Complications during colonoscopy: prevention, diagnosis, and management

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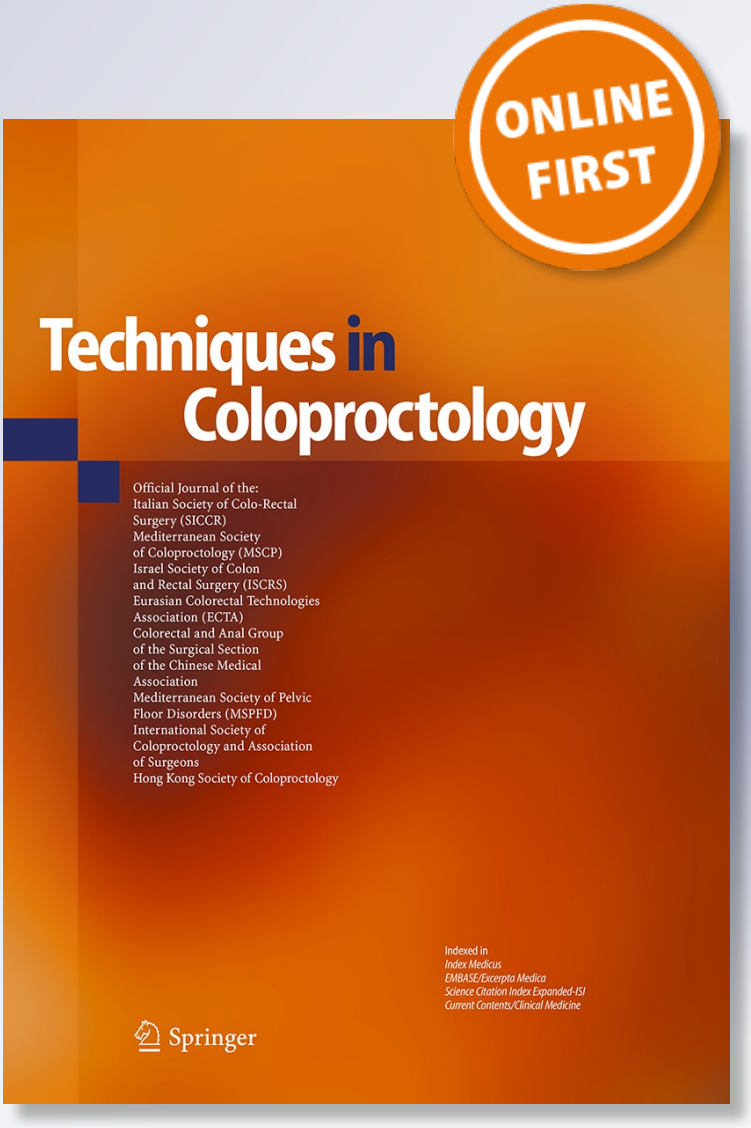

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REVIEW

Complications during colonoscopy: prevention, diagnosis, and management

R. Manta[1] · F. Tremolaterra[2] · A. Arezzo[3] · M. Verra[3] · G. Galloro[4] · L. Dioscoridi[1] · F. Pugliese[1] · A. Zullo[5] · M. Mutignani[1] · G. Bassotti[6]

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Abstract Colonoscopy is largely performed in daily clinical practice for both diagnostic and therapeutic purposes. Although infrequent, different complications may occur during the examination, mostly related to the operative procedures. These complications range from asymptomatic and self-limiting to serious, requiring a prompt medical, endoscopic or surgical intervention. In this review, the complications that may occur during colonoscopy are discussed, with a particular focus on prevention, diagnosis, and therapeutic approaches.

