#Reviewer 1 comment (03251358)

Nice review of colonoscopy-related adverse events (particularly perforation and bleeding), based on recent large-scale studies. The manuscript is well written and concise. Figures and tables are informative; there is not redundancy with what is contained in the main body of text. However, there are some margins for improvement. Throughout the manuscript the use of the word "fatal" should used correctly. Fatal consequence means something leading to the death of the patient. Therefore, for example the sentence "In particular, perforations in elderly patients can lead to highly fatal consequences" should be "In particular, perforations in elderly patients can lead to a high proportion of fatal consequences".

Response: We appreciate this comment. As suggested by the reviewer, we have changed the word 'fatal' as below.

A colon perforation is a severe complication with a relatively high mortality rate.

In particular, perforations in elderly patients can lead to a high proportion of fatal consequences.

They can also cause serious conditions in healthy people.

Consider reporting the definition of perforation (e.g. localized or diffuse release of gas or intestinal fluids into the peritoneum diagnosed with a CT scan…), and those of immediate or early bleeding and delayed bleeding (definitions more commonly reported in articles or better in guidelines).

Response: Thank you for this comment. We have defined perforation and bleeding (immediate and delayed) as follows.

Generally, colonoscopy perforation was defined as intraperitoneal fat or viscera seen during

the colonoscopy, or the presence of radiographic abnormalities (intra-abdominal free air on X-ray or localized or diffuse release of gas or intestinal fluid into the peritoneum on CT scan)[5,9,14].

The definition of post-colonoscopy bleeding was somewhat different among the studies: lower-GI bleeding after colonoscopy with/without polypectomy requiring a transfusion of packed red blood cells, hospitalization, emergency room visit, or need for repeat colonoscopy in the setting of hematochezia[5,9,10,37]. *Generally, immediate bleeding was defined as that occurring within 1 day after an endoscopic procedure, and delayed bleeding as that occurring from 24 hours to 14 days after an endoscopic procedure*[8,37,38].

As results are currently presented, they only constitute a list of extracted data. For each section (perforation and bleeding), to facilitate readers understanding the data that were presented, it is necessary to summarize them as aggregate results. For example, all data analyzed, is perforation or bleeding more common in screening cases or in diagnostic cases? And why? Is it possible to rank the risk factors according to their incidence (e.g. more probable in screening or diagnostic patients, after polypectomy, for polyps >10 mm, elderly patients, patients with co-morbidities…) It would be appropriate to add a Discussion section also, to comment the aggregated results. The section "Challenges" derives from the points commented and debated in Discussion.

Response: We agree that our data need to be summarized, and that we should comment on the aggregated results. Based on the extracted data, we have summarized the incidence of complications according to the indication for colonoscopy or whether polypectomy is performed. Also, we have added the risk factors in each study to Table 6. Finally, we have added Tables 4, 5, and 6 and revised the Discussion section as per your advice.

Discussion

Large-scale studies can provide more comprehensive information on post-colonoscopy

complications. In single-institution studies, the number of subjects is small and only specific indications, such as polypectomy, are evaluated. However, population-based research using national data has the advantage of enabling unbiased conclusions to be reached.

We summarized the incidence of post-colonoscopy complications according to colonoscopy indication and procedure (Tables 4 and 5). Table 4 shows the post-colonoscopy perforation rates stratified by colonoscopy indication and procedure type. The rate of perforation in screening/surveillance colonoscopy was 0.010% to 0.067%. However, the rate of perforation in symptomatic/diagnostic colonoscopy was 0.022% to 0.268%. Arora et al[72] reported the incidence and risk of colonic perforation according to colonoscopy indication. In this study, 22% of all colonoscopies were conducted for screening purposes (58,457/269,712). The identification of diarrhea and obstruction as indications for a colonoscopy was related to a higher incidence of perforation (0.140% and 0.374%, respectively) compared with screening colonoscopy (0.067%)[72]. Another study involved a subgroup analysis according to colonoscopy indication[16]. Of the total of 1,144,443 colonoscopies, 544,474 were for screening or surveillance. The perforation rate was 0.011% in the screening/surveillance group and 0.022% in the symptomatic/surveillance group. ASA class IV/V was most significantly associated with an increased risk of perforation in the screening/surveillance group[16]. Hamdani et al[73] showed that the incidence of perforation in a diagnostic colonoscopy group was 20-fold that in the screening colonoscopy group. A recent large-scale study analyzing health insurance data showed that the risk of perforation is significantly increased for emergency colonoscopy (OR: 4.63, CI: 3.52–6.10)[29]. The aforementioned large-scale studies showed that the incidence of complications is lower for screening/surveillance colonoscopies than for other indications. A recent meta-analysis also indicated that the incidence of complications varies according to indication[5]. In general, screening or surveillance populations tend to be less likely to require additional procedures because they have a higher percentage of health status.

