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What Influences the Quality of Prevention Colonoscopy?

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Keywords
Colonoscopy · Colonoscopy methods · Water-aided colonoscopy · Cap-assisted colonoscopy · Carbon dioxide insufflation · Colorectal neoplasms · Mass screening

Summary
Background: Colorectal cancer still has a high incidence and mortality. Although colonoscopy is considered as gold standard of colorectal cancer screening, there still exists an unsatisfactory level of adenomas missed in screening and surveillance colonoscopy. Furthermore, patients bear the burden of potentially unpleasant and painful examination and preparation procedures. **Method:** A search of the literature using PubMed was carried out, supplemented by a review of the programs of the Digestive Disease Week (DDW) and the United European Gastroenterology Week (UEGW) 2011–2013. **Results:** Several new approaches to colonoscopy were described: water, CO_2 and cap colonoscopy, and application of spasmolytics such as hyoscine butylbromide and glucagon. The use of these methods does not necessitate the purchase of new endoscopes. They are feasible and safe, facilitate achieving the aim of more comfort and less pain, and perhaps allow lower doses of sedatives to be used. However, a clear effect on procedure time is lacking. Furthermore, the published data do not consistently answer the question of whether these techniques have a positive impact on the most important goal, the better detection of carcinoma precursors. **Conclusion:** More efforts to optimize bowel preparation have to be made to improve visualization of the mucosal surface. The most reliable criteria for the quality of screening and surveillance colonoscopy remain a minimum cecal intubation rate of >90%, a withdrawal time of at least 6 or better 9 min, and an adenoma detection rate of >20%. These results should be achieved with a complication rate lower than 1%, including polypectomy.

Schlüsselwörter
Koloskopie · Koloskopie-Methoden · Wasser-gestützte Koloskopie · Kappen-assistierte Koloskopie · Kohlendioxid-Insufflation · Kolorektale Tumoren · Vorsorgeuntersuchung

Zusammenfassung
Hintergrund: Es besteht weiterhin eine hohe Inzidenz und Mortalität an kolorektalen Karzinomen. Obwohl die Koloskopie als Goldstandard für die kolorektale Karzinomvorsorge gilt, besteht weiterhin ein unbefriedigendes Niveau übersehener Adenome bei der Screening- und Nachsorge-Koloskopie. Weiterhin tragen die Patienten die Last einer gelegentlich unangenehmen und schmerzhaften Untersuchung und Vorbereitung. **Methode:** Eine Literaturrecherche über PubMed-Abfragen, ergänzt durch eine Durchsicht der Programme von Digestive Disease Week (DDW) und United European Gastroenterology Week (UEGW) 2011–2013, wurde durchgeführt. **Ergebnisse:** Verschiedene neue Ansätze zur Koloskopie werden beschrieben: Wasser-, CO_2- und Kappen-Koloskopie sowie die Anwendung von Spasmolytika wie Butylscopolamin und Glucagon. Die Anwendung dieser Methoden erfordert nicht, in neue Endoskope zu investieren. Sie sind praktikabel und sicher und erleichtern es, die Zielsetzung von mehr Komfort und geringeren Schmerzen zu erreichen. Möglicherweise sind niedrigere Dosen von Sedativa möglich, aber eine eindeutige Verkürzung der Untersuchungsdauer war nicht festzustellen. Die veröffentlichten Daten können auch die Frage, ob diese Techniken das wichtigste Ziel – die bessere Erkennung von Karzinomvorstufen – verbessern, nicht einheitlich beantworten. **Schlussfolgerung:** Weitere Bemühungen zur Optimierung der Darmvorbereitung müssen mit dem Ziel einer verbesserten Visualisierung der Schleimhautoberfläche unternommen werden. Die zuverlässigsten Kriterien für die Qualität von Screening- und Überwachungskoloskopien bleiben ein Erreichen des Zökums in >90%, eine Rückzugszeit von mindestens 6 bzw. besser 9 min und eine Adenom-Erkennungsrate von >20%. Diese Ergebnisse sollten mit einer Komplikationsrate unter 1% einschließlich Polypektomie erzielt werden.