Keywords Colon · Complications · Colonoscopy · Lower endoscopy · Perforation · Bleeding

✉ R. Manta
r.manta@libero.it

[1] Diagnostic and Interventional Digestive Endoscopy Unit, Niguarda Cà-Granda Hospital, Milano, Italy

[2] Digestive Endoscopy Unit, San Carlo Hospital, Potenza, Italy

[3] Department of Surgical Sciences, University of Torino, Torino, Italy

[4] Unit of Surgical Digestive Endoscopy, Department of Clinical Medicine and Surgery, Federico II University of Naples, Naples, Italy

[5] Gastroenterology and Digestive Endoscopy, Nuovo Regina Margherita Hospital, Rome, Italy

[6] Gastroenterology, Hepatology and Digestive Endoscopy Section, Department of Medicine, University of Perugia Medical School, Perugia, Italy

Introduction

Colonoscopy is commonly performed worldwide for diagnosis and treatment of different diseases, as well as for colorectal cancer screening in developed countries. Although colonoscopy is generally safe and well tolerated, particularly when a conscious sedation is performed, nearly one-third of patients complain of transient gastrointestinal symptoms. These include bloating (until to 25 %), abdominal discomfort (10.5 %), diarrhea (6.3 %), nausea (4 %), and self-limiting bleeding (3.8 %) [1–4]. Fortunately, major complications are uncommon. In a systematic review of 12 studies including 57,742 screening colonoscopies, the rate of serious adverse events was found to be as low as 0.28 % [5]. Another study, based on a database of 2.3 million colonoscopies performed between 1997 and 2004, found that a complication requiring hospitalization occurred in 1.9 per 1000 colonoscopies [6]. In addition, >85 % of major complications were observed following an interventional colonoscopy [5]. Of note, a near sevenfold increased risk of bleeding or perforation has been observed following polypectomy [7]. Overall, the procedure-related mortality was reported to be as low as 0.09 % [8]. This review specifically focused on prevention, diagnosis, and therapeutic approaches of colonoscopy-related complications, while those associated with bowel preparation, which is performed before colonoscopy, are available elsewhere [9, 10].

Cardiopulmonary adverse events

Different types of cardiopulmonary adverse events have been described in the literature. Fluctuations in the heart rate and/or oxygen saturation are relatively common, but they are generally mild and probably of minor clinical relevance [11].

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Significant complications are prolonged hypoxia, cardiac arrhythmias, vasovagal syndrome, hyper- or hypotension, and myocardial ischemia [10]. The incidence of these complications varies between 0.2 and 0.5 %, with a mortality rate ranging from 0.03 to 0.05 % [12]. Risk factors predisposing to cardiopulmonary adverse events include advanced age, associated comorbidities (particularly pulmonary diseases), anemia, presence of active bleeding, obesity, long-lasting or emergency procedures, and American Society of Anesthesiologists (ASA) III–IV class [13].

Excessive sedation may cause hypoxemia, aspiration, hypotension, arrhythmias, and vasovagal syndrome. Transient hypoxemia has been described in 0.23 % of cases, while prolonged hypoxemia is extremely rare, the incidence being only 7.8 on 100,000 colonoscopies [14]. It is noteworthy that the association between midazolam and an opioid, such as meperidine, increases the risk of hypoxemia as compared to the use of midazolam as a single agent [12]. Patients with severe chronic obstructive pulmonary disease (COPD) are at increased risk of hypercapnia during colonoscopy. Therefore, sedation in these patients should be appropriately balanced, and the endoscopic examination should be discontinued in case of excessive difficulty in colonoscope progression or excessive pain during the procedure. A review on sedation-related complications, including those occurring with propofol use, has been recently published [15].

Hypotension occurs in 0.48 % of colonoscopies, and it may depend not only on sedation but also on dehydration secondary to bowel preparation [12]. The vasovagal syndrome has been reported to occur in 0.19 % of colonoscopies, and it is maybe the result of a painful intubation, especially in the presence of a short mesosigma or patient anxiety [16]. The most frequent cardiac arrhythmia is sinus tachycardia [17], whereas bradycardia occurs in 0.28 % of cases, and more serious arrhythmias are extremely rare [12, 18].

When a severe disease (such as heart disease or COPD) is present, a careful evaluation of risk by a specialist before colonoscopy may be useful. Appropriate pulse-oximetry monitoring before, during, and after the procedure, and the adoption of minimum effective dose of sedatives, especially in patients with COPD, is mandatory. In addition, if the patient develops vasovagal syndrome or severe hypotension, the procedure should be stopped as should any infusion of fluids or atropine. Similarly, emergency colonoscopies in unstable patients should be avoided to reduce the risk of complications.