Unlike perforation, few large-scale studies have assessed the incidence of bleeding by colonoscopy indication (Table 5). Two studies that, together, analyzed more than 50,000 colonoscopies reported the incidence of bleeding according to colonoscopy indication. Crispin et al[46] reported similar rates of bleeding in screening and symptomatic colonoscopy groups (0.240% vs. 0.210%); however, the OR was higher in the symptomatic group (1 [reference]

vs. 1.312 [1.042–1.655]). Warren et al[47] showed that the rate of bleeding after colonoscopy was higher in the diagnostic group than the screening group (0.206% vs. 0.375%). The risk per 1,000 persons of post-colonoscopy bleeding was also similar (2.1 vs. 3.7). In another meta-analysis, the symptomatic group had a higher bleeding rate than the screening/surveillance group (2.4 [0.9–4.6] vs. 4.6 [0.1–15.8], P < 0.001)[5].

Polypectomy also affects the incidence of perforation. According to six large-scale studies, the rate of perforation for polypectomy was 0.037% to 0.091%, compared to 0.005% to 0.077% for colonoscopy without polypectomy (Table 4) [27,30,47,52,72,73]. During polypectomy, perforation may occur due to grabbing of deep colonic wall layers or excessive thermal injury. The rate of complications during screening colonoscopy differs significantly depending on whether polypectomy was performed[30]. Polypectomy has a marked effect on the incidence of bleeding (Table 5). The rate of post-colonoscopy bleeding in the non-polypectomy group was 0.001% to 0.336%, compared to 0.092% to 1.136% in the polypectomy group (Table 5). Polypectomy is itself a risk factor for bleeding. In addition, the polyp size, morphology, and number (risk factors for post-polypectomy bleeding) exert a synergistic effect on the risk of bleeding.

To date, diverse risk factors for colonoscopic perforation and bleeding have been identified. Patient-related factors (old age, female gender, multiple comorbidities, large polyp) and the need for additional intervention such as polypectomy are among these risk factors[14,16]. Three studies have evaluated the risk factors for post-colonoscopy bleeding[5,8,9]; these are listed in Table 6. Polypectomy, polyp size, and old age are common risk factors for post-colonoscopy perforation and bleeding in several studies.

Table 4 Perforation rates per colonoscopy indication and procedure type from recent studies with sample sizes > 50,000 cases

	Indication		*Procedure*	
Author	*Screening/surveillance*	*Symptomatic/diagnostic*	*Without polypectomy*	*With polypectomy*
Sieg et al[27]	-	-	*0.005%*	*0.063%*
Crispin et	*0.040%*	*0.030%*	-	-

al[46]				
Warren et al[47]	*0.056%*	*0.050%*	*0.052%*	*0.070%*
Arora et al[72]	*0.067%*	*0.086%*	*0.077%*	*0.077%*
Pox et al[30]	*0.016%*	*-*	*0.012%*	*0.046%*
Hamdani et al[73]	*0.010%*	*0.268%*	*0.010%*	*0.037%*
Rutter et al[52]	*0.063%*	*-*	*0.031%*	*0.091%*
Bielawska et al[16]	*0.011%*	*0.022%*	*-*	*-*

Table 5 Bleeding rates per colonoscopy indication and procedure type from recent studies with sample sizes > 50,000 cases

