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Complications of Colonoscopy

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1. Introduction

Colonoscopy is a common procedure in medical practice for a variety of gastrointestinal indications. It is widely used in the United States, especially since 2001, when Medicare expanded its coverage for screening for colorectal cancer to include colonoscopy. An estimated 14.2 million colonoscopies were performed in 2002 in the United States, with screening indications representing half of cases [1]. Although generally considered a safe procedure, complications of colonoscopy as an invasive procedure should be noted. Complications vary from minor symptoms such as minor abdominal discomfort to more serious complications such as colonic perforation, cardiopulmonary arrest, or even death (Table). Although most studies have focused on serious complications, the less serious complications are important because they are more frequent than reported and may have an impact on willingness of patients and their peers to undergo future colonoscopy. Colonoscopy complications are categorized as immediate; occurring during the procedure or before discharge from endoscopy unit, or delayed; occurring within 30 days of the procedure. We will present in this chapter these potential complications in detail.

2. Complications of colonoscopy

2.1. Death

Death has been reported as a complication of colonoscopy in 30 days from the procedure. Its rate varies between studies from 0 to 83.3 per 10,000 colonoscopies [2-15]. In 3 studies with a total of 16,747 patients of mean age 59 years, there was no single death within 30 days of colonoscopy [6-8]. In a study in outpatient colonoscopy in the Medicare population by using Surveillance,

Epidemiology and End Result (SEER) database, there were 53 deaths within 30 days of 53,220 patients (9.9 deaths per 10,000 colonoscopies) [2]. The main focus in that study was not the death rate but the serious gastrointestinal and cardiopulmonary events which increased with advance age, history of stroke, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), atrial fibrillation, diabetes mellitus (DM), and use of polypectomy.

Most deaths are not related directly to the procedure itself, rather to severe underlying comorbidities such as CHF, severe underlying coronary artery disease, COPD, cirrhosis, stroke, and pneumonia [3,4,11]. In a study of 9,223 patients from the UK, there were 10 deaths within 30 days of procedure (10.8 deaths per 10,000 colonoscopies); however, four cases were considered to be due to severe comorbidities rather than the procedure itself [4]. The mean age of study population was 58 years (range: 16-95 years) with 14.1% were 75 years or older. The reported causes of death were pneumonia, CHF, myocardial infarction, stroke and cirrhosis [4]. In a study of 13,580 patients, one single death occurred during colonoscopy in patient with massive GI bleeding (0.7 deaths per 10,000 colonoscopies) [5]. One single death occurred in 26,162 colonoscopies in another study done by Tran (0.38 deaths per 10,000 colonoscopies) which occurred in a patient with underlying coronary artery disease and COPD who developed perforation and died postoperatively from myocardial ischemia [11].

Polypectomy has been shown to be an independent risk factor for death. In a study from Germany with 82,416 colonoscopies, death rate was 0.1 per 10,000 colonoscopies, which was 7-fold higher if polypectomy was performed [9].

However, the mortality rate was as high as 83.3 deaths per 10,000 colonoscopies in an Australian study of 23,508 outpatients with 196 deaths within 30 days of the procedure, although only 3 deaths were attributed to the colonoscopy itself (1.2 deaths per 10,000 colonoscopies) [13]. In a 2010 review of complications of colonoscopy from large studies, there were 128 deaths attributed to colonoscopy among 371,099 colonoscopies (3.4 deaths per 10,000 colonoscopies) [14,15].

2.2. Cardiopulmonary complications

Cardiopulmonary complications may be related to the preparation, conscious sedation, or the procedure itself. It might occur during or immediately after the procedure, including respiratory depression, hypoxia, dyspnea, hypotension, hypertension, bradycardia, tachycardia, vasovagal reactions, cardiac arrhythmias, and chest pain. Most of these events occur at endoscopy unit; however, they may occur days after the procedure. Fortunately, most of these complications are self-limited and resolve with minor interventions. In a study of 21,375 patients by Ko, et al. there were 160 cases of respiratory depression (74.8 per 10,000 colonoscopies) [3]. Also in this study, there were 105 cases of immediate cardiovascular complications (49.1 per 10,000 colonoscopies), with the vast majority being hypotension (65 cases; 30.4 per 10,000 colonoscopies) and bradycardia (32 cases; 14.9 per 10,000 colonoscopies). Vasovagal reaction occurred in 14 cases (6.5 per 10,000 colonoscopies), tachycardia in 2 cases (0.9 per 10,000 colonoscopies), and hypertension in one case (0.4 per 10,000 colonoscopies). One hundred and thirty four cases required supplemental oxygen (62.6 per 10,000 colonoscopies), 48 cases intravenous fluids (22.4 per 10,000 colonoscopies), 29 cases nalox-

one (13.5 per 10,000 colonoscopies), 20 cases atropine (9.3 per 10,000 colonoscopies), and 16 cases required flumazenil (7.4 per 10,000 colonoscopies).