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Introduction

Introduced into the diagnostic spectrum in 1969, colonoscopy has been accepted worldwide as gold standard in the diagnosis of diseases of the large bowel, especially in the detection of colon cancer precursors. Diagnosis of over 1.3 million new cases of colorectal cancer (CRC) was estimated in 2012, hereof 447,000 cases in Europe. CRC is the third most common cancer in men, and the second most common cancer in women. Worldwide mortality is lower with 694,000 per year. In Germany, CRC is responsible for approximately 40,000 deaths/year, being the second most common cause of cancer deaths [1, 2].

According to the adenoma-carcinoma sequence, it has become widely accepted that resection of adenomas of the colon reduces the incidence and consequently the mortality of CRC. The promise of elimination of desirably all carcinoma precursors can only be fulfilled when the detection rate is 100%. The adenoma detection rate is defined as the proportion of patients with at least one adenoma detected during one colonoscopy [3]. However, many studies, and most recently Samadder et al. [4], have demonstrated the reality and importance of interval carcinoma. This is defined as CRC that occurs after a previous and before the next screening/surveillance examination. In their series, 126,936 persons underwent colonoscopy (1995–2009) with the result of 2,659 persons with carcinoma detected; however, in 3.5 and 6%, carcinomas were found 6–36 and 60 months, respectively, later, particularly in the proximal colon and in patients with prior polypectomy. Also recently, Corley et al. [5] (20,079 colonoscopies 1998–2010, 716 subsequent post-colonoscopy CRC within 10 years) demonstrated very clearly that 'cancer risk increases linearly with decreasing physician adenoma detection rate and there was no clear threshold above which there was no further improvement'. Reasons other than missed adenomas may be the rapid development of particularly serrated adenomas, and the overestimation of adenoma resection. This data highlights the demand for further optimization of screening and surveillance colonoscopy. In particular, further progress is desirable and necessary to achieve the following aims: i) improvement of diagnostic quality, particularly with regard to the detection of colon carcinoma precursors; ii) minimization of the rate of interval colorectal carcinomas; iii) increase in patients' comfort and thus acceptance of the procedure; iv) avoidance of or dose-reduced sedatives; v) minimization of the procedural risk; and vi) cost reduction.

In the last decade, several primary technical innovations have been developed such as the Third Eye Retroscope (Avantis Medical, Sunnyvale, CA, USA), retroflexion colonoscopy, the Invendo Endoscopy System (Invendo Medical, Garden City, NY, USA), the G-Eye colonoscope (Smart Medical Systems, Ra'anana, Israel), colon capsule, and in situ low coherence enhanced backscattering spectroscopy (LEBS). While these topics and the spectrum of dye-based and virtual chromoendoscopy (chromoscopy) are covered by Kiesslich et al. in another contribution in this special issue, this article deals primarily with the following recent improvements, mainly published in the last 5 years, which can in the majority be achieved with existing endoscope systems: i) preparation of the bowel; ii) rinsing and cleaning systems; iii) carbon dioxide (CO_2) colonoscopy; iv) water colonoscopy; v) cap colonoscopy; and vi) administration of spasmolytics. The special aspects of screening colonoscopy in patients with inflammatory bowel diseases are excluded in this contribution.

Colon Preparation

At first, we set our focus on recent studies investigating proper bowel preparation and the subsequent recommendations. It is accepted that endoscopy of an inadequately prepared bowel is more time-consuming with regard to both cecal intubation and complete withdrawal, and also brings about impaired diagnostic quality, particularly concerning the detection of small and large adenomas [6]. Adequate preparation means 'that lesions other than small (5 mm) polyps' are not obscured [3]. In several publications, 20–40% of the investigated patients showed inadequate cleansing [7, 8]. Several authors have proposed scales for measuring colon cleansing for colonoscopy – most recently the Chicago scale (table 1) which gave an overview of other until then used scales, e.g. the Boston and Ontario scale [9]. In future, such standardized scales may be helpful to design comparable or superior multicenter studies to evaluate different modes of preparation. The results of recent bowel preparation studies can be summarized as follows [6, 10]: Split-dosing and same-day dosing of polyethylene glycol electrolyte lavage solution (PEG-ELS) are more efficient than evening-before dosing, and this split-dosing mode is better tolerated among standard preparations; the application of 4 l PEG-ELS remains the gold standard for efficacy; and intake of a fiber-free and low-residue diet 1 day before colonoscopy may improve preparation quality. Patients should be asked to describe their last rectal effluent as a predictor of preparation quality; if it was a brown liquid or solid, further oral preparation or enemas are recommended [6, 11]. In the hospital setting, it would be very helpful if the nursing staff supervised and supported the inpatients during the preparation and assessed the quality of their rectal effluent. If there are predictors (see below) of inadequate preparation, the cleansing process should be intensified, e.g. by additional administration of bisacodyl [12], magnesium citrate, or sodium picosulphate. The European Society of Gastrointestinal Endoscopy (ESGE) recommends the latter two drugs as 'valid alternatives' [10]. Addition of simethicone [13], lubiprostone [14], metoclopramide, domperidone, cisapride, and tegaserod did not improve the result. Simethicon, however, is recom-