	Indication		*Procedure*	
Author	*Screening/surveillance*	*Symptomatic/diagnostic*	*Without polypectomy*	*With polypectomy*
Sieg et al[27]	*-*	*-*	*0.001%*	*0.270%*
Crispin et al[46]	*0.240%*	*0.210%*	*-*	*-*
Warren et al[47]	*0.206%*	*0.375%*	*0.336%*	*0.874%*
Pox et al[30]	*0.020%*	*-*	*0.001%*	*0.092%*
Rutter et al[52]	*0.647%*	*-*	*0.102%*	*1.136%*

Table 6 Summary of major risk factors for perforation and bleeding related to colonoscopy from recent studies with sample sizes > 50,000 cases

Author	*Risk factors for perforation*	*Risk factors for bleeding*

Rabeneck et al[77]	*Comorbidity score ≥ 3 [OR: 3.73, 95% CI: 1.59 – 8.77], Polypectomy [OR: 2.96, 95% CI: 2.31 – 3.80], Old age [OR: 2.06, 95% CI: 1.79 – 2.37]*	*Polypectomy [OR: 10.32, 95% CI: 6.52 – 16.34], Old age [OR: 1.61, 95% CI: 1.20 – 2.16]*
Crispin et al[46]	*Polyp size: 0.5 – 1 cm [OR: 11.93, 95% CI: 3.02 – 47.13] Polyp size: 1 – 3 cm [OR: 28.12, 95% CI: 7.82 – 101.09] Polyp size > 3 cm [OR: 31.49, 95% CI: 6.37 – 155.66] Polypectomy [OR: 2.27, 95% CI: 1.39 – 3.70], Old age [OR: 1.00, 95% CI: 1.00 – 1.00]*	*Polyp size: 0.5 – 1 cm [OR: 5.25, 95% CI: 3.42 – 8.06] Polyp size: 1 – 3 cm [OR: 16.84, 95% CI: 11.14 – 25.46] Polyp size > 3 cm [OR: 27.52, 95% CI: 17.20 – 44.05] Polypectomy [OR: 60.21, 95% CI: 35.90 – 100.99] Biopsy [OR: 8.88, 95% CI: 5.06 – 15.59], Colonoscopy in patients with symptoms [OR: 1.31, 95% CI: 1.04 – 1.67], Pedunculated polyp [OR: 1.55, 95% CI: 1.26 – 1.90], Number of polyps: 2 – 4 [OR: 1.26, 95% CI: 1.06 – 1.50], Old age [OR: 1.00, 95% CI: 1.00 – 1.00]*
Arora et al[72]	*Colonoscopy indication (obstruction) [OR: 5.09, 95% CI: 3.17 – 8.20], Colonoscopy procedure[1] [OR: 6.12, 95% CI: 3.16 – 11.83], Comorbidity score ≥ 2 [OR: 1.52, 95% CI: 1.12 – 2.06], Old age [OR: 1.01, 95% CI: 1.00 – 1.02]*	-
Pox et al[30]	*Polypectomy*	*Polypectomy*
Hamdani et al[73]	*Colonoscopy indication : Crohn's disease [OR: 5.16, 95% CI: 1.79 – 14.88], Colonoscopy indication : abdominal pain*	-

