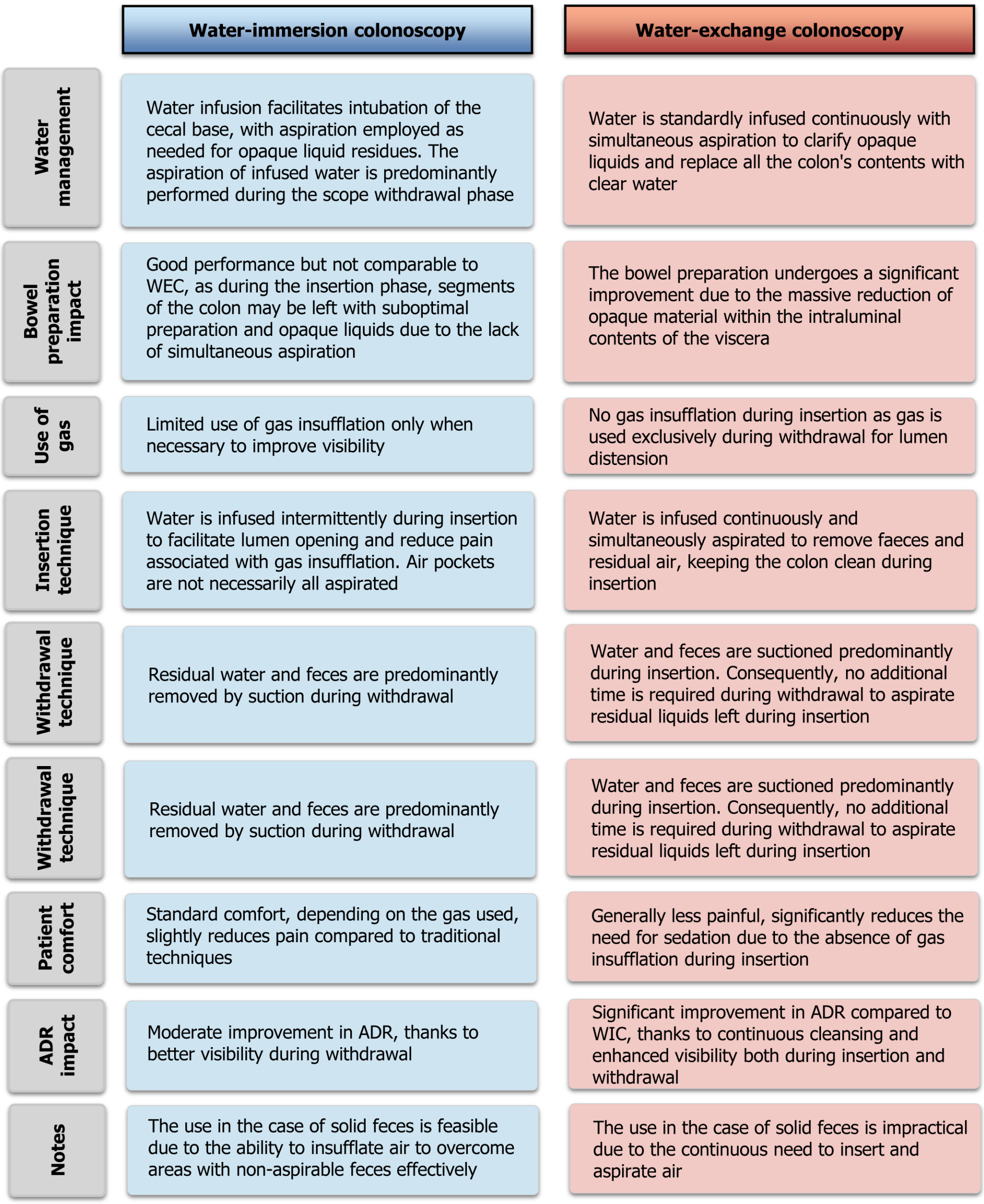

Figure 1 The main differences between water-immersion and water-exchange colonoscopy techniques are as follows: Both techniques, derivatives of water-assisted colonoscopy, utilize water to facilitate the completion of the examination, with distinct differences between them. Compared to standard techniques, water-immersion (WIC) and water-exchange (WEC) offer numerous advantages regarding inflammatory bowel disease (IBD). They facilitate reaching the caecal base with a higher likelihood of achieving terminal ileum intubation. They assist in colorectal cancer screening colonoscopy, which these patients are more susceptible to, by increasing adenoma detection rates both during instrument withdrawal (WIC) and throughout the procedure, including insertion (WEC). Moreover, procedural comfort for patients with IBD, who already suffer from gastrointestinal disorders, is improved to varying degrees with both techniques. In the figure, what pertains (for each parameter indicated in the grey-background boxes) to the WIC is in the blue boxes, while what pertains to the WEC is in the red boxes. WEC: water-exchange colonoscopy; ADR: adenoma detection rate.

the afferent endings and consequently lowering the activation threshold[30].