Perforation

Undeniably, perforation is the most worrying complication of diagnostic or therapeutic colonoscopy. In diagnostic colonoscopy, a perforation may develop either during or immediately after the examination. The mechanisms involved are mechanical trauma caused by direct pressure from the endoscope against the colon wall (usually in the rectosigmoid segment or in the rectum during the retroflexion maneuver of the endoscope in a small rectum) or barotrauma due to excessive distension of the bowel (usually in the cecal region). Perforations occurring in diagnostic colonoscopies are generally large (>2 cm), while those that occur postoperatively due to thermal injury, such an argon plasma coagulation or electrocautery, are smaller. Both degree and duration of electrocautery play a role [19, 20]. An experimental study on polypectomy in pigs found that the use of tungsten instead of steel snares was significantly associated with a lower depth of tissue injury, suggesting a potential effect on reducing the risk of perforation [21]. The presence of adhesions, severe diverticular disease, mucosal inflammation, stenosis, comorbidities, advanced age, incorrect use of cutting or coagulation current, and limited operator experience are associated with a higher risk of perforation in diagnostic colonoscopies [6, 7, 22–24].

As expected, the incidence of perforation after therapeutic colonoscopy is distinctly higher than after diagnostic colonoscopy, and the risk varies according to the procedure (Table 1). Following standard polypectomy with snare, a perforation develops more frequently when polyps are >1 cm in the right colon or >2 cm in the left colon or when multiple polyps are removed [17, 25]. The mortality rate associated with iatrogenic perforation ranges from 0 to 0.65 % [26]. It has been suggested that an incidence of perforation greater than 1 out of 500 colonoscopies or greater than 1 out of 1000 in screening colonoscopies should prompt an audit for revision of procedures [27].

Perforation may occur during dilation of colonic stenosis, generally performed in Crohn's disease patients in one or more sessions. A systematic review found that a dilation-related perforation in these patients occurred in 13 (2 %) out of 347 cases, and no death plausibly related to pneumatic dilatation was described [28]. Another recent

Table 1 Incidence rates of perforation associated with colonoscopy procedures

Procedure	Perforation (%)
Screening colonoscopy	0.01–0.1
Snare polypectomy	0.17
Endoscopic mucosal resection (EMR)	0–5
Endoscopic submucosal dissection (ESD)	5–10
Anastomotic stricture dilation	0–6
Crohn's disease stricture dilation	0–18
Colonic stent placement	4
Decompressive probe positioning	2

review evaluated data of balloon dilatation of benign rectal anastomotic strictures [29]. Overall, there were 9 (1.1 %) perforations following 850 procedures performed on 405 patients.

Stenting of either neoplastic or benign strictures is another therapeutic procedure potentially causing colon perforation. A recent meta-analysis found that perforation occurred in 207 (7.4 %) out of 4086 patients who underwent colorectal stent placement [30]. Stent type, benign etiology, and bevacizumab therapy were identified as risk factors for perforation following stenting as well as post-procedural reintervention dilation with the stent in situ, while intraprocedural stricture dilation either before or after stent placement was not associated with perforation.

Local mucosal resections, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), are increasingly performed to remove early neoplastic lesions in the colon. A definite risk of complications following these procedures is reported, even in expert hands (Fig. 1a). A meta-analysis of four Japanese studies, with data concerning 566 EMR and 661 ESD procedures, found that procedure-related complications occurred in 37 (5.8 %) and 56 (8.4 %) cases, respectively [31].