	[OR: 5.79, 95% CI: 2.64 – 12.74], *Colonoscopy indication : diagnostic* *[OR: 15.33, 95% CI: 7.79 – 30.18],* *Inpatient [OR: 11.05, 95% CI: 5.14 – 23.75],* *ICU patient* *[OR: 5.83, 95% CI: 2.80 – 12.14],* *Low albumin (≤ 4.0)* *[OR: 3.58, 95% CI: 1.72 – 7.47]* *Old age [OR: 1.03, 95% CI: 1.01 – 1.05]*	
Samalaviciu s et al[79]	*Low-volume practice center*	-
Blotière et al[29]	*Age: 60 – 69 [OR: 2.91, 95% CI: 1.66 – 5.10],* *Age: 70 – 79 [OR: 5.38, 95% CI: 3.08 – 9.40],* *Age ≥ 80 [OR: 7.51, 95% CI: 4.20 – 13.45],* *Emergency colonoscopy* *[OR: 4.63, 95% CI: 3.52 – 6.10],* *Polyp size ≥ 1cm* *[OR: 2.72, 95% CI: 2.05 – 3.60]*	*Age: 60 – 69 [OR: 1.70, 95% CI: 1.18 – 2.43],* *Age: 70 – 79 [OR: 2.55, 95% CI: 1.77 – 3.66],* *Age ≥ 80 [OR: 3.23, 95% CI: 2.21 – 4.73],* *Emergency colonoscopy* *[OR: 5.99, 95% CI: 5.01 – 7.15],* *Polyp size ≥ 1cm* *[OR: 5.12, 95% CI: 4.33 – 6.04],* *Chronic disease [OR: 1.76, 95% CI: 1.53 – 2.02],* *Gender (male) [OR: 1.64, 95% CI: 1.43 – 1.87]*
Rutter et al[52]	*Polypectomy,* *Location of polyp (cecum)* *[OR: 5.60, 95% CI: 1.37 – 22.83]*	*Polypectomy,* *Location of polyp (cecum)* *[OR: 13.50, 95% CI: 3.93 – 46.42],* *Increasing polyp size* *[OR: 4.92, 95% CI: 2.84 – 8.51]*
Bielawska et al[16]	*Age: 60 – 74 [OR: 2.69, 95% CI: 1.83 – 3.98],* *Age ≥ 75 [OR: 5.63, 95% CI: 3.73 – 8.49],* *Gender (female)* *[OR: 2.00, 95% CI: 1.43 – 2.80],* *ASA class III* *[OR: 2.14, 95% CI: 1.22 – 3.75],*	-

ASA class IV/V
[OR: 7.20, 95% CI: 2.41 – 21.50],
Hospital setting: university
[OR: 2.83, 95% CI: 1.85 – 4.31],
Hospital setting: VA/military
[OR: 3.74, 95% CI: 2.37 – 5.89],
Any therapy [OR: 3.93, 95% CI: 2.05 – 7.56],
Polyp size ≥ 1 cm
[OR: 4.14, 95% CI: 2.58 – 6.65],
Endoscopy specialty: surgery or unknown
[OR: 2.00, 95% CI: 1.30 – 3.08]

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[1]*Colonoscopy procedure includes treatment of foreign-body, submucosal injection, hemostasis, endoscopic ultrasound, transmural or intramural aspiration or biopsy.*

Due to the fact that different definitions of early and delayed bleeding are often used across articles, probably some limitations in the analysis of extracted data should be acknowledged by the authors.

Response: We have added the use of different definitions of early and delayed bleeding as a limitation of the study.

This review article is limited by the use of different definitions of immediate and delayed bleeding among the included studies.

#Reviewer 2 comment (02543017)

The authors have worked hard and put together all this data related to complications of colonoscopy. Although subject matter is timely, would be nice to include/ discuss different mechanisms of each complication.

Answer: Thank you for this comment. We think that it is so interesting and valuable work to include difference mechanisms of each complication in manuscript. We added several sentences as below.

Colonoscopy perforations may occur by several mechanisms, such as mechanical trauma, barotrauma, thermal energy, and removal of a tissue lesion[14]. Iqbal et al[13] classified the injury characteristics, based on the mechanism of perforation, into thermal, polypectomy, and blunt. Blunt injury is caused by direct trauma or torque from the endoscope; this mechanism results in the largest perforations[13]. The cecum is the most frequent site of perforation due to thermal energy and polypectomy, and the rectosigmoid colon due to blunt injuries[13].

Bleeding after a diagnostic endoscopy is very rare. If it occurs, it is typically associated with biopsy. This may occur when the blood vessel structure is directly biopsied, especially in patients with abnormal blood coagulation function[39]. It is also rarely seen in cases of severe mechanical friction due to the endoscope.

