REVIEW

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Painless colonoscopy: fact or fiction?

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Although colonoscopy is a routinely performed procedure, it is not devoid of challenges, such as the potential for perforation and considerable patient discomfort, leading to patients postponing the procedure with several healthcare risks. This review delves into preprocedural and procedural solutions, and emerging technologies aimed at addressing the drawbacks of colonoscopies. Insufflation and sedation techniques, together with various other methods, have been explored to increase patient satisfaction, and thereby, the quality of endoscopy. Recent advances in this field include the prevention of loop formation, encompassing the use of variable-stiffness endoscopes, computer-guided scopes, magnetic endoscopic imaging, robotics, and capsule endoscopy. An autonomous endoscope that relies on self-propulsion to completely avoid looping is a potentially groundbreaking technology for the next generation of endoscopes. Nevertheless, critical techniques need to be refined to ensure the development of effective and efficient endoscopes.

Keywords: Colonoscopy; Endoscopy; Patient comfort

INTRODUCTION

A colonoscopy is a medical procedure performed to screen, diagnose, or treat colonic abnormalities such as inflammation, polyps, or tumors. Colorectal cancer (CRC) is currently the second most frequent cause of mortality in both males and females, and the incidence of CRC is increasing even more in the older population.[1,2] Colonoscopy remains the gold standard for CRC screening, followed by personal and familial history screening and fecal occult blood testing using fecal immunochemistry tests (FIT). Delaying colonoscopy in FIT-positive patients is associated with an increased risk of advanced adenoma and CRC.[3] Moreover, it has been estimated that noncompliance with colonoscopy in a FIT-positive population doubles the risk of CRC-related mortality.[4] Although colonoscopy with polypectomy reduces the risk of CRC mortality by 60%, only 72.5% of patients exhibiting FIT-positivity respond to subsequent colonoscopies.[5,6]

Patient reluctance to undergo colonoscopy is due to two major problems. First, colonoscopy is an invasive endoscopic procedure requiring bowel preparation and carries inherent procedural risks, including minor issues such as flatulence and abdominal distention as well as severe complications including perforation, (post-polypectomy) bleeding, bacterial transmission, and, rarely, death.[7,8] Overall, the incidence of complications in diagnostic colonoscopy ranges between 0.14% and 1.1%.[9] Second, anxiety regarding possible discomfort and pain is a major concern for patients. During the procedure, traction of the colonoscope to solve loops or overcome an angulated colon is the main cause of abdominal pain. Additionally, the insufflation of air or carbon dioxide (CO_2) may cause discomfort and pain. Hence, many patients require sedation, which can lead to adverse sedation-related effects.[10] In this narrative review, we describe potential (pre-)procedural actions to overcome abdominal discomfort and increase patient satiety.

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PREPROCEDURAL ACTIONS

Sedation

Even though sedation for endoscopic procedures is becoming increasingly common, a notable interest has been observed in non-sedated endoscopy. Non-sedated endoscopy has several potential advantages, including reduced cost, broad accessibility, low risk, increased efficiency, and diminished postprocedural impairment. This allows patients to resume activities, such as driving or returning to work, immediately after the procedure. Although motivated patients can successfully undergo non-sedated endoscopy, most patients in developed countries still prefer sedation. The overarching trend in gastrointestinal (GI) endoscopy leans towards more potent forms of sedation than less potent ones.[11] The initial methods of sedation for GI endoscopy include moderate sedation with agents such as midazolam, diazepam, pethidine, fentanyl, remifentanil, and/or meperidine. Intravenous benzodiazepines, midazolam, and diazepams have potent sedative, anxiolytic, hypnotic, and amnestic properties. In contrast, fentanyl, remifentanil, meperidine, and intravenous opioid analgesics exhibit minimal sedative effects. Typically, moderate sedation is induced by a combination of a benzodiazepine sedative and an opioid analgesic, leveraging their complementary and synergistic effects. Midazolam and fentanyl (MF) have emerged as the most commonly used agents for moderate sedation in the United States and many other countries. Moderate sedation with MF has been proven to be efficient for standard GI endoscopy, with a safety profile comparable to that of propofol.[12] Research indicates that the incidence of cardiopulmonary complications associated with MF sedation is typically low, ranging from 0.05% to 0.10% during colonoscopies.[13] In a recent meta-analysis encompassing 27 studies, many of which were randomized controlled trials, propofol was identified to be associated with comparable risks of hypoxia (odds ratio [OR], 0.82; 95% confidence interval [CI], 0.63–1.07) and hypotension (OR, 0.92; 95% CI, 0.64–1.32) when compared to MF or other traditional sedative agents. In addition, for non-advanced procedures, propofol was associated with a low likelihood of complications (OR, 0.61; 95% CI, 0.38–0.99).[13]