Table 1. Chicago bowel preparation scale (BPS) for colon cleansing [9]

Chicago BPS
0 = Unprepared colon segment with stool that cannot be cleared (>15% of the mucosa not seen)
5 = Portion of mucosa in segment seen after cleaning, but up to 15% of the mucosa not seen because of retained material
10 = Minor residual material after cleaning, but mucosa of segment generally well seen
11 = Entire mucosa of segment well seen after cleaning
12 = Entire mucosa of segment well seen without washing (suctioning of liquid allowed)
Chicago BPS rating for the amount of fluid in the whole colon
3 = Large amount of fluid (>300 cc)
2 = Moderate amount of fluid (151–300 cc)
1 = Minimal amount of fluid (51–150 cc)
0 = Little fluid (≤50 cc)
Chicago BPS total score
Calculated by adding the scores of the right, transverse, and left colon segments; ranges from 0 (very poor) to 36 (outstanding); score for the fluid in the whole colon is reported separately

Table 2. Predictive factors for quality of bowel preparation independent of colon cleansing agent [8, 11, 15]

Patient-related factors
Age > 65 years
Male sex
History of prior inadequate preparation
Prior colon resection
Comorbidities
Diabetes
Chronic constipation
Stroke disease
Dementia
Low activation
Constipating drugs, e.g. opioids, psychopharmaca
Inpatient status
Low socioeconomic status
Procedure-related factors
Timing of purgative administration
Appointment waiting times
Adherence to bowel preparation instructions
Ingestion of <90% of the preparation

mended by the ESGE to reduce bubbles in the colonic fluid [10]. Predictors of inadequate preparation have been identified; they can be classified as medical- or patient-related, and are listed in table 2 [11, 15]. Language difficulties can also have a considerable impact on preparation [8], an emerging problem in modern societies with a higher degree of immigration. Some authors emphasize the importance of adequate written instruction and activation of patients before preparing for colonoscopy [8, 10]. Others reported a significantly improved quality of colon preparation using an educational video [16]. It may be helpful to offer written instructions in a patient's native language.

New Colonoscopy Methods

Rinsing and Cleaning Systems

Because bowel preparation remains unsatisfactory in a significant proportion of patients, several intraprocedural rinsing and cleaning systems have been developed. The ClearPath System (EasyGlide Ltd., Kfar Truman, Israel) with 4 nozzles for rinsing and a wide channel for suction is mounted on the end of the endoscope. The only available study based on 57 partly prepared porcine colons assessed this technique as an easy-to-perform, effective, and safe method [17]. Another innovation with which the intestine can be flushed during examination is the Med-Jet system (TavTech Ltd., Yehud, Israel). A catheter is advanced through the working channel through which the intestinal wall can be rinsed with CO_2 or water. After use of the system, 18 adenomas and 1 colon cancer hidden behind stool remnants were detected in 11 of a total of 32 patients with incomplete bowel preparation [18]. The JetPrep device is a similar disposable through-the-scope system (JetPrep Ltd., Herzliya, Israel) [19, 20] which allows rinsing of the colon with predefined pressure and flow rates. Another interesting and innovative approach is the liquefying of stool through application of endoluminal ultrasound; however, it yet resides in the phase of an animal model [21]. All these additional systems are naturally more time-consuming, and clinical experience and evaluations in comparison with other procedures are lacking, both as a single and an additional procedure.

Carbon Dioxide Colonoscopy

Insufflation of the bowel with air causes considerable pain and bloating in many patients due to slow absorption and persisting distension. CO_2, however, shows rapid absorption. Several recent studies [22–26] and meta-analyses [27] have demonstrated lower pain, bloating, need for sedation on demand, and stress factors, and a higher degree of comfort during and after colonoscopy. This method is safe [28] and has the potential to improve patient acceptance and patient comfort without time consumption and at a low cost.