From the available randomised controlled trials (RCT) comparing air and CO_2 in gas-aided colonoscopy, a clear superiority of CO_2 emerges when analysing intraprocedural and postprocedural pain (within 360 minutes of the procedure)[31]. This advantage is observed without a significant difference in the duration of the procedure or the ileocecal intubation rate[31]. However, when this analysis is combined with water-aided techniques, WEC outperforms all others in pain scores, while gas techniques (particularly those using air) are the least effective[8].

Nonetheless, the water-aided and CO_2 techniques are superior to the air-aided techniques during the insertion phase of colonoscopy performed without sedation[32].

Unfortunately, despite the numerous advantages provided by colonoscopy in the diagnostic, therapeutic, and preventive oncological pathway for IBD, these benefits often clash with the necessary therapeutic adherence required from patients. Unsurprisingly, endoscopy faces predictably poor compliance from these patients, with procedural pain being one of the primary reasons cited[33].

Despite these potential disadvantages, colonoscopy is a tool of great importance in the diagnostic-therapeutic setting of IBD and encompasses various indications, ranging from initial diagnosis to disease monitoring during follow-up[34,35]. Nonetheless, CRC screening represents a cornerstone indication in the context of IBD[36], where the risk of CRC significantly increases compared to the general population[37].

In this context, whether performed using white light or advanced imaging techniques such as chromoendoscopy, colonoscopy allows for identifying precancerous lesions and facilitates secondary cancer prevention, provided that bowel preparation is adequate and employs methods that avoid mucosal damage[18]. Moreover, it is essential to note that a significant proportion of IBD patients undergo endoscopic examinations during active disease. Consequently, techniques that increase procedural speed while maintaining safety (regarding iatrogenic mucosal damage and intra- and post-procedural complications) and ensuring patient well-being are highly desirable. In IBD, most research on water-assisted techniques (*i.e.*, WIC or WEC) has concentrated on minimising procedural pain.

In a trial, Shi *et al*[38] compared WIC and WEC with standard air-performed colonoscopy in approximately one hundred patients with UC. The WIC and WEC techniques (with no significant differences) demonstrated the ability to achieve caecal intubation in over 90% of patients, in contrast to the air technique, which achieved it in less than 80% of patients. Additionally, there was a concomitant reduction in abdominal pain and an improvement in bowel preparation with the water-assisted techniques. In this study, abdominal pain was assessed in detail using a visual analogue scale ranging from 0 to 10, obtained by directly asking the patient during the procedure. There was a slight, though not significant, superiority of the WEC compared to the WIC when comparing the predicted pain scores. However, despite these data, it is essential to highlight the limited sample size of this study (with just over fifty patients in both the WIC and WEC groups), which necessitates studies with larger sample sizes. This is essential not only to obtain further data on the potential of WIC/WEC in reducing colonoscopy-associated pain in IBD patients (especially in unsedated colonoscopy) but also to conduct subgroup analyses to determine whether the disease phenotype or other IBD-specific variables might impact and influence the technical success of these two water-assisted colonoscopy methods.

In a previous study, nearly one hundred IBD patients were randomised at 1:1 to receive water-assisted or air-based colonoscopy[39]. Among the endpoints, the authors identified the rate of unsedated colonoscopy using a discomfort score on a scale of 0-10. This study also highlighted the superiority of the water-assisted technique during both the insertion and withdrawal phases of the procedure. Figure 2 summarises the differences in pain scores identified by these studies.

THE ADVANTAGES OF WATER-AIDED COLONOSCOPY IN CAECAL AND TERMINAL ILEUM INTUBATION: FROM GENERAL PRINCIPLES TO IBD APPLICATION

What are the already-known advantages of water-assisted colonoscopy in caecal and terminal ileum intubation?

Key performance indicators such as the caecal intubation rate, ADR, and colonoscope withdrawal time are essential for defining high-quality colonoscopy[40]. A high-quality colonoscopy includes a comprehensive colon examination, achieved by fully intubating the cecum[41]. A low caecal intubation rate results in an increased interval of CRC[42]. Although maximizing caecal intubation rates is associated with positive outcomes, this is not feasible in all patients, so recommended rates may not reach 100%[43]. Even for experienced endoscopists, colonoscopy may be difficult in 10%-20% of cases, and in about half of these, caecal intubation, and thus the completeness of the examination, is not achieved [43]. The leading causes of difficult colonoscopy include individual and technical factors (*e.g.*, adhesion syndrome, redundant colon, segments with diverticula), which cannot always be predicted before the examination.