Monitored anesthesia care by anesthesiologists involves the administration of propofol to induce deep sedation without patient intubation. This approach is widely used in GI procedures and is among the most frequently used sedation methods in North America and Europe. A meta-analysis of 22 randomized controlled trials demonstrated that propofol exhibited advantages such as enhanced patient cooperation, reduced recovery scores, and superior sedation.[14] Nurse- or computer-administered propofol sedation is a recent alternative that is not widely available. To overcome the cardiorespiratory risks of propofol sedation, a Chinese research group demonstrated that a combination of propofol and esketamine significantly reduced the propofol volume per minute, while also resulting in hemodynamic instability.[15]

Insufflation by CO_2 or air: a no-brainer from the patients and safety perspective

Established in 1952, the use of room air for colonic insufflation is a prevailing practice and continues to be the most extensively employed method worldwide.[16] Alternative approaches to air insufflation have been documented for nearly four decades. The use of CO_2 as a substitute for room air has been recognized as a viable alternative.[17] Moreover, CO_2, which is more swiftly absorbed than air, is easily expelled through respiration and has the added benefit of being noncombustible. Furthermore, CO_2 is well-documented as a superior alternative to air in terms of patient comfort; therefore, European guidelines now recommend the routine use of CO_2 insufflation for colonoscopy.[17,18] Nevertheless, the adoption of CO_2 insufflation has been notably low, with only 4.2% of endoscopists opting to use CO_2 as an insufflation agent. Surprisingly, in the practice pattern survey, more than half of the responding endoscopists were unaware that CO_2 was a viable alternative to room air.[19,20] Despite an extensive body of evidence spanning more than 30 years supporting CO_2, obstacles persist in its implementation. These barriers include perceived costs, technical challenges, and lack of apparent benefits. Notably, currently, a dearth exists of high-level studies confirming the equivalence of CO_2 insufflation to that of room air concerning key performance indicators in endoscopy, such as sedative levels, polyp detection rates (PDRs), polypectomy rates, and procedure times. In a recent meta-analysis, 23 well-designed randomized controlled trials were scrutinized, presenting the outcomes for patients who underwent colonoscopy with either CO_2 or air insufflation.[21] The utilization of CO_2 is correlated with a marked enhancement in patient comfort throughout and following the procedure while maintaining the procedure time, cecal intubation rates, and PDRs without causing a noteworthy increase in systemic CO_2 absorption. Employing CO_2 insufflation is an efficient and secure method for enhancing the overall colonoscopy experience and is an important quality indicator for the procedure. Moreover, CO_2 insufflation significantly reduced the number of hospital admissions after endometrial resection of large colonic lesions, primarily driven by reduced postprocedural pain.[22]

In contrast, deflation of the bowel by insertion of a rectal tube after colonoscopy does not affect abdominal bloating, pain, or discomfort during recovery from the procedure or over the subsequent 24 hours, nor does it affect overall patient satisfaction.[23]

In cases of perforation during diagnostic colonoscopy, the use of CO_2 insufflation is generally advised to reduce the risk of intraperitoneal pressurization and decrease pain.

PROCEDURAL SOLUTIONS

Patient positioning and loop resolving (scope guide, magnetic unlooping)

Colonoscopy is traditionally initiated with the patient in the left lateral (LL) position.[24] However, no empirical evidence supports this as an optimal practice. The left colon, particularly the sigmoid colon, poses a particular challenge during colonoscopy. Beginning a colonoscopy in the LL position causes air to rise away from the left colon, leading to the collapse of the colon.[24] This results in acute bends in the sigmoid region, potentially making navigation challenging for flexible endoscopes. In contrast, positioning the patient on the right side allows air to fill and dilate the left colon, reducing bowel angulation and potentially facilitating the passage of the endoscope.[24] The right or left in colonoscopy (ROLCOL) study investigated whether right- vs. left-sided starting position could improve insertion time to reach the cecum and reduce patient discomfort. The results demonstrated that colonoscopy was performed rapidly (median cecal intubation time [CIT] 507 vs. 720 seconds, $p=0.007$) and comfortably (visual analog score 2 vs. 3, $p=0.0001$) when initiated in the right-sided position.[25] Dynamic changes in patient position during withdrawal have also been demonstrated to increase adenoma detection rates (ADRs).[24]