Complications	Rate of complications (cases per 10,000 colonoscopies)
Death	0-83.3
Cardiopulmonary events	
Hypotension	0.2-48
Hypertension	0.4-2.1
Vasovagal reaction	6.5-19
Arrhythmia	1.9-102
Bradycardia	0.3-28
Tachycardia	0.7-0.9
Chest pain	0.7-45.2
Pulmonary edema	0.2-57.3
Transient hypoxia	0.8-23
Respiratory depression	0.7-74.8
Perforation	0.4-19
Bleeding	8.5-63.8
Postpolypectomy electrocoagulation syndrome	0.3-9.3
Gas explosion	Case reports in the literature
Infections	
Bacterial endocarditis	Case reports in the literature
Acute diverticulitis	0.8-8.4
Pneumonia	0.4-0.9
Per-perineum infections	0.9-3.1
Minor GI symptoms	133.1-4100
Cerebrovascular events	0.8-6.5

Table 1. Rate of complications of colonoscopy

In a retrospective study of 174,255 colonoscopies in the Clinical Outcomes Research Initiative (CORI) database, there were 1995 unplanned cardiopulmonary events (114.4 per 10,000 colonoscopies) which were significantly higher than in EGD [16]. Hypotension occurred in 867 cases (48 per 10,000 colonoscopies), bradycardia in 507 cases (28 per 10,000 colonoscopies), vasovagal reaction in 341 cases (19 per 10,000 colonoscopies), transient hypoxia in 410 (23 per 10,000 colonoscopies), low oxygen saturation in 128 (7 per 10,000 colonoscopies),

prolonged hypoxia in 14 cases (0.7 per 10,000 colonoscopies), hypertension in 38 cases (2.1 per 10,000 colonoscopies), arrhythmia in 34 cases (1.9 per 10,000 colonoscopies), chest pain in 14 cases (0.7 per 10,000 colonoscopies), respiratory distress in 13 cases (0.7 per 10,000 colonoscopies), tachycardia in 13 cases (0.7 per 10,000 colonoscopies), pulmonary edema in 4 cases (0.2 per 10,000 colonoscopies), wheezing in 3 cases (0.1 per 10,000 colonoscopies), and tracheal compression in one case (0.05 per 10,000 colonoscopies) [16]. The risk factors were advanced age, high *American Society of Anesthesiologists* (ASA) class, inpatient status, trainee participation, and non-university and veterans hospitals [16].

Higher doses of meperidine required for colonoscopy were associated with higher cardiopulmonary events, whereas there was an inverse association with doses of fentanyl and midazolam in the study by Sharma [16]. The association between lower dose of benzodiazepines use in endoscopy and cardiopulmonary events was suggested first in a small earlier study [17]. Droperidol has been used effectively for conscious sedation in difficult endoscopy, but has notable potential complications including QT prolongation and torsade de pointes. In one study, the use of droperidol for conscious sedation was not associated with increased cardiopulmonary events [16].

In a study of 53,220 outpatient colonoscopies in the Medicare population using the SEER database and diagnosis coding system, there were total of 1030 cardiovascular events (193.5 per 10,000 colonoscopies) with arrhythmias comprised more than half events which were statistically significant than matched group [2]. There were 241 cases of acute coronary syndrome and 115 cases of cardiopulmonary arrest in 30 days which was not statistically significant from matched group. Advanced age, polypectomy during procedure, CHF, atrial fibrillation, DM, COPD, and stroke were the independent risk factors for adverse cardiovascular events [2]. It has been shown that life expectancy decreases significantly for patients with 3 or more chronic conditions at the time of colon cancer diagnosis, illustrating importance of considering chronic comorbidities in elderly patients when evaluating for screening colonoscopy [18].

In a study of 82,416 colonoscopies from Germany, there were 12 cases of cardiopulmonary complications during the procedure (1.4 per 10,000 colonoscopies); oxygen desaturation in 7 cases (0.8 per 10,000 colonoscopies) which were treated by oxygen supplement or flumazenil, bradycardia in 3 cases (0.3 per 10,000 colonoscopies) which were treated by atropine, and hypotension in 2 cases (0.2 per 10,000 colonoscopies) which were treated by intravenous fluids [9]. Most of these complications occurred in patients received the combination of benzodiazepines with opioids, whereas no cardiopulmonary event was recorded when use propofol [9].

Appropriate evaluation for anesthesia risk, identifying high-risk patients, consulting other specialties based on their comorbidities, and appropriate monitoring before, during and after the procedure may reduce the rate of cardiopulmonary complications.

2.3. Perforation

Colonic perforation may occur due to therapeutic endoscopic interventions, barotrauma due to air insufflation during colonoscopy, mechanical forces against colon wall, or during maneuvering of the scope. Persistent abdominal pain after colonoscopy and abdominal disten-

sion may present initially, however a late presentation with abdominal abscess is possible. Although plain X-Rays may reveal sub-diaphragmatic free air, CT scan is more sensitive to detect any free air in the abdomen and pelvis which should be considered in cases with high suspicion of perforation. The rate of perforation varies between studies from 0.4-19 cases per 10,000 colonoscopies.

There were 4 cases of perforation in a study of 82,416 colonoscopies without polypectomy (0.4 per 10,000 colonoscopies), but it was 14 times higher if polypectomy was performed during the procedure (6.3 per 10,000 colonoscopies) [9]. Although the majority of polypectomy was done in the left colon, half of the perforations after polypectomy occurred in the right colon [9].

In another study of 21,375 patients, there were 4 cases of perforation (1.8 per 10,000 colonoscopies); all of them female, two occurred without biopsy or polypectomy [3]. The risk of serious complications including perforation, GI bleeding, post-polypectomy syndrome and diverticulitis (all combined) increased with pre-procedure warfarin use and performance of polypectomy with cautery [3].