Indeed, various potential risk factors can be hypothesized, including age over 50 years, female sex, body mass index less than 23 kg/m^2, previous surgery (particularly hysterectomy), the presence of diverticular disease, stenosis, and abdominal adhesions[44,45]. Technical factors that can complicate colonoscopy include the formation of scope loops in the sigmoid and transverse colon and the presence of redundancy in the transverse colon due to a mobile mesentery[43]. Sometimes, a hard-to-complete colonoscopy can be finalised through various manoeuvres, such as changing the patient's position from left lateral to supine and/or abdominal compression. Isolated studies comparing positional variations and compression manoeuvres generally favour the former; nevertheless, the two manoeuvres can be combined to maximise their advantages. Other strategies include using a paediatric colonoscope, gastroscope, or double-balloon enteroscope[46, 47]. In light of the above, water-aided colonoscopy thus addresses all these needs by increasing the probability of caecal intubation and reducing the necessity for these ancillary manoeuvres[48].

Compared to gas-aided, water-aided colonoscopy might involve using a shorter length of the colonoscope to pass the sigmoid colon, thus leaving more tube length available to reach the cecum. By infusing water just beyond the anal canal and suctioning air, weighing down the left colon, a straightened pathway is achieved, minimising the formation of loops [49]. In an RCT, the primary outcome was determining whether cap-aided and water-aided colonoscopy increased the insertion success rate through the sigma without loop formation. WIC significantly increased the insertion success rate through the sigmoid colon without loop formation (53.5% compared to 37.5% in the gas-aided group and 40% in the cap group). In contrast, no significant differences were found between the groups regarding caecal intubation rate and caecal intubation time[50].

A meta-analysis comparing 23 studies showed that WEC and WIC had a higher caecal intubation rate than CO_2 insufflation. CO_2 insufflation, on the other hand, ranks as the technique with the lowest caecal intubation rate[8]. Possible explanations for why WEC was the most satisfactory technique include infusing water and easily aspirating it to minimise pain from the manoeuvres and the infusion of warm water, which can reduce colonic spasms[28]. WEC, as already postulated, also leads to better intestinal cleansing, resulting in improved mucosal visualisation[20].

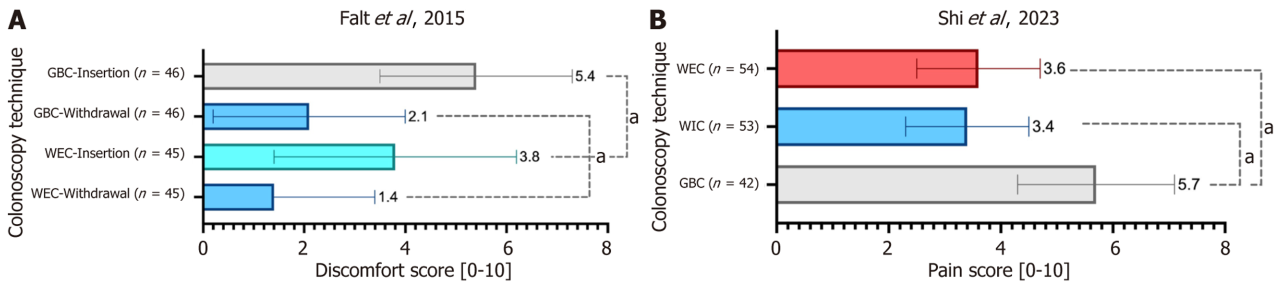

Figure 2 Pain-related data emerged from the two primary studies (A and B) conducted in an inflammatory bowel disease setting, comparing water-assisted colonoscopy techniques with standard gas-based colonoscopy. In both cases, pain was graded using a Likert scale from 0 to 10. A: A discomfort score in the paper by Falt *et al*[39]; B: A pain score by Shi *et al*[38]. Unlike the latter, the former study recorded these scores separately for the insertion and withdrawal phases of the procedure. The results from the first study (A) indicate that the water-exchange technique (WEC) was drastically and significantly superior to the gas-based colonoscopy (GBC) technique during both the insertion and withdrawal phases. In the second study (B), a broader comparison was conducted, including GBC, WEC, and the water-immersion technique (WIC). Although WIC and WEC did not show significant differences in pain scores, both were superior to the GBC technique. Continuous numerical values are expressed in both graphs (*i.e.*, A and B) as means and SD of the respective means. The sample size (*n*) reported in each study is also indicated for each group. $^{a}P < 0.05$, statistical significance.