Water Colonoscopy

Numerous recent studies and 3 meta-analyses have demonstrated that the instillation of water instead of air while inserting the colonoscope reduces pain, discomfort, and the need for sedation [29–32]. Other advantages are questionable. Data on the detection of adenomas are conflicting [33–36]. Procedure time seems to be higher compared with the usual air insufflation. The cecal intubation rate using water colonoscopy varies between studies and was inferior in a recent review [34]. Finally, there is a learning curve even for experienced colonoscopists [37, 38]. In a study comparing water with CO_2 colonoscopy, water colonoscopy was similar with regard to the required sedation/analgesia [24]. There is a consensus that water colonoscopy has no additional risk. Possible reasons for

the better acceptance are stretching of the sigmoid and flexures, avoidance of loop formation, and, particularly when warm water is used, prevention of colonic spasms. Intensive flushing improves the optical view. Falt et al. [39], however, found no differences regarding cecal intubation rate, procedure time, need of sedation, pain, and adenoma detection between the instillation of cold (20–24 °C) and warm water (37 °C). This might improve the feasibility of water colonoscopy in daily routine.

Two modes of water colonoscopy are distinguished: water exchange, which means removal of the infused water predominantly during insertion; and water immersion, defined as removal of the infused water during withdrawal. The first method is clearly particularized in the editorial of F.W. Leung [40]. Considering different parameters, it seems unclear which method has more advantages [41].

Cap Technology

A transparent (endoscopic submucosal dissection) cap or hood mounted on the tip of the endoscope allows flattening of haustral folds and improves mucosal exposure, particularly behind the flexures or the ileocecal valve. This method, too, comes with no additional risk. Most studies evaluating cap-fitted colonoscopy emphasized better patient comfort [42–44] or shorter time for cecal intubation [42, 43, 45], while others could not confirm these effects [42, 46]. These data did not show an improved cecal intubation rate. More important, however, is the outcome in terms of result quality. Some authors reported a significantly lower miss rate for all adenomas (21 vs. 33%; n = 100) compared with usual colonoscopy [47]. Furthermore, higher adenoma detection (mean number of detected adenomas per procedure 2.0 vs. 1.2; n = 295) was reported [45], but the majority of studies investigating this parameter did not confirm this [42–44, 46] or reported lower adenoma detection [48]. These studies with an inferior or equal result represent a total of 3,684 patients. Thus, the significance of cap-fitted colonoscopy might lie more in facilitating celiac intubation and adenoma resection than better detection.

Administration of Spasmolytics

Hyoscine butylbromide and glucagon have been tested for facilitating colonoscopy and improving the adenoma detection rate. Particularly in a hypercontractile colon, these substances might reduce the amount of air needed for inflation, yield a better endoscopic view, and consequently result in an enhanced polyp detection rate. We have considered 5 recent studies. The first 2 studies could not show benefits in cecal intubation rate, neither for hyoscine butylbromide nor for glucagon [49, 50]. In another study, glucagon reduced cecal intubation time, scores and markers for pain, abdominal fullness, scope manipulation, and stress compared with placebo [51]. 2 of these studies, including a total of 717 patients, reported non-significantly increased adenoma and polyp detection rates, one for the entire study group [52], the other for the subgroups with a moderate to marked degree of colonic spasm only [53]. However, Tamai et al. [51] in their abovementioned trial also observed a non-significantly lower polyp detection rate [51]. Only mild adverse effects have been reported, mainly tachycardia.

The Role of the Endoscopist

As cited above, the adenoma detection rate varies considerably between experienced endoscopists. Finally, we briefly discuss the importance of several endoscopist-related factors which have been discussed in the literature and have led to several proposals and guidelines. Increased attention should be paid to the visualization of the so-called blind zones of the colon, namely the proximal sides of folds, flexures, rectal valves, and behind the ileocecal valve. For this purpose, adequate colonic distension, and perhaps repeated suctioning and cleansing are necessary. The colonoscopist has to take into account the increasing importance of the predominantly right-sided, flat, depressed, and serrated adenomas which when missed may be a reason for occurrence of interval carcinomas. Therefore, Bourke et al. [54] pointed out to 'think flat, depressed, and serrated', due to the observation that many adenomas are not even elevated but flat. Another advice is to examine the right colon twice, particularly when polyps are detected from the cecum to the hepatic flexure. Comparison between the second examination in retroflexion or forward view revealed equal results (miss rate of 33% for both methods) [55].