In a population-based cohort study of 67,632 colonoscopies performed in persons between 50-75 years of age, there were 37 cases of perforation (5.4 per 10,000 colonoscopies); 57% were detected on the day of procedure, 92% within 2 days, and all within 5 days [19]. In 62% of these cases snare polypectomy was performed. The median length of stay was 6 days (0-18), comparing to 2 days (0-15) when GI bleeding occurred as a complication of colonoscopy. Although 68% of them underwent surgery; one of them died after hemicolectomy, 32% were treated conservatively without mortality [19].

In a study of 53,220 Medicare beneficiaries (age 66-95 years) who had outpatient colonoscopy, there were 33 cases of perforation (6.2 per 10,000 colonoscopies) with 21 cases of them (63.6%) underwent polypectomy [2]. The independent risk factors for serious gastrointestinal complications including perforation and GI bleeding were advanced age, DM, CHF, COPD, atrial fibrillation, stroke, and performing polypectomy [2].

A study from the UK with 9,223 pediatric and adult patients, there were 12 cases of perforation (13 per 10,000 colonoscopies); half of them diagnosed at the time of colonoscopy, another two before discharge from the unit, and the rest presented 1, 7, 16, and 24 days after the procedure [4]. Four of the perforations followed biopsy or polypectomy from 1841 patients underwent any kind of therapeutic or diagnostic interventions (21.7 per 10,000 colonoscopies).

There were 15 cases of perforation in a study of 16,318 patients (9.1 per 10,000 colonoscopies); 12 cases either had biopsy or polypectomy (80%) [12]. The rate of serious complications (including perforation, bleeding, diverticulitis, postpolypectomy syndrome; all combined) after removal of polyps larger than 10 mm was significantly higher than in those with removal of smaller polyps. All perforations were detected in 7 days of the procedure. The risk factors were increasing age, female gender, and polypectomy.

In a large retrospective cohort study of 277,434 patients, 228 cases of perforation occurred (8.2 per 10,000 colonoscopies) [20]. The predictors for perforation were advanced age, ob-

struction as an indication for the colonoscopy, significant comorbidities, and performance of invasive interventions during the procedure.

In an Australian study of 23,508 patients over 10 years, there were 23 perforations (9.7 per 10,000 colonoscopies), 78% occurred with a mucosal intervention (hot snare polypectomy) [13]. The rectosigmoid was the most common site of perforation, followed by the cecum. Surgical intervention was performed in 83%, and one death occurred. Median time to diagnosis was 1 day (0-5 days) with length of hospitalization stay 8 days (3-26 days).

The sigmoid colon is probably susceptible to perforation due to the mechanical forces on the sigmoid during colonoscopy, the common occurrence of diverticular disease in sigmoid, and frequency of colonic polyps in this area. The relatively thin-walled right colon is more predisposed to barotrauma and thermal injury during polypectomy.

Twenty cases of perforation occurred in a study of 10,486 patients (19 per 10,000 colonoscopies); 65% in sigmoid colon and 25% in cecum [10]. Comparing to flexible sigmoidoscopy, there were only two cases of perforation in 49,501 sigmoidoscopies (0.4 per 10,000 sigmoidoscopies). Although most of perforations (91%) detected in 2 days of colonoscopy, 9% presented after 2 weeks with abdominal abscess. All patients except an 87 year old who died underwent surgery with 37% required only simple closure without any resection. The average length of stay was 7.7 ± 2.8 days. Female gender was an independent risk factor for perforation. Transmural electrocautery burns (36%), mechanical injury (32%) from the tip and shaft of scope, and barotrauma (5%) were the main mechanisms of perforation [10]. Defects caused by diagnostic intervention tend to be larger than those caused by electrocautery injury.

Perforations occurring more often in female which may be due to frequency of pelvic surgery in females, diverticular disease, or the higher likelihood of looping because of longer colonic lengths [3,10,21].

In a large study of 116,000 patients underwent colonoscopy at ambulatory centers, 37 cases of perforation occurred (3.1 per 10,000 colonoscopies); most of them female (73%), 49% had diverticular disease, 54% had history of pelvic or colon surgery [21]. Sigmoid colon was the most common site of perforation (62%) then ascending colon (16%). The time to diagnosis ranged from immediate (29 patients) to 3 days (8 patients). Surgery was performed in 95%, and conservative treatment in the rest. No mortality occurred.

Although surgery consultation should be obtained in any case of perforation, conservative treatment with bowel rest, hydration, and intravenous antibiotics has been increasingly used in selected cases [5,19,21]. There are also case reports revealing successful closure with endoscopic clips to repair perforations [22].

In a study of 97,091 outpatient colonoscopies, the rate of perforation was 8.5 per 10,000 colonoscopies. The risk factors for colonoscopy-related perforation were older age, increased comorbidity score, polypectomy, and low-volume endoscopists (when perforation combined with bleeding) [23]. However, this finding was different from a study by Wexner which showed neither an absolute number of prior colonoscopies, nor any ongoing annual experi-

ence affected the serious complication rates [5]. Also Ko and colleagues did not find any relation between complication rate and annual colonoscopy volume, trainee participation, or practice setting [3].