A study comparing the WIC with gas insufflation concerning caecal intubation rates and times demonstrated that the observed differences are contingent upon the quality of bowel preparation. With optimal bowel preparation, caecal intubation was achieved in 100% of cases in the water immersion group and 97.4% in the gas insufflation group, with no significant differences observed in the times to intubate the splenic flexure and hepatic flexure. In conditions of suboptimal bowel preparation, the caecal intubation rates remained comparable; however, the time to achieve caecal intubation was significantly prolonged in the water immersion group, likely due to the mixing of faecal residues with water, thereby diminishing visibility[51].

What data are available on the IBD population?

All these considerations are highly pertinent, as a thoroughly conducted endoscopic examination (extending even to the terminal ileum) allows for a comprehensive assessment of UC (both in diagnostic phases, follow-up, and CRC screening) and optimally evaluates Crohn's disease (CD) with localization in the lower gastrointestinal tract[34,52-54]. Failure to visualise the ileum in patients with chronic diarrhoea and suspected IBD prevents an early diagnosis, adversely affecting the patient's quality of life and general health and leading to substantial healthcare costs[55,56].

The Falt *et al*[39] study evaluated the application of water-aided colonoscopy in 92 IBD patients. Specifically, they were randomised to undergo water-aided or gas-aided colonoscopy. The terminal ileum intubation success rate was figured out among the secondary outcomes. In water-aided colonoscopy, the terminal ileum was successfully intubated in 84.8% compared to 80.4% in the gas-aided group.

Shi *et al*[38] prospective single-blind RCT recruited 172 UC patients to evaluate the rate of ileo-caecal intubation in the gas-aided, WIC, and WEC techniques. It was found that the rate of caecal intubation was higher in the WIC (91.4% *vs* 75.0%) and WEC (93.1% *vs* 75.0%) groups than in the gas-aided group, with no significant difference between the WIC and WEC groups[38]. One reason for the failure of a gas-aided colonoscopy was abdominal pain.

In summary, WIC and WEC may significantly increase the ileo-caecal intubation rate in IBD patients. This could be attributed to the injection of water instead of air, which aligns the intestinal lumen and reduces pressure on the intestinal canal. Moreover, the temperature and volume of water are crucial factors in water-aided colonoscopy. Injecting warm water can relax the intestinal musculature, reducing spasms and abdominal pain. It is generally believed that a temperature around 37-42 °C effectively mitigates abdominal discomfort[32].

WATER-AIDED COLONOSCOPY AS A WINNING TOOL IN COLORECTAL SCREENING

What advantages have emerged from studies in the general population?

CRC ranks as the third most common cancer by incidence and the second by mortality[57]. Secondary prevention of CRC typically involves a screening programme that includes the detection of faecal occult blood (FOB). Traces of blood can signal the presence of tumours or polyps that may become malignant[58]. Colonoscopy is crucial for diagnosing and treating CRC, especially when there are positive FOB results. This topic is of utmost relevance, considering what has already been outlined for colitis-associated CRC. One primary quality indicator for colonoscopy is the ADR, reflecting the ability to detect polypoid and non-polypoid adenomas during the procedure[59]. ADR is vital for reducing the incidence of interval CRC, tumours found after a negative screening test or colonoscopy and before the subsequent recommended examination[60]. An increase of 1% in ADR correlates with a 3% decrease in CRC incidence and a 5% decrease in CRC-related mortality[61]. An overall ADR of ≥ 25% (≥ 30% in men and ≥ 20% in women) is considered acceptable for CRC screening colonoscopies[62].

The increased incidence of interval CRC is generally due to missed lesions during the procedure, with contributing factors including lesion size, sessile morphology, location, and inadequate bowel preparation[63]. In patients with IBD, the risk of post-colonoscopy CRC is far from negligible, and adequate bowel preparation and IBD-related high-risk features[36] remain extremely influential factors[64].

Modern approaches to increasing ADR, such as high-definition endoscopes, and virtual/dye-based chromoendoscopy, have been developed[65].