The mechanism of post-polypectomy bleeding varies depending on polyp morphology. In the case of pedunculated polyps, a large feeding vessel usually passes through the stalk. Insufficient electrocoagulation during stalk cutting with a snare may cause pulsatile bleeding[40]. In the case of sessile polyps, the polypectomy section is usually deep and wide, which may result in insufficient electrocoagulation of the interior, resulting in bleeding from the internal margin of the section. In addition, exposed vessels are often located in the submucosal layer, which may increase the risk of delayed bleeding[41,42].

#Reviewer 3 comment (02542039)

The review article entitled "Adverse events related to colonoscopy: global trend and future challenges" has summarized important data in the trend of colonoscopy related adverse events. The manuscript is well written but there are

certain needs to make it more useful in those who are interested in this subject.

1. The writing style is very descriptive, the authors should summarize the risk factor for each complication and try to calculate the odd ratio if possible. Perhaps they may put it as a table.

Response: We appreciate this comment. We have summarized the risk factors for complications in Table 6.

Table 6. Summary of major risk factors for perforation and bleeding related to colonoscopy from recent studies with sample sizes > 50,000 cases

Author	*Risk factors for perforation*	*Risk factors for bleeding*
Rabeneck et al[77]	*Comorbidity score ≥ 3 [OR: 3.73, 95% CI: 1.59 – 8.77], Polypectomy [OR: 2.96, 95% CI: 2.31 – 3.80], Old age [OR: 2.06, 95% CI: 1.79 – 2.37]*	*Polypectomy [OR: 10.32, 95% CI: 6.52 – 16.34], Old age [OR: 1.61, 95% CI: 1.20 – 2.16]*
Crispin et al[46]	*Polyp size: 0.5 – 1 cm [OR: 11.93, 95% CI: 3.02 – 47.13] Polyp size: 1 – 3 cm [OR: 28.12, 95% CI: 7.82 – 101.09] Polyp size > 3 cm [OR: 31.49, 95% CI: 6.37 – 155.66] Polypectomy [OR: 2.27, 95% CI: 1.39 – 3.70], Old age [OR: 1.00, 95% CI: 1.00 – 1.00]*	*Polyp size: 0.5 – 1 cm [OR: 5.25, 95% CI: 3.42 – 8.06] Polyp size: 1 – 3 cm [OR: 16.84, 95% CI: 11.14 – 25.46] Polyp size > 3 cm [OR: 27.52, 95% CI: 17.20 – 44.05] Polypectomy [OR: 60.21, 95% CI: 35.90 – 100.99] Biopsy [OR: 8.88, 95% CI: 5.06 – 15.59], Colonoscopy in patients with symptoms [OR: 1.31, 95% CI: 1.04 – 1.67], Pedunculated polyp [OR: 1.55, 95% CI: 1.26 – 1.90], Number of polyps: 2 – 4 [OR: 1.26, 95% CI: 1.06 – 1.50],*

		Old age [OR: 1.00, 95% CI: 1.00 – 1.00]
Arora et al[72]	*Colonoscopy indication (obstruction) [OR: 5.09, 95% CI: 3.17 – 8.20], Colonoscopy procedure[1] [OR: 6.12, 95% CI: 3.16 – 11.83], Comorbidity score ≥ 2 [OR: 1.52, 95% CI: 1.12 – 2.06], Old age [OR: 1.01, 95% CI: 1.00 – 1.02]*	-
Pox et al[30]	*Polypectomy*	*Polypectomy*
Hamdani et al[73]	*Colonoscopy indication : Crohn's disease [OR: 5.16, 95% CI: 1.79 – 14.88], Colonoscopy indication : abdominal pain [OR: 5.79, 95% CI: 2.64 – 12.74], Colonoscopy indication : diagnostic [OR: 15.33, 95% CI: 7.79 – 30.18], Inpatient [OR: 11.05, 95% CI: 5.14 – 23.75], ICU patient [OR: 5.83, 95% CI: 2.80 – 12.14], Low albumin (≤ 4.0) [OR: 3.58, 95% CI: 1.72 – 7.47] Old age [OR: 1.03, 95% CI: 1.01 – 1.05]*	-
Samalaviciu s et al[79]	*Low-volume practice center*	-
Blotière et al[29]	*Age: 60 – 69 [OR: 2.91, 95% CI: 1.66 – 5.10], Age: 70 – 79 [OR: 5.38, 95% CI: 3.08 – 9.40], Age ≥ 80 [OR: 7.51, 95% CI: 4.20 – 13.45], Emergency colonoscopy [OR: 4.63, 95% CI: 3.52 – 6.10], Polyp size ≥ 1cm [OR: 2.72, 95% CI: 2.05 – 3.60]*	*Age: 60 – 69 [OR: 1.70, 95% CI: 1.18 – 2.43], Age: 70 – 79 [OR: 2.55, 95% CI: 1.77 – 3.66], Age ≥ 80 [OR: 3.23, 95% CI: 2.21 – 4.73], Emergency colonoscopy [OR: 5.99, 95% CI: 5.01 – 7.15], Polyp size ≥ 1cm [OR: 5.12, 95% CI: 4.33 – 6.04], Chronic disease [OR: 1.76, 95% CI: 1.53 – 2.02],*