Preventative measures to avoid perforation have been suggested, including decreasing the risk of barotrauma by minimal air insufflation, minimizing loop formation, encouraging the use of cold techniques in the removal of small polyps, and injection of saline into the submucosa for removal of flat or sessile polyps [14,15].

2.4. Bleeding

Colonic bleeding is the most common serious complication following colonoscopy. Although it may occur after diagnostic procedure, it mostly follows therapeutic colonoscopy from either biopsy or polypectomy, and can be immediate or delayed up to several weeks after colonoscopy.

In a population-based study of 97,091 patients aged 50-75 years, bleeding rate within 30 days was 16.4 per 10,000 outpatient colonoscopies. The independent risk factors for colonoscopy-related bleeding were older age, male gender, polypectomy, and low-volume endoscopists [23].

In another population-based, matched cohort study of 53,220 Medicare patients of age 66-95 years, there were 340 cases of GI bleeding (63.8 per 10,000 outpatient colonoscopies) which was significantly higher than matched group [2]. The risk of bleeding was 4 times higher when polypectomy was performed (21 bleeding episodes per 10,000 colonoscopies without polypectomy compared to 87 per 10,000 colonoscopies with polypectomy). Older age, history of COPD, CHF, atrial fibrillation, and stroke were other independent risk factors for serious GI events (bleeding and perforation) [2].

In a study of 23,508 patients, 49 cases of GI bleeding occurred (20.8 cases per 10,000 colonoscopies); all cases associated with biopsy or polypectomy, median time to presentation with bleeding was 6 days (0-14 days), and length of stay was 2 days (1-18 days) [13]. No death was contributed to bleeding, none required surgery, colonoscopic interventions was performed in 4 cases (8%), and blood transfusion in 7 cases (14%) [13].

Use of aspirin or any other non-steroidal anti-inflammatory drugs (NSAIDs) alone does not increase risk of postpolypectomy bleeding. Thus, the American Society for Gastrointestinal Endoscopy (ASGE) recommends continuing aspirin and NSAIDs if one of them is used alone and if its use is necessary [24-27]. However, there is some evidence that combination of aspirin with one or more NSAIDs may increase the risk of bleeding after polypectomy; therefore discontinuation of NSAIDs 2-3 days before polypectomy is recommended in patients receiving aspirin [24-27]. Also, use of clopidogrel alone does not increase risk of postpolypectomy bleeding; however, concomitant use of aspirin or any other NSAIDs increases the risk of bleeding [3,24,25,28].

Pre-procedure warfarin use increases risk of bleeding after colonoscopy, thus discontinuation of warfarin is recommended 3-5 days before colonoscopy, however bridging with hepa-

rin or its equivalents is important in high risk patients for thrombosis such as a mechanical cardiac valve [3,14,24,25,29].

A prospective cohort study of 21,375 patients of age over 40 years using CORI database, there were 34 cases of GI bleeding requiring hospitalization within 30 days following colonoscopy (15.9 per 10,000 colonoscopies), and half of them required blood transfusion [3]. Pre-procedure warfarin use and snare polypectomy with cautery had an increased risk of serious complications. Risk increased even further if more than one polypectomy with cautery was done.

Size of resected polyps, number of polyps removed, and histology type of polyps have been reported as increased risk factors for postpolypectomy bleeding [3,28-30].

Management of bleeding detected during colonoscopy can be performed with endoscopic approach; however, delayed bleeding is managed conservatively with bowel rest, intravenous hydration and blood transfusion if required. Repeat colonoscopy is often required for hemostasis. Angiographic embolization and surgery are preserved for selected cases with massive, severe, persistent bleeding [3,15,31]. However, many cases of bleeding are minimal and self-limited.

Twenty one cases of bleeding occurred within 30 days in a study of 24,509 patients aged 16 years or older who underwent lower GI endoscopy including colonoscopy and sigmoidoscopy (8.5 per 10,000 colonoscopies) [31]. Seven of them required blood transfusion, 15 required repeat endoscopy and 2 required laparotomy. The average time to present was 6 days (0-16 days).

Some measures suggested to decrease the bleeding rate after polypectomy including use of cold snare instead of hot biopsy forceps, prophylactic use of mechanical methods such as clips and detachable snare loops, and injection of epinephrine into submucosa of large sessile polyps [14,15,32].

2.5. Postpolypectomy electrocoagulation syndrome

Postpolypectomy syndrome results from electrocoagulation injury to the bowel wall when electrocautery is used which causes transmural burn and focal peritoneal inflammation without radiologic evidence of frank colonic perforation. It is characterized by severe localized abdominal pain, fever, localized peritonitis signs, and leukocytosis without any radiologic evidence of perforation. Patients usually present within 1-5 days after colonoscopy performed with electrocautery polypectomy. The rate of this syndrome varies from 0.3 to 9.3 cases per 10,000 colonoscopies, depending on differences in defining this syndrome [12,14,15,31].

In a study of 16,318 patients aged 40 years or older, 6 cases of postpolypectomy syndrome occurred in 11,083 colonoscopies with biopsy performed (5.4 cases per 10,000 colonoscopies) [12].