Numerous studies have established that water-aided colonoscopy supports an increase in ADR. In a multicentre trial, 224 patients aged 50-70 years undergoing screening colonoscopy were randomised in a 1:1:1 ratio to receive WEC, WIC, or gas-aided colonoscopy. The primary endpoints revealed a significantly higher ADR for WEC (49%) compared to gas-aided (40.4%) and WIC (43.4%)[66]. Secondary endpoints indicated a higher ADR for WEC in the right colon, where diminutive polyps with flat or depressed morphology and more advanced histological patterns are more common[66]. One possible explanation is that WEC improves colon cleansing overall, particularly in the right colon, where residual faeces are often most abundant[26]. In a study aggregating data from three RCT, Cadoni *et al*[67] examined water-aided colonoscopy concerning the ADR in the right colon. Specifically, WEC was associated with a significantly higher ADR in the right colon than WIC and gas-aided colonoscopy for lesions < 10 mm: 11.9% *vs* 6.9% and 7.2%, respectively. However, ADR for lesions of any size was comparable among the three groups. Overall ADRs were comparable among the groups, but WEC, as predicted, demonstrated significant superiority in colon cleanliness, with higher overall and segmental Boston bowel preparation scale (BBPS) scores.

The BBPS is a pillar indicator of colonoscopy quality. BBPS values ≥ 6 indicate adequate bowel preparation, allowing better visualization of possible polypoid lesions, mainly flat lesions[68]. Inadequate bowel preparation is associated with increased rates of missed adenomas. In contrast, no significant differences in ADRs were found between intermediate and high levels of bowel preparation[62]. An additional parameter to be considered in this matter is the hyperplastic polyp detection rate (HPDR), given that in IBD, there are certain factors where even a benign polyp like this can include adenomatous areas with transformative potential[69]. A retrospective study of 704 patients, including 173 screening cases, evaluated the efficacy of WEC compared to WIC and gas-aided one in ADR/HPDR, particularly in the ascending colon[70], due to the higher prevalence of CRC, particularly interval CRC, in the right colon[71]. The superior efficacy of WEC compared to other techniques was also documented for flat or slightly elevated adenomas, particularly within the right colon, encompassing adenomas of any size and those measuring less than 10 mm[70].

Based on these findings, water-aided colonoscopy is an innovative technique that facilitates the inspection of the proximal colon (especially the right colon), making it desirable for CRC screening and prevention[72]. However, most studies possess small sample sizes and are conducted within single centres. To substantiate the advantages of this technique, further multi-centre studies with larger patient cohorts are imperative.

What evidence exists from targeted studies on IBD?

In the coming years, CRC screening programmes are set to expand, resulting in more patients with UC or CD undergoing screening due to their heightened risk for CRC. It is estimated that 18%-20% of patients with UC will develop CRC within 30 years of diagnosis[73]. Continuous mucosal inflammation and regeneration in UC patients can precipitate dysplastic changes, leading to CRC[74]. Endoscopic examination is recommended to commence 8-10 years after the onset of symptoms in UC patients, with screening colonoscopy every 1-3 years, depending on different risk factors[36]. In these patients, surveillance colonoscopy allows for the early detection of dysplasia or CRC in up to 66% of cases, and water-assisted colonoscopy can be utilised to enhance mucosal visualisation and increase the ADR[75].

The advantages of water-assisted colonoscopy in CRC screening are not confined to patients with UC; patients with CD can also derive substantial benefits from this technique. CD patients may present with extensive strictures along the large bowel. In several cases, scar tissue and inflammation may contrast the passage of the colonoscope, complicating the complete intubation of the caecum and terminal ileum. This also considers that patients with colonic CD, albeit to a lesser extent than patients with UC, experience a specific increase in CRC risk compared to the general population[76,77]. As already mentioned, the water-assisted technique has demonstrated particular potential in the presence of strictures or adhesions, facilitating the smoother passage of the instrument through these critical points. Despite these significant potentialities, there is very little evidence of the relationship between WIC and WEC and CRC screening performance in patients with IBD. In the already mentioned Shi *et al*[38] trial, the authors also focused on ADR. No significant differences in ADR were observed among the WIC and WEC. In cases of moderate-to-severe UC, mucosal patina and suboptimal bowel preparation impacted ADR.

In conclusion, the benefits of water-aided colonoscopy in screening and surveillance colonoscopy for IBD patients include enhanced mucosal visualisation, and a potential increase in ADR. However, studies comparing water-assisted colonoscopy in UC and CD are limited by small, single-centre samples. Future research with larger, multi-centre cohorts is necessary to assess water-assisted colonoscopy application further and demonstrate its superiority over air-insufflation colonoscopy.

UNDERWATER RESECTION IN IBD: WHY CHOOSE IT OVER THE TRADITIONAL METHOD?