Prevention

During the diagnostic phase, colonoscope progression should be performed gently and cautiously, and loop formation should be avoided [32]. When abdominal pain occurs during the examination, alternative maneuvers (ancillary maneuver, compression, decubitus changes) should be used, and when an objective difficulty in progressing is observed, to desist is better than to inflict damage. The use of a pediatric colonoscope (or a standard gastroscope) may facilitate the passage through a substenotic or fixed colonic segment, which may occur in the sigmoid tract with diverticula. A judicious use of air insufflation may reduce the risk of perforation due to a barotrauma, especially in the presence of visceral stenosis [33]. The use of CO_2 or water, instead of air, further minimizes bowel distension, abdominal discomfort, and the risk of perforation [34–36]. However, some studies reported that water use for bowel distension could affect the adenoma detection rate [37, 38].

In the interventional procedures, the diathermy snare must be accurately positioned by promoting the lifting of the mucosa from the underlying muscle. It is also important to limit the amount of tissue included in the loop to a maximum of 2 cm. A prepolypectomy, submucosal injection of saline solution for creating a fluid cushion which separates the mucosa–submucosa layers (lifting) has been found to reduce the risk of electrocoagulative damage of muscularis propria [24]. Special attention should be paid during removal of polyps in the cecal region, where the thin wall may predispose to perforation. The use of mixed current mode may lead to far less deep tissue damage than pure coagulation mode. Some studies reported an increased risk of perforation in the course of small polyp removal with a hot biopsy forceps [39], while a low risk is associated with cold snaring polypectomy [40, 41].

As far as stenting treatment of malignant stenosis is concerned, a higher rate of perforation was reported in patients receiving chemotherapy with bevacizumab [42–44]. Therefore, stent placement in these patients should be discouraged. In addition, dilation of a stenotic area before or after stent placement is not advisable [45]. Similarly, dilation of either tumoral masses or actively inflamed segments in Crohn's disease patients should be avoided [28]. Finally, limited operator experience, i.e., during the learning curve, is associated with an increased risk perforation during EMR or ESD procedures [46, 47].

Diagnosis

Generally, a perforation occurs during or within the first 24 h after the procedure [48–50]. This is an advantage for

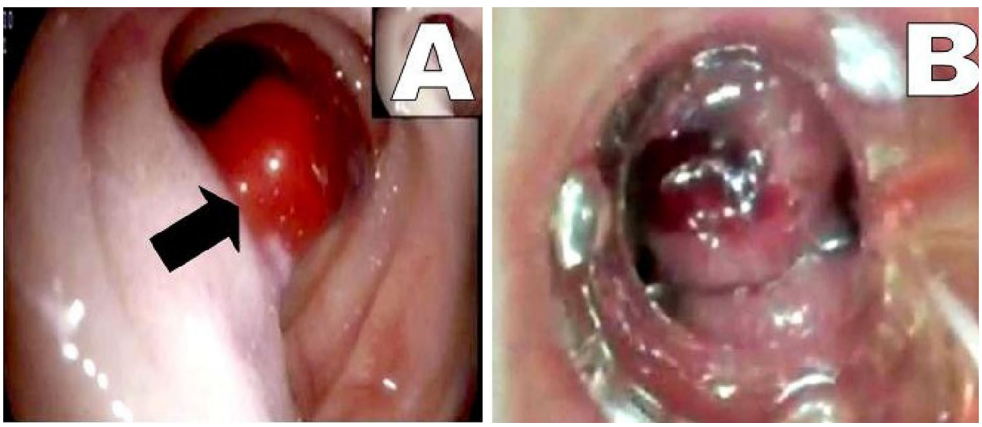

Fig. 1 Postpolypectomy bleeding (*black arrow*) (**a**) and endoscopic treatment with an over-the-scope clip (**b**)

both early detection and prognosis. Indeed, the colon is still clean so that the infection risk is reduced. During colonoscopy, the diagnosis is usually performed by direct vision of the wall defect or, after resection, by the so-called target sign, i.e., evidence of a muscle layer section on the resected lesion. In case of suspicion, an abdominal X-ray (1b) and/or abdominal CT scan (1c), with or without soluble contrast, are indicated. A late perforation should be suspected when abdominal pain, distension, signs of circumscribed peritonitis, fever, and/or leukocytosis occur following the procedure. The onset of generalized peritonitis, sepsis, and hemodynamic instability represents negative prognostic factors [51], requiring urgent surgery. The conventional surgical treatment of perforative complications is associated with a relatively high morbidity (between 5 and 30 %) and mortality [52].