The recognition of postpolypectomy syndrome is of importance because it does not require surgical treatment as frank perforation. The diagnosis can be made by CT scan in the appro-

priate clinical scenario which shows focal thickening of the colonic wall at a polypectomy site with peri-colonic fat stranding [33]. The treatment is conservative, including bowel rest, intravenous hydration and antibiotics [15,33]. Outpatient management with oral antibiotics also has been reported [12].

Postpolypectomy syndrome occurs more often with resection of large sessile polyps when prolonged, high thermal energy is applied. Therefore saline injection into the sub mucosa of large sessile polyps before polypectomy may decrease the rate of this complication [33].

2.6. Gas explosion

Gas explosion during colonoscopy is rare but has potential life-threatening consequences including death. It triggers when three elements are available in the colon lumen: high level of combustible gases such as hydrogen and methane produced by fermentation of non-absorbable carbohydrates by colonic flora, high level of oxygen, and electrical energy that produces heat such as electrocautery and argon plasma coagulation [15,34,35]. High levels of hydrogen and methane are produced in the colonic lumen by fermentation of non-absorbable carbohydrates (lactulose, mannitol) or incompletely absorbed carbohydrates (lactose, fructose, sorbitol) by the colonic bacteria, or the presence of stool in the colonic lumen due to poor cleansing preparation or using enema for sigmoidoscopy [15,34-38]. In a review in 2007 searching from 1952-2006, there were only ten cases reported in the literature including one case from the reviewer [15,34]. Most of cases caused colonic perforation with one death. Bowel preparation using manitol which is rarely used in current practice for colonic cleansing, using cleansing solutions containing sorbitol, or using enemas containing no fermentable agents were participating factors for gas explosions [34]. Newer bowel preparation solutions such as polyethylene glycol (PEG) and sodium phosphate are safer for electrocautery and argon plasma coagulation by not producing inflammable levels of hydrogen and methane. Using argon plasma coagulation during sigmoidoscopy following enemas carries risk for gas explosion which should only be performed after complete colonic preparation with new solutions not containing manitol or sorbitol. It has been suggested using frequent air insufflation and suction before performing these procedures, using carbon dioxide during colonoscopy, and using oral antibiotics to decrease combustible levels of hydrogen and methane in colonic lumen when using manitol or sorbitol [15,35-37].

2.7. Acute diverticulitis

Acute diverticulitis is another potential complication of colonoscopy. It is caused by microscopic perforation of the colon which may develop following colonoscopy in persons with pre-existing diverticulosis due to barotrauma or mechanical forces from the endoscope. Acute diverticulitis following colonoscopy has been poorly investigated and infrequently mentioned in studies reporting other complications of colonoscopy. The rate of diverticulitis as a complication of colonoscopy has been reported from 0.8 to 8.4 cases per 10,000 colonoscopies [3,12,14,31].

In a study of 16,318 patients aged 40 years or older, there were 6 cases of diverticulitis within 30 days of colonoscopy (3.6 cases per 10,000 colonoscopies); 2 cases required surgery and the rest were treated conservatively, 5 of them developed in colonoscopy with biopsy performed [12].

In another study of 21,375 patients aged 40 or older, there were 18 cases of diverticulitis within 30 days of colonoscopy (8.4 per 10,000 colonoscopies) with majority did not require hospitalization [3]. The risk factors for serious GI complications (perforation, bleeding, postpolypectomy syndrome, and diverticulitis) were prior warfarin use, and polypectomy with cautery; however, these risks were not individualized to each complication but all combined [3].

In third study of 24,509 outpatients who underwent colonoscopy or sigmoidoscopy, there 2 cases of acute diverticulitis within 30 days of colonoscopy (0.8 per 10,000 colonoscopies) [31].

2.8. Infection

Transient bacteremia can occur during and after colonoscopy due to bacterial translocation of normal colonic flora to blood stream. Then these bacteria may potentially adhere to distant tissue such as endocardium and artificial devices, however clinical infections are rare. Transient bacteremia associated with colonoscopy occurs in average of 4.4% ranging from 0-25% [24,39,40]. However, harmless transient bacteremia occurs in some daily activities such as tooth brushing in 23-68% [24,39,41]. These isolated bacteria during colonoscopy are generally believed to have little potential to cause endocarditis. The most common isolated organisms are normal skin flora which could contamination during blood draw [24,42,43]. Despite more than 14 million colonoscopies are performed each year in the United States, there have been only 15 reported cases of infectious endocarditis with temporal relation with colonoscopy; thus, potential side effects of prophylactic antibiotic outweigh their possible benefit of preventing endocarditis [24,39,44]. Due to the lack of convincing evidence of risk of endocarditis, both the American Heart Association (AHA) and ASGE have revised their recommendations against prophylactic antibiotics before colonoscopy [39,44].

In cirrhotic patients with or without ascites in the absence of acute GI bleeding who undergo colonoscopy, the risk of bacteremia is low. In a study of 58 cirrhotic patients who underwent colonoscopy, there were 4 cases of positive blood culture (6.9%) without in development of infections [42].

Patients on peritoneal dialysis may be at risk for infectious complications after colonoscopy. There are several reported cases of peritonitis in patients on peritoneal dialysis after colonoscopy especially postpolypectomy [45,46]. The International Society for Peritoneal Dialysis (ISPD) in 2005 recommended prophylactic antibiotics and emptying the peritoneal fluid before colonoscopy; however 2010 ISPD recommendations did not address these prevention strategies [47,48].