Patients with IBD, as previously mentioned, are at an increased risk of developing colonic and rectal neoplasia. Carcinogenesis in this context differs from that of sporadic CRC (*i.e.*, the conventional adenoma-carcinoma sequence) as it involves an advanced mutational burden (particularly affecting genes such as *p53*, *K-RAS*, and *APC*) in the intestinal tissue subjected to chronic inflammatory processes, which in turn leads to the development of dysplasia[52]. This,

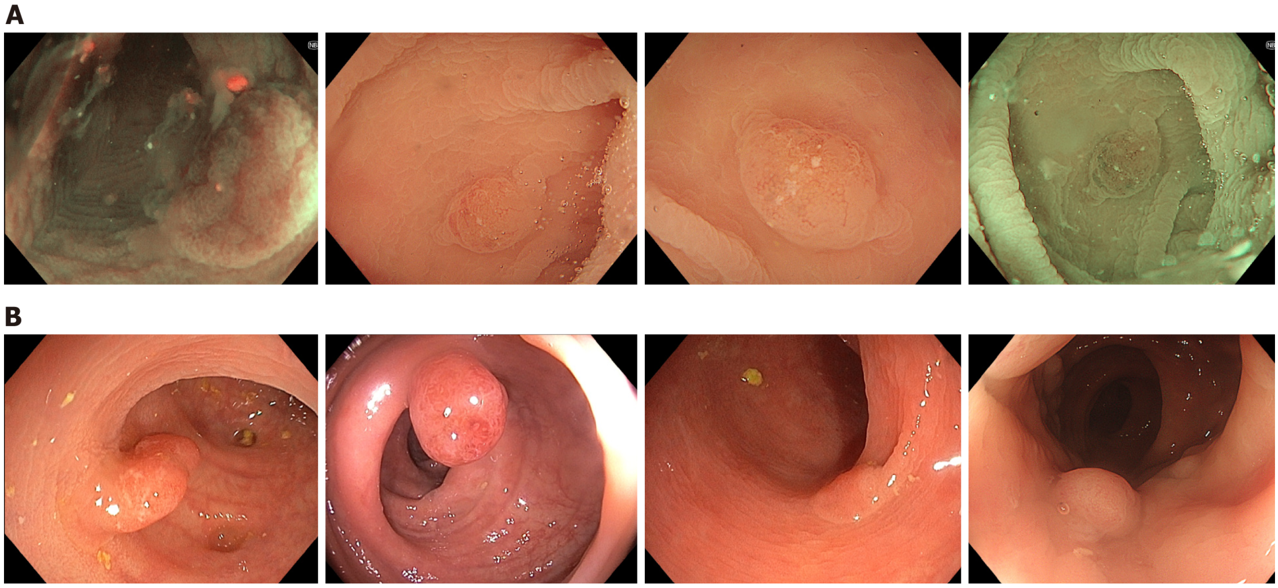

Figure 3 Colonic fold distension during water-aided and gas-aided colonoscopy. A: An example of how the water-assisted colonoscopy technique avoids excessively distending the folds of the colon; B: In contrast to the gas-assisted technique.

therefore, necessitates the imperative to promptly and effectively treat colitis-associated neoplasia upon detection. Additionally, as already written, it requires the establishment of a distinct endoscopic surveillance protocol compared to that of the general population, which considers colitis-specific risk factors such as the inflammatory burden and the disease duration[36]. Colitis-associated CRC also has a poorer prognosis compared to sporadic cancer when matched for stage[74,78-80].

Over time, the diagnosis of polypoid and non-polypoid formations associated with IBD has been enriched by integrated classifications incorporating specific parameters for IBD and those traditionally used for the general population. An example is the classification of Frankfurt Advanced chromoendoscopic IBD lesions (*i.e.*, FACILE)[81]. The FACILE classification integrates the Kudo pit pattern[6], the lesion morphology according to the Paris classification[82], the mucosal surface (roundish, villous, irregular), the vascular profile (based on its regularity and visibility), and the presence of macroscopic signs of colitis. All of this is instrumental in determining the resectability of the lesions, as advanced imaging[83], which is further enhanced by water-assisted techniques, underpins the optical diagnosis that predicts the endoscopic (rather than surgical) resectability of colorectal lesions identified during colonoscopy.

In addition to standard endoscopic resection techniques, the management of neoplasms associated with IBD in the lower gastrointestinal tract employs advanced endoscopic resection techniques to ensure adequate radicality of resection (*i.e.*, R0 resection) and to avoid surgery. Techniques involved include EMR, endoscopic submucosal dissection (ESD), as well as intermediate techniques such as hybrid ESD-EMR, all of which have been shown through meta-analyses to be practical and applicable in IBD contexts[84].