Looping during colonoscopy is another important factor that causes discomfort in patients. Ancillary nursing assistance is a potential solution; however, it is not always efficient. Procedural pain can also be controlled by adjusting endoscope stiffness. A variable-stiffness colonoscope significantly reduced patients' pain scores for both experienced and less experienced endoscopists when compared to traditional colonoscopes.[26] In addition, this type of endoscope was associated with a high cecal intubation rate and a decreased need for sedation.[26,27] Integrated magnetic scope guide (ScopeGuide; Olympus) technology offers a real-time three-dimensional representation of the shape and position of the endoscope while performing colonoscopy. Thus, the guide was designed to improve procedural efficiency and increase patient comfort. A recent prospective randomized trial demonstrated no improvement in the CIT when used by expert endoscopists, nor did it affect the frequency of ancillary maneuvers or patient discomfort.[28] However, electromagnetic scope guidance could be helpful in training as it displays a poor appreciation of loop formation by endoscopists.[29] More recently, another loop-resolving device, the Endorail (EndoStart), was introduced. The device comprises a handpiece containing an adjustable magnet, balloon catheter, and a ferromagnetic fluid (i.e., water-based iron powder dispersion)-prefilled syringe. In the case of a loop, the balloon catheter can be inserted through the scope and filled with ferromagnetic fluid. A magnetic handpiece was placed on the patient to anchor the catheter to the abdominal wall. The loop was resolved by gently retracting the scope of the fixed catheter. Repici et al.[30] demonstrated in a phantom colon that this technology has the potential to facilitate loop-solving in patients; however, further research is required. Currently, a randomized control trial is actively enrolling patients to investigate the safety and efficacy of Endorail in enhancing colonoscopy completion rates in long-term procedures (NCT05626738).

Underwater colonoscopy

Water-exchange (WE) colonoscopy involves the infusion of water instead of air or CO_2 insufflation during the insertion phase. WE was adapted from water immersion, where the removal of infused water mainly occurs during withdrawal. In contrast to water immersion, WE involves the suction of all residual air and the predominant removal of infused water during insertion.[31] Numerous prospective studies conducted in the United States and Europe, primarily addressing the potential reduction in insertion pain and enhancement of the ADR, have suggested that WE may offer improvements.[32,33] A systematic review also hinted at the potential benefit of WE in improving the ADR compared to the benefit of water immersion in resolving ADR.[31] A Chinese prospective randomized trial demonstrated in WE colonoscopy that the mean maximum pain score was significantly lower than that in the air insufflation group (3.57 ± 2.01 vs. 4.69 ± 1.83, $p<0.001$).[34] For patients with a history of abdominal or pelvic surgery and those who were overweight, the maximum pain scores were lower in the WE group than those in the air insufflation group (3.67 ± 1.95 vs. 4.88 ± 1.80,

p<0.001; 3.40±1.96 vs. 4.79±1.97, p<0.001, respectively). Moreover, CIT and PDR remained unchanged. The procedure is deemed safe, although WE may not be suitable for patients with contraindications to colonoscopy. Although perforation is a potential complication of polypectomy, it is independent of the WE method. Water intoxication was a concern; however, blood chemistry findings revealed no significant changes.[35]

Robotic colonoscopy

Robotic colon (RC) systems are the most recent advancement in endoscopic procedures and have attracted increasing attention in scientific publications. These innovative endoscopes hold great promise because of their unique ability to move and adapt to the contours of the lower GI tract.[36] Studies have demonstrated that these characteristics offer advantages over conventional colonoscopy (CC), benefiting both patients and medical professionals. Notably, robotic colonoscopy offers a more comfortable and less painful alternative to standard colonoscopy.[37]