Three parameters count as key quality indicators: i) cecal intubation rate; ii) withdrawal time; and iii) adenoma detection rate. Another key criterion, of course, is a low rate of complications (see below). A minimum cecal intubation rate of 95% has been demanded for screening colonoscopies, others consider a rate of >90% as an 'acceptable standard' [56]. It is recommended that the time for the withdrawal manoeuver, the phase of intensive diagnostic evaluation of the colonic mucosa, should not fall below 6–10 min, excluding the time needed for biopsies, polypectomy, and additional cleansing. A current publication proposed a withdrawal time of 9 min based on the comprehensive experience from the New Hampshire Colonoscopy Registry with nearly 8,000 colonoscopies [57]. The adenoma detection rate of a colonoscopist should average at least 25% in men older than 50 years and 15% in women older than 50 years at the first screening examination. This depends, of course, on age, gender, race, and a physician's specialty [5].

A minimum volume of procedures is not published as mandatory for successful performance of screening/surveillance colonoscopies, but there are recommendations of >300 colonoscopies per year to be performed by an endoscopist fully trained in colonoscopy, biopsy, and polypectomy [56].

Endoscopic polypectomy should be performed on all polyps or flat lesions detected during colonoscopy with the ex-

Table 3. Complications of screening/surveillance colonoscopy quality improvement targets [3, 58]

Type of complication	Target, %
Incidence of minor sedation reactions, such as unplanned reversal of sedation	<1
Incidence of more serious adverse reactions, such as need for mask ventilation or endotracheal intubation	<0.33
Incidence of perforation by type (mechanical, small polyp, large polyp)	<0.05–0.1
Incidence of postpolypectomy bleeding (immediate and delayed) for cases involving polypectomy[a]	<1

[a]Expected rate varies depending on the volume of the removed large polyps.

ception of hyperplastic polyps in the rectosigmoid. They can be characterized as multiple, small (usually 1–5 mm), pale, sessile lesions [3]. The method of resection depends on site, size, macroscopic pattern, and the personal expertise of the endoscopist. These topics will be presented in detail in other contributions in this issue.

Furthermore, the recovery of the resected specimen is of substantial importance. The histopathologic finding forms the basis for decisions regarding surveillance interval, approach for repeated resection, or surgery. Thus, a good rapport and collaboration between the endoscopist and pathologist are essential.

Regarding the risk-benefit assessment of colonoscopy, we have to consider potential risks including polypectomy or endoscopic resection. Table 3 contains the quality targets for different degrees of colonic intervention. Recently reported complication rates show that these goals can be reached [58–61].

Conclusion

It cannot be emphasized enough that the most important precondition for performing successful colonoscopy with the aim of reducing the morbidity and mortality of CRC through detection and elimination of its precursors is adequate bowel preparation. Additional cleaning and rinsing devices cannot replace cleansing but might be helpful in certain circumstances, e.g. when managing bleeding. Other supportive procedures, such as cap, water-assisted and CO_2 colonoscopy, as well as administration of spasmolytics, are safe, and most investigators are consistent that these methods improve patient comfort and lower pain and abdominal fullness during and after colonoscopy. These procedures may represent the next step towards achieving the goal of unsedated colonoscopy; however, there are conflicting data concerning advantages for adenoma detection. CO_2 insufflation is easy to use (instead of air), incurs low costs, consumes no additional time, and can therefore be recommended for everyday use. Cap-fitted colonoscopy is helpful when complex adenoma resection is anticipated. On the basis of the published data, we have discussed the mentioned methods as single additions to standard colonoscopy. However, it is uncertain how the combination of different methods may work, e.g. installation of water during endoscope insertion and insufflation with CO_2 at withdrawal. The most urgent task remains the improved detection of cancer precursors, particularly of flat, serrated adenomas. The endoscopist has to face this new challenge by on the one hand training his visual skills and attention to these lesions, and on the other hand further mastering demanding resection techniques in a wholesome and safe way.

Disclosure Statement

The authors report no conflicts of interest.

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