Applying water-aided colonoscopy to basic or advanced resection techniques has shown promising results. For example, Garg *et al*[85] conducted a meta-analytic review of nearly two thousand endoscopic resections using EMR for non-pedunculated polyps larger than one cm. They demonstrated a good efficacy profile for the underwater technique and an advantage in reducing long-term recurrence. Compared to conventional EMR, the underwater variant is based on the principle that the colon is subjected to less tension (induced by gas-aided colonoscopy), making the submucosal injection unnecessary to create a protective cushion for the colon's muscular wall (which could damage and lead to iatrogenic perforation, Figure 3)[86]. Additionally, this technique provides a greater possibility of *en bloc* resection of large lesions compared to the conventional form, as such lesions, with less colonic wall tension, occupy less space and are more easily targeted by the resection snare[86]. Despite the lack of solid evidence, this technique has also been applied to ESD resections[86].

A recent RCT compared fifty-six patients, dividing them 1:1 between underwater ESD and conventional ESD for the resection of laterally spreading tumours (with an average size of approximately 3 cm) and with the presence of fibrosis in over 60% of cases[87]. The data demonstrated that underwater ESD provided an advantage in overall procedure time of approximately thirty minutes, accompanied by a gain of about 6.7 mm^2/minute in dissection speed[87]. This was not associated with differences in the rates of radical resection, *en bloc* resection, or iatrogenic perforations[87]. These findings, although from a trial not explicitly designed for patients with IBD, nonetheless offer a promising perspective for resections performed in IBD, where radicality, speed, and managing intestinal fibrosis are significant considerations.

Despite these advantages, the patient must undergo adequate bowel preparation to perform an underwater EMR/ESD [86]. In patients with IBD, it is well-known that achieving this outcome can often be challenging[18,19]. The prominent detailed cases of underwater EMR in patients with IBD[88,89] are presented in Table 1.

The reports indicate a significant advantage of underwater EMR, particularly in resecting polypoid formations over one cm that have undergone prior biopsy sampling (and thus have fibrosis in the relative submucosa). This fibrosis could lead to a reduction in lesion lifting after submucosal injection, which the underwater technique helps to avoid (Figure 4).

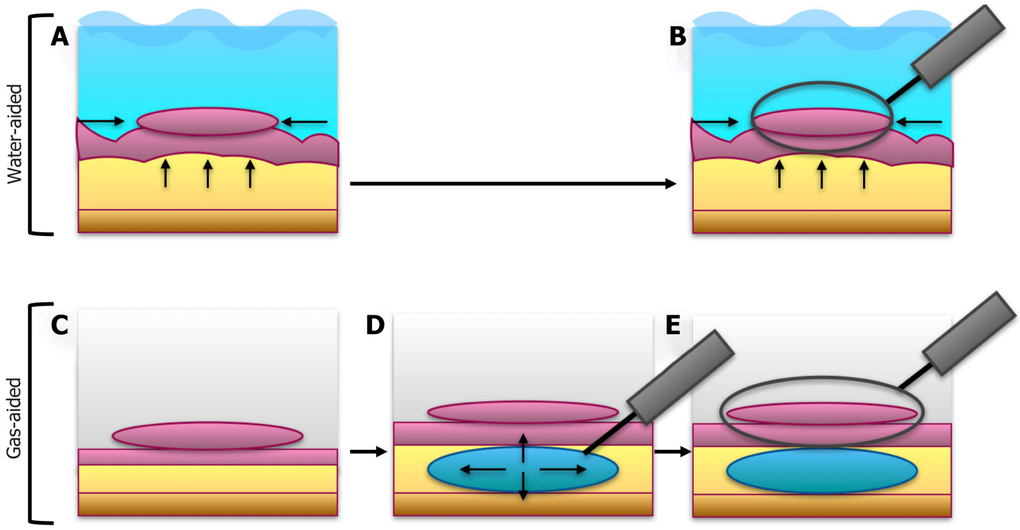

Figure 4 Advantages of water-aided colonoscopy in colonic mucosal lesion resections. A: In the water-aided technique (upper portion of the figure), the introduction of water into the colon lumen allows for de-tensioning of the colonic walls and elevation of the mucosa (in pink) and submucosa (in yellow); B: This facilitates the removal of the mucosal lesion, as in an endoscopic mucosal resection using a snare; C: Conversely, in the gas-aided technique (lower portion of the figure), this elevating effect is absent, and the tension of the colonic walls is increased, resulting in reduced thickness of the mucosa and submucosa; D and E: Consequently, the submucosa must be elevated by injecting substances (*e.g.*, diluted adrenaline in saline solution (D), to enable mucosal resection (E).