Treatment

The management of colonic perforation depends on several factors, such as the site and characteristics of damage, and the clinical condition of the patient. Endoscopic treatment with endoclip positioning allows the closure of perforations, with a success rate raging from 60 to 100 %, the success being higher in smaller defects [53]. However, a recent case report described a successful closure of a large colonic perforation (30 mm), following an endoscopic resection of a submucosal leiomyoma, by applying seven endoclips [54]. Another device, available since 2007, is the over-the-scope clip (OTSC, Ovesco GmbH, Tuebingen, Germany). This system consists of a nitinol clip shaped as a 'trap' or 'bear trap,' making it possible to include a larger amount of tissue ($\geq$20 mm). In a case series, treatment with OTSC application achieved a success rate of 100 % in 11 patients without a recurrence [55]. A systematic review on OTSC use in gastrointestinal perforations showed a procedural success rate as high as 80–100 %, and a clinical success rate ranging from 57 to 100 %, without major complications [56]. More recent studies showed resolution of perforation in 95 % of cases, as well as in over 80 % of anastomotic leakages, suggesting that OTSC positioning may reduce the need for surgery in several patients [57, 58]. When presence of extraluminal infection is excluded or the cavity is adequately drained by another route, partially or totally covered stents may be used to allow the closure of perforation. However, there is a high probability of stent migration, even in the presence of stenosis, and a potential risk of intolerance or tenesmus in the case of low rectal stent positioning. Finally, the assessment of safety and effectiveness of a novel suturing device, the Overstitch endoscopic suturing device (Apollo Endosurgery, Austin, TX, USA), is ongoing, so that the endoscopist will have another 'ace up his/her sleeve' to repair bowel perforation before resorting to a surgical approach [59, 60].

Bleeding

Bleeding is usually associated with polypectomy or other operative procedures and rarely develops following a diagnostic colonoscopy [61–63] (Fig. 2a). Indeed, the overall rate of bleeding varies from 0.1 to 1 % [1], being distinctly lower following diagnostic or screening examinations without polypectomy (0.2–0.4 %) than following operative colonoscopies with polypectomy (near 1 %) [64]. After polypectomy, bleeding can occur immediately, after a few days (usually 5–7) or even after 3–4 weeks [65]. Basically, the use of cutting or mixed current causes immediate bleeding, whereas pure coagulation current is associated with delayed hemorrhage [66, 67]. However, the use of mixed current far outweighs the risk of immediate bleeding, which is usually easily controlled. Higher rates of immediate (10 %) and delayed (14 %) bleeding were reported following resection of large (>2 cm) polyps, especially in the right colon [3, 20, 68–74]. A retrospective evaluation of 4592 polypectomies showed that for every 1-mm increase in polyp diameter, the risk of hemorrhage increased by 9 % [75]. The role of polyp size in bleeding has also been confirmed in another analysis on 6617 polypectomies performed in Japan [73]. Sessile polyp, multiple polypectomies, unfavorable histology (villous or tubulo-villous histotype), use of anticoagulants or dual antiplatelet therapy, presence of coagulopathy or cardiovascular diseases, and limited experience in operative endoscopy (<80 procedures) are additional risk factors for bleeding [20, 50, 67, 76, 77].

Prevention

The injection of saline or other fluids to dissociate the base of the polyp from the submucosal arterioles is thought to reduce the risk of hemorrhage. Addition of adrenaline in the solution can lower the incidence of immediate bleeding without affecting delayed hemorrhage [78, 79]. The diathermic snare needs to be closed slowly, coagulation current should be used predominantly, and the grip of polypoid tissue in the diathermic snare should not exceed 2 cm. For larger pedunculated polyps, the effectiveness of detachable snare positioning has been demonstrated [80], while the effectiveness of endoclips affixed to the base of the stalk is more controversial [81, 82]. Likewise, the use of hemoclips after polypectomy as bleeding prophylaxis is still a matter of debate [83–85]. Based on the available data, the prophylactic placement of endoscopic clips seems