Infections in prosthetic joints has been reported after colonoscopy, however the risk is too low which led ASGE to recommend against using prophylactic antibiotics for patients who have prosthetic orthopedic devices undergoing colonoscopy [39,49,50].

Acute appendicitis following colonoscopy has been described in the literature. In a review in 2008, there were only 12 cases reported in literature from 1985 to 2007 [51]. Pre-existing sub-clinical disease of the appendix, barotrauma, impaction of stool into the appendix, direct intubation of appendiceal lumen, and focal edema in appendiceal orifice from trauma leading to obstruction are proposed mechanisms of acute appendicitis after colonoscopy [51].

Pneumonia within 30 days of colonoscopy has been reported. In a study of 21,375 patients, there were 2 cases of pneumonia within 30 days of colonoscopy (0.9 cases per 10,000 colonoscopies) [3]. Another study of 24,509 patients, 1 case of pneumonia developed in 30 days of colonoscopy (0.4 per 10,000 colonoscopies) [31]. The mechanism is mostly aspiration secondary to sedation and anesthesia more than related to the procedure itself.

Local infections in perineum including perianal abscess and Fournier's gangrene have been described following colonoscopy. In a study of 3,196 patients, there was one case of Fournier's gangrene occurring 2 days after colonoscopy (3.1 cases per 10,000 colonoscopies) [6]. In another study of 21,375 patients, 2 cases of perirectal abscess occurred during 30 days of colonoscopy (0.9 per 10,000 colonoscopies) [3]. The mechanism is local mechanical trauma to the perineum area during the procedure.

2.9. Abdominal pain and other minor GI symptoms

Although abdominal pain can be the symptom of above mentioned serious complications, less severe abdominal discomfort is more common following colonoscopy. The mechanism is multifactorial including mechanical trauma, barotrauma, gaseous distension secondary to air insufflation. It is usually self-limited and rarely required hospitalization; however it is of importance because it may affect the adherence for any future surveillance colonoscopy. In a study by Ko et al. there were 5 cases of abdominal pain requiring hospitalization (2.3 cases per 10,000 colonoscopies) [3]. In a study of 53,220 patients, abdominal pain occurred in 176 patients (33 cases per 10,000 colonoscopies), paralytic ileus in 172 patients (32.3 cases per 10,000 colonoscopies), and nausea and vomiting in 361 patients (67.8 cases per 10,000 colonoscopies) which all were significantly higher compared to the matched group [2]. The risk of these symptoms was higher if polypectomy was performed.

Minor adverse events that defined as any health problem that patient experienced in 30 days of colonoscopy not requiring a hospital visit were reported in telephone interview in 466 patients of a study of 1,528 patients (41%) with majority were GI symptoms including 195 cases of abdominal discomfort, 64 cases of self-limited rectal bleeding which lasted 1-3 days, 6 cases of nausea, and 62 cases of change in bowel habits including diarrhea (n=20), constipation (n=11), flatulence (n=8), fecal incontinence (n=3), fecal urgency (n=3), and mucus discharge (n=2) [8]. There were also 2 cases of severe abdominal pain that required hospitalization. Among the patients who were not retired and reported minor adverse events, 26.1% missed one extra day of work after the day of procedure, 5.9% missed 2 days beside the day of colonoscopy, and 8.8% missed 3 days or more [8].

Minor complications occurred in 162 subjects (34%) in a prospective cohort study by Ko et al. most commonly bloating (25%) and abdominal pain (11%) [52]. Minor adverse events

were more common in women, and when the procedure lasted 20 minutes or longer. Colonic preparation was reported by patients as the most difficult part of the procedure in 77%. Most patients (94%) missed 2 or fewer days from normal activities for the preparation, procedure itself, or recovery [52].

These minor adverse events have 3 aspects of effect; they are inconvenience to patients, have indirect cost by missing work, and can affect the willingness of patients to undergo any further colonoscopy in future if need it.

Reducing looping of the endoscope and minimizing air insufflation may decrease some of these symptoms [53]. It has been also suggested using carbon dioxide, which is rapidly absorbed and excreted through lungs, as an insufflating gas for colonoscopy to reduce these symptoms [54,55]. Also water immersion technique instead of air insufflation has been proposed to reduce these minor events especially in cases of minimal sedation [56] (Leung 2010).

2.10. Miscellaneous

The most serious miscellaneous complications have reported within 30 days of colonoscopy are cerebrovascular accident (CVA), transient ischemic attack (TIA), and pulmonary embolisms which most likely related to temporary cessation of anticoagulation agents and antiplatelet medications peri-procedure period [3,6-8,13].

Stroke or TIA occurred within 30 days of colonoscopy in 3.3 cases per 10,000 colonoscopies in study of 21,375 patients [3]. In a study of 1,528 patients, there was one case of TIA, and one case of pulmonary embolism within 30 days of colonoscopy (6.5 cases of each per 10,000 colonoscopies) [8]. A third study of 23,508 patients, there were two cases of TIA and reversible ischemic neurologic deficit lasting 24 hours and 72 hours, occurring in recovery period following the procedure (0.8 per 10,000 colonoscopies) [13]. However, these rates are comparable with the expected annual adjusted rate of stroke in general population [3].