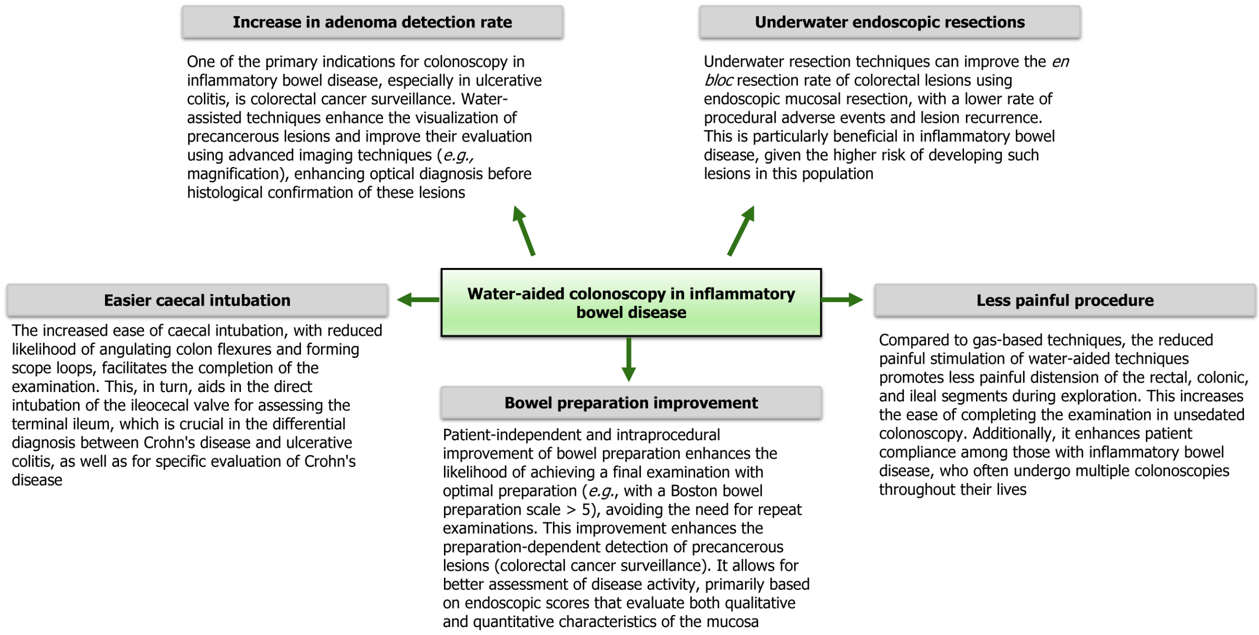

Figure 5 Benefits that water-assisted colonoscopy techniques can provide in patients with inflammatory bowel disease. Within this patient group, where colonoscopy serves multiple diagnostic, therapeutic, and preventive purposes (screening and surveillance for colorectal cancer), water-assisted techniques' advantages can prove particularly beneficial, especially considering the frequent need for these patients to undergo multiple colonoscopies throughout their chronic disease.

CONCLUSION

Based on the available evidence, water-assisted colonoscopy techniques (primarily represented by WIC and WEC) are perfectly suitable for gastrointestinal-sensitive patients such as those with IBD. The advantages offered by WIC and WEC techniques are manifold (Figure 5) and highly appropriate for IBD application, serving the multiple purposes that colonoscopy fulfils in this patient population. Perhaps it would take a greater effort from international scientific societies focusing on IBD to promote the adoption of such techniques, encourage endoscopist training in this regard, and formulate guidelines advocating the use of these techniques in routine clinical practice for IBD specialists.

Table 1 Relevant reports on advanced resection techniques using water-aided (*i.e.*, underwater) methods in patients with known inflammatory bowel disease

Ref.	Sex, age	IBD details (Montreal classification)	Polyp type, size, (chromoendoscopy)	Resection technique	Histologic diagnosis
Hosotani *et al*[89], 2022	M, 73	UC (E3)	Flat, elevated, 15 mm (JNET2A)	*En bloc* UEMR	Low-grade tubular adenoma with submucosal severe fibrosis (previous biopsy)
Takabayashi *et al* [88], 2022	F, 52	UC (not specified)	Flat, elevated, 15 mm (JNET2A)	*En bloc* UEMR	Low-grade tubular adenoma

M: Male; F: Female; UC: Ulcerative colitis; JNET: Japan narrow-band imaging expert team classification type; UEMR: Underwater endoscopic mucosal resection; IBD: inflammatory bowel diseases.

FOOTNOTES

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