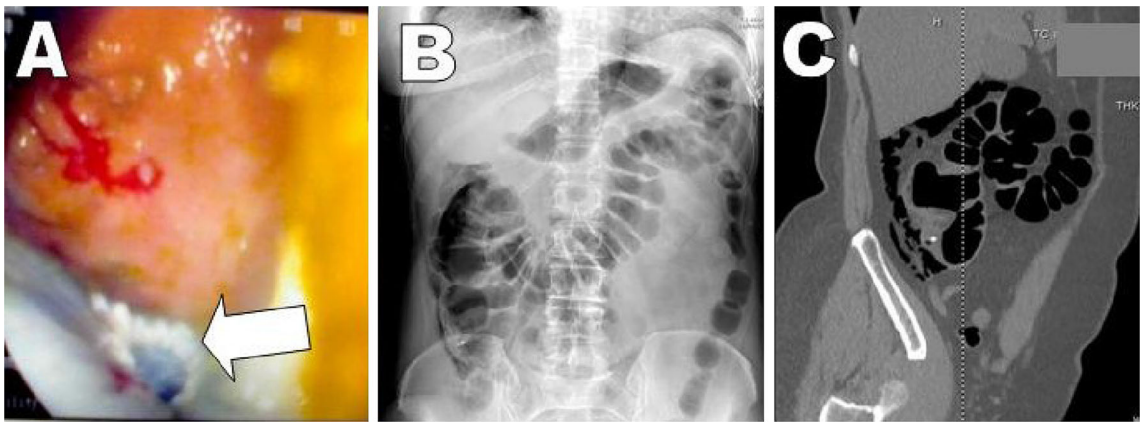

Fig. 2 Postendoscopic mucosal resection (EMR) perforation (*white arrow*) (**a**) with free air in the abdomen on X-ray (**b**) and computed tomography scan (**c**)

to be a cost-effective strategy only for those patients receiving antiplatelet or anticoagulation therapy [86]. However, if the polyp is very large (>2 cm) and positioned proximal to the splenic flexure, application of clips to prevent delayed bleeding could be a prudent approach. For small polyp resection, the use of a mini-snare without electrocautery instead of hot biopsy forceps is recommended [33]. Indeed, polypectomy with hot biopsy causes more submucosal damage, and it is associated with an increased risk of bleeding, especially when used in the right colon [32, 87].

Several studies showed that the use of aspirin is not associated with an increased risk of postpolypectomy bleeding, and therefore, aspirin therapy should not be interrupted for preventive purposes [69, 88]. However, in the presence of polyps at potentially higher risk of complications (for instance very large lesions, right localization), suspension of aspirin taken for primary cardiovascular prevention from 5 days before until 5 days after polypectomy would appear to be a judicious approach. Similarly, the American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommend discontinuation of oral anticoagulants 5 days before the procedure, and replacement with low molecular weight heparin in patients at high risk of thromboembolism [89, 90]. Although warfarin should be reintroduced on the evening of the procedure, a delayed resumption of therapy should be considered, at least for high-risk polypectomies [67].

Diagnosis

The diagnosis of immediate bleeding is usually intraprocedural. The diagnosis of delayed bleeding is made within 48 h in most cases, and it is heralded by the appearance of frank rectal bleeding or by detection of anemia with or without associated systemic symptoms of hemodynamic instability.

Treatment

Bleeding is essentially treated with an endoscopic approach, and surgery should be reserved only for those patients in whom endoscopic hemostasis is not effective. In case of mild bleeding, submucosal injection of adrenaline solution (dilution 1:10,000) can be effective, while in the presence of more severe hemorrhage, especially when the source of bleeding is visible, the application of endoclips ensures an high success rate [91, 92]. It should be considered that in case of bleeding after resection of pedunculated polyps, the stalk can be grasped and held tightly for a few minutes with the same diathermic snare. Then, a detachable snare or endoclips can be easily placed at the base. When massive bleeding after removal of a large and standard endoscopic clips are not sufficient to ensure an adequate compression of a large vessel, the application of an OTSC has been found to be successful without complications [93] (Fig. 2b). Hemostasis with electrocautery should be used with caution, particularly in the ascending colon, due to the increased risk of perforation.