At present, the endotics system is the sole RC system available for clinical use; however, other systems have been developed. A detailed overview of the different robots and their specifications is provided in Table 1.[38-42] In 2017, Tumino et al.[43] demonstrated that RC with the endotics system was successfully performed in 93.1% of patients in whom CC had previously failed because of procedural pain. In terms of metrics, a prospective study demonstrated that the CIT and colonoscopy duration were significantly inferior to those of CC, but the PDR and ADR were comparable. Furthermore, a significantly low proportion of patients undergoing an RC procedure require procedural sedation.[44] In line with this finding, a study conducted by Cosentino et al.[38] revealed that the stress pattern in the colonic mucosa associated with RC was significantly lower (approximately 90%) than that associated with CC. Another potential advantage of RC is that the insertion phase provides sufficient visualization of the colonic mucosa, while the withdrawal phase offers an opportunity to review what was observed during insertion. Consequently, research suggests that RC may exhibit higher diagnostic accuracy than CC owing to its lower insufflation rate, allowing for the visualization of small lesions that are not easily detected using traditional colonoscopy.[44] However, noting that both RC

Table 1. Robotic colonoscopy systems

Robotic colonoscopy system	Manufacturer	Characteristic	Availability	Reference
Endotics system	Era Endoscopy, Pisa, Italy	- Electro-pneumatic self-advancing locomotion - The device is controlled remotely by a hand-held control device	Available for clinical practice	Cosentino et al. 2009[38]
Neoguide endoscopy system	Neoguide Endoscopy System Inc., Los Gatos, CA, USA	- Electro-mechanical propulsion via follow-the-leader principle) - 16-segment insertion tube controlling the snake-like movement - Position sensors at the distal tip and external base for live scope positioning and 3-dimensional colon mapping	Not available	Eickhoff et al. 2007[39]
Invendoscope SC40	Invendo Medical GmbH, Weinheim, Germany	- Electro-mechanical propulsion with an inverted sleeve mechanism - Hand-held remote for tip control	Not available	Rösch et al. 2008[40]
Aer-O-Scope system	GI View Ltd., Ramat Gan, Israel	- Self-steering, self-propelling and disposable colonoscope - Inflation and deflation of two inflatable balloons (proximal and distal) together with pneumatic pressure control in between the two balloons is used for movement	Not available	Vucelic et al. 2006[41]
ColonoSight system	Stryker GI Ltd, Haifa, Israel	- Electo-mechanical self-propulsion - Exists of a reusable part (the colonoscope) and a disposable part (multi-lumen sheath with working channel)	Not available	Shike et al. 2008[42]

and CC demonstrate comparable ADRs, even though the time required to complete an RC is typically long, is important.[36]

In addition, 92.7% of patients were willing to undergo repeat endovascular procedures. Anecdotal data suggests the possibility of successful RC in a patient with dolichocolon characterized by severe angulation who refused to undergo CC with or without sedation because of the fear of perforation.[36] Although these developments are technically impressive, their exact applicability in improving patient discomfort is not clear, and they are unlikely to be cost-effective when compared to the economical techniques mentioned above.

CONCLUSION

Patient experience and satisfaction are important quality indicators of colonoscopy and are mainly driven by pain and discomfort during the procedure.[18,45] Although sedation provides good pain control in most patients, colonoscopy is performed with minimal or no sedation in several countries. In such cases, the aforementioned techniques can help improve the general tolerability of colonoscopy. The first simple measure is CO_2 insufflation, which is preferred over air insufflation owing to its superior absorbance. Even sedated colonoscopy improves postprocedural pain due to reduced persistent intestinal insufflation. In an unsedated colonoscopy, WE is a viable option for the reduction of intra-and postprocedural discomfort, when compared to air or CO_2 insufflation. Moreover, WE has been demonstrated to increase ADR, although it is both elaborate and time-consuming.

New robotic colonoscopy techniques have demonstrated positive outcomes in alleviating the pain and discomfort associated with CC. Despite these promising results, their widespread adoption remains limited, and obvious questions remain unanswered regarding the cost-effectiveness of these devices, especially in light of minimal supporting evidence.

Conflicts of Interest

Raf Bisschops is currently serving as an associate editor in *Clinical Endoscopy*; however, he was not involved in the peer reviewer selection, evaluation, or decision process of this article. Raf Bisschops received speaker's fees, consultancy, and research support from Pentax, Fujifilm, and Medtronic. The other authors have no potential conflicts of interest.

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