Splenic hematoma and rupture, intramural hematoma, subcutaneous emphysema in the absence of frank colonic perforation, tearing of mesenteric vessels with intra-abdominal bleeding, thrombosis in carotid-subclavian artery bypass graft, thrombophlebitis in the intravenous site, intestinal obstruction, and ischemic and chemical colitis secondary to glutaraldehyde or air insufflation have been reported following colonoscopy in literature [3,14,15,23,31,57,58].

2.11. Polyp and cancer miss rates

Although it is not a true complication of colonoscopy, missing colorectal polyps and cancer is of importance because it affects patient's safety, malpractice, and determining the surveillance interval for repeat colonoscopy. In a study of 235 patients, the miss rate for advanced adenomas which defined as polyps ≥ 10 mm with or without a villous component or high-grade dysplasia was 2.5% and 3.3% for patients who had complete colonoscopy and satisfactory colon preparation on second and third repeat colonoscopy, respectively [59]. There was no cancer missed [59].

In another prospective study with repeated colonoscopy performed within 2 months of first colonoscopy, the miss rate of colorectal polyps was 21.2%; however, as number of polyps found on first colonoscopy increased, the miss rate increased to reach 77.8% when 4 polyps found [60]. The miss rate decreased inversely with polyps' size from 23.9% with polyps of 1-4 mm to 10% for polyps of size ≥ 10 mm [60].

However, the overall miss rate for adenomas was as high as 24% in a study of 183 patients who underwent 2 consecutive colonoscopies on the same day. The miss rate increased with number of polyps detected on first colonoscopy, inversely with polyps' size, and right colon [61].

In a systematic review of 6 studies of a total of 465 patients, the pooled polyps miss rate was 22% which increased inversely with polyps' size to reach 26% for polyps of 1-5 mm [62].

Also withdrawal time of endoscope is an important factor for detecting adenomas with minimal recommended time of 6 minutes. The detection rates for adenomas ≥ 10 mm were only 2.6% for endoscopists with mean withdrawal time less than 6 minutes, compared to 6.4% for those with withdrawal time greater than 6 minutes [63]. Therefore, polyp miss rate increases with short withdrawal time.

3. Complications associated with specific colonoscopic interventions

3.1. Colonoscopic tattooing

Colonic tattooing is an injection of permanent dye into the submucosal layer of colon wall that adjacent to the lesion for easier future localization either for surgical resection or colonoscopic follow-up. Although three studies with a total of 264 patients who underwent colonoscopic tattooing reported no fever, abdominal pain, or any major complications [64-66], a systematic review of 447 patients with colonoscopic tattooing described 5 cases of complications with only one was an overt clinical complication (22.3 per 10,000 tattooing) [67].

It has been reported cases of intramural hematoma, colonic abscess, rectus muscle abscess following colonoscopic tattooing, bowel obstruction, retroperitoneal colonic perforation due to localized necrosis, adhesion ileus, and spread of the dye following colonoscopic tattooing [68-75].

3.2. Colonic balloon dilation

Colonic dilation has been used as a non-surgical treatment for benign strictures that associated with Crohn's disease and those at surgical anastomoses [76].

In a systematic review in 2007 of 13 studies with 347 patients with Crohn's disease with colonic strictures who underwent 695 sessions of colonic dilation, there were 14 cases of major complications (201.4 cases per 10,000 colonic dilations); 13 cases being bowel perforation (92.8%) [77].

Two prospective studies with a total of 42 patients with benign colorectal anastomotic stenosis, not associated with Crohn's disease, who underwent 81 sessions of colonic dilation reported no procedure-related complications [78,79].

3.3. Colonic stent placement

Self-expandable metal stents (SEMS) have been used in the management of colorectal obstruction as a bridge to surgery or as a palliative treatment especially malignant obstruction. In a pooled analysis of 54 studies with 1,198 patients who underwent colonic stent placement, the major complications related to stent placement included stent migration (11.81%), reobstruction (7.34%), perforation (3.76%), and mortality (0.58%) [80]. The risk factors for stent migration which may occur proximally or distally were using covered stent, laser treatment, dilation prior stent insertion, and the use of chemotherapy and radiotherapy. The causes for reobstruction were tumor ingrowth (73.2%), fecal impaction, mucosal prolapse, stent migration, tumor overgrowth, and peritoneal seeding. The reobstruction was significantly higher in uncovered stents. The perforation was related to stent wires, balloon dilation, guide wires, or related to laser recanalization prior stent placement. The death was related to colonic perforation and its consequences in majority of cases [80].

In another systematic review of 1,785 patients with 1,845 stent placements, colonic reobstruction in 12%, migration of the stent occurred in 11%, perforation in 4.5%. Other reported complications of stent placement included GI bleeding, anal pain, abdominal pain, and tenesmus which were relatively rare and generally well tolerated by patients [81]. It is not recommended to perform dilation around the time of stent placement due to increased perforation risk [76,80].

Despite of the early termination of 3 randomized controlled trials comparing SEMS to surgery because of high rate of complications in SEMS groups, a recent systematic review in 2012 with 234 patients including these 3 trials showed that the clinical perforation rate was 6.9% and the silent perforation rate 14%. There was no difference between SEMS arm and emergent surgery in primary anastomosis, permanent stoma, in-hospital mortality, anastomotic leak, 30-day reoperation and surgical-site infection rates [82-85].