During local mucosal resection (EMR, ESD), when clips may interfere with the procedure, application of monopolar current or bipolar forceps for oozing-type bleeding is particularly useful in the case of arterial bleeding [94]. In case of unsuccessful of endoscopic hemostasis, there is an indication for arterial embolization or surgery.

Postpolypectomy electrocoagulation syndrome

The reported incidence of postpolypectomy syndrome ranges from 0.003 to 0.1 % [1]. It is due to a full-thickness damage of colon wall by electrocoagulation during a polypectomy. The transmural burn reaching the serosa causes localized peritoneal irritation not associated with a radiologically evident perforation [95]. It occurs most

frequently after removal of large sessile polyps or large (>2 cm) lateral spreading tumor (LST), which generally require greater amounts of current [22]. Fasting, intravenous antibiotic therapy, and hospitalization when needed generally resolve the symptoms in a few days. The submucosal injection of large amount of fluids would theoretically minimize the occurrence of this complication. Of note, the accidental capture in the diathermy snare of a portion of the adjacent normal, i.e., without submucosal injection, can cause transmural burn syndrome in the involved area [22].

Infections

Transient bacteremia after a colonoscopy with or without polypectomy occurs in approximately 4 % of cases. However, these events are rarely symptomatic and usually not clinically relevant [96]. Sporadic cases of *Salmonella*, *Klebsiella*, *Enterobacter*, *Serratia*, and hepatitis B and C virus transmission have been described in the literature [97, 98], generally associated with an accidentally ineffective reprocessing of colonoscope. A recent review established that almost all cases of infection after colonoscopy are the consequence of defective endoscope cleaning or poor adherence to the procedures recommended in the guidelines [99, 100]. As a result, the only way to reduce the infection risk is a careful observation of standard cleaning procedures [94, 101].

Neither the American Heart Association nor the ASGE recommends antibiotic prophylaxis prior to colonoscopy in routine practice [94, 102]. However, sporadic cases of endocarditis have been described [103], so that prophylaxis in high-risk patients, such as those with prosthetic heart valves or previous endocarditis, would be appropriate. The decision should be performed on a case-by-case basis with the cooperation of a cardiologist [97].

Gas explosion

Large bowel explosions during colonoscopy have been reported only rarely but, as expected, with serious consequences. Indeed, a review of 9 cases reported 8 colonic perforations and 1 death following bowel explosion [104]. Explosion occurs when the concentration of hydrogen or methane in the colon is so high that the electrocautery energy used during an operative procedure may trigger the combustion in the presence of oxygen. The use of non-absorbable sugars, such as mannitol, lactulose, and sorbitol, for bowel preparation is an additional contributing factor [105, 106]. Similarly, an inadequate cleaning of the colon, particularly when only enemas are used as in the case of rectosigmoidoscopies, may predispose to the colon explosion during an operative procedure [107]. As a preventive measure, insufflation with CO_2, instead of air, has been proposed [108].

Miscellaneous complications

Rare complications of colonoscopy include hematoma or rupture of the spleen [109], acute appendicitis [110], ischemic colitis [111], and strangulation of hernias [112]. Chemical colitis due to glutaraldehyde has been also reported, when it used for sterilization and the endoscope was not properly rinsed, requiring hospitalization in some cases [113]. Chemical colitis due to peracetic acid has been also described, but it is generally self-limiting, and without consequence for the patient [114].

Conclusions

Colonoscopy has an important diagnostic and therapeutic role in the management of many colonic diseases. Its use in colorectal cancer screening has been implemented in several developed countries. Therefore, thousands of colonoscopies are performed every day worldwide. Although colonoscopy is generally a safe procedure, some adverse events and complications may occur. The knowledge of different complications, their estimated frequency, and the risk factors involved are crucial for early diagnosis and management in order to reduce the risks for the patient and to improve the quality of colonoscopy.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent In this article no participants were included.

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