3.4. Colonic decompression tube placements

Transanal endoscopic decompression tube placement has been used in acute colorectal obstruction or pseudo-obstruction before surgery or stenting.

In 5 series consisting of 153 patients with acute colonic obstruction treated with transanal decompression tube placement, two cases of bowel perforation occurred (1.3%) [86-90].

In a series of 50 patients with acute colonic pseudo-obstruction who underwent 54 decompression tube placements, one case of bowel perforation occurred (2%), and overall in-hospital mortality was 30% reflecting severe underlying comorbidities [91].

3.5. Percutaneous endoscopic colostomy

Percutaneous endoscopic colostomy (PEC) is considered a minimally invasive endoscopic procedure that has been used as an alternative modality to surgery in poor surgical candidates who have recurrent sigmoid volvulus, recurrent colonic pseudo-obstruction, neurogenic bowel or severe slow-transit constipation [76,92-94].

The complications of PEC that has been reported are fecal peritonitis (8.5%), fecal leakage, recurrent infections (77%), buried internal bolster, abdominal wall bleeding and pain [92-94]. All-cause mortality has been reported as high as 26% reflecting the often frail patients who undergo PEC [92-94].

3.6. Colonic hemostasis

Colonic hemostasis devices are used to treat GI bleeding including diverticular bleeding, postpolypectomy bleeding, angiodysplasia, and radiation-induced angioectasias. Colonic hemostasis devices include contact thermal devices (eg, heater probe [HP], multipolar electrocautery [MPEC] probes, and hemostatic graspers), noncontact thermal devices (eg, argon plasma coagulator [APC]), mechanical devices (eg, band ligators, clips, and loops) and injection needles [95].

Initial worsening of bleeding may occur when applying any of these devices which can be successfully treated by an additional application of the same or different device [15]. Colonic perforation especially right colon has been reported as high as 2.5% with thermal devices [15,95,96]. Distention of the GI tract with argon gas, submucosal emphysema, pneumomediastinum, pneumoperitoneum, and gas explosion has been reported as complications of APC [95,97,98].

There are multiple reports of premature deployment of the clip, and the failure to separate the clip from the catheter after deployment [95]. Colonic perforation, initial worsening bleeding, clip retention, immediate or delayed bleeding secondary to slippage of loop when using detachable loop ligating devices have been described [95,99].

The complications of injection needles are usually related to injected substances such as cardiac arrhythmias and hypertension due to epinephrine, however, there are reports of needles separating from the catheter in the patient and requiring retrieval, and of needles failing to extend from their sheaths [95].

3.7. Foreign body removal

Colorectal foreign bodies may result from the insertion in the rectum for sexual pleasure, non-sexual purposes such as body packing of illicit drugs for transportation purposes, accidentally, by swallowing solid objects such as bones and toothpicks, or migration into the colon from the adjacent organs such as intrauterine contraceptive devices and inguinal hernia mesh [15,100-103]. Numerous kinds of objects have been described in the literature including fruits, vegetables, cans, bottles, bull horn, batteries, light bulbs, cosmetic containers, and children or sex toys [100,104]. The presenting symptoms of colorectal foreign bodies are pel-

vic pain, abdominal pain, the peritoneal signs if perforation occurs, rectal bleeding, rectal mucous drainage, fecal incontinence, bowel obstruction, or drug overdose if bag ruptures during removal attempts in body packing of illicit drugs [15,100,101,104].

These symptoms and the management varies considerably based on the type of inserted objects (sharp versus blunt), traumatic or not, and illicit drug involved or not [15,101]. Management of colorectal foreign bodies can be challenging and a systematic approach should be employed including abdominal plain film and CT scan to evaluate for free intra-abdominal air, shape and size of object, and its location and relations to the pelvis [15,100,101]. The majority of cases can be successfully managed conservatively, but occasionally such as large objects or tightly wedged in the pelvis surgical intervention is warranted [15,100]. It is not recommended removing drug-containing bags endoscopically because of potential rupture of bags that can lead to systemic absorption of the drug which may cause death from rapid drug overdose [15,105].

3.8. Advanced techniques for colonoscopic tissue removal

These advanced techniques include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) that have been used to remove benign and early malignant lesions that confined to superficial layers (mucosa and submucosa) [15,106]. Perforation and bleeding are the most common complications for EMR and ESD which are more frequent than with standard polypectomy [15]. The size of lesion, location, histology, the type of device used, and operator experience are the factors that affects complication rates [15,107-109].

Intraprocedural bleeding rate has been reported over 10% in several large studies with delayed bleeding to up to 14% [15,101,102]. Bleeding usually is managed endoscopically, although it may require blood transfusion [15,110].

Perforation may occur in 0-5% and 5-10% in EMR and ESD respectively which is usually recognized during the procedure and managed endoscopically, although delayed perforation has been reported in 0.4% [15,107-111].

4. Conclusion

Despite these varieties of potential complications of colonoscopy and colonoscopic interventions, they occur in low rate. It is important for both patients and physicians to know these potential complications. Informing patients regarding the symptoms of these complications is of importance to seek medical attention in timely manner without delay. Also knowledge of these potential complications their frequency, risk factors, and appropriate interventions is essential for endoscopists to minimize their incidence, detect and treat them without delay.

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