		Gender (male) [OR: 1.64, 95% CI: 1.43 – 1.87]
Rutter et al[52]	*Polypectomy, Location of polyp (cecum) [OR: 5.60, 95% CI: 1.37 – 22.83]*	*Polypectomy, Location of polyp (cecum) [OR: 13.50, 95% CI: 3.93 – 46.42], Increasing polyp size [OR: 4.92, 95% CI: 2.84 – 8.51]*
Bielawska et al[16]	*Age: 60 – 74 [OR: 2.69, 95% CI: 1.83 – 3.98], Age ≥ 75 [OR: 5.63, 95% CI: 3.73 – 8.49], Gender (female) [OR: 2.00, 95% CI: 1.43 – 2.80], ASA class III [OR: 2.14, 95% CI: 1.22 – 3.75], ASA class IV/V [OR: 7.20, 95% CI: 2.41 – 21.50], Hospital setting: university [OR: 2.83, 95% CI: 1.85 – 4.31], Hospital setting: VA/military [OR: 3.74, 95% CI: 2.37 – 5.89], Any therapy [OR: 3.93, 95% CI: 2.05 – 7.56], Polyp size ≥ 1 cm [OR: 4.14, 95% CI: 2.58 – 6.65], Endoscopy specialty: surgery or unknown [OR: 2.00, 95% CI: 1.30 – 3.08]*	-

[1]Colonoscopy procedure includes treatment of foreign-body, submucosal injection, hemostasis, endoscopic ultrasound, transmural or intramural aspiration or biopsy.

2. There certain type of colonoscopy related perforation. Scope related or polypectomy related? The size and danger cause to different outcomes. Immediate detection has shown a better result. Endoscopic treatment has emerged as a promising approach. I need the authors discussing in these issues.

Response: Thank you for this comment. We have added the rates of perforation and the outcomes of colonoscopy, and a discussion of endoscopic treatment of perforations.

Colonoscopy perforations may occur by several mechanisms, such as mechanical trauma, barotrauma, thermal energy, and removal of a tissue lesion[14]. Iqbal et al[13] classified the injury characteristics, based on the mechanism of perforation, into thermal, polypectomy, and blunt. Blunt injury is caused by direct trauma or torque from the endoscope; this mechanism results in the largest perforations. The cecum is the most frequent site of perforation due to thermal energy and polypectomy, and the rectosigmoid colon due to blunt injuries[13]. The outcome varies depending on the type of perforation. In particular, blunt injuries have larger perforations and a higher rate of fecal diversion than polypectomy injury and, therefore, a worse prognosis[13]. In addition, immediate detection of perforation results in less intraperitoneal contamination than delayed detection. In general, perforations detected during or immediately after colonoscopy have a better prognosis than those whose detection is delayed, and less frequently require surgical treatment[8,13,15].

Surgery plays an important role in the treatment of post-colonoscopy perforation. Recent advances in endoscopic techniques have enabled treatment of < 10 mm immediately detected colonoscopy-related perforations in patients with good bowel preparation and stable vital signs[18]. The ESGE recommends the use of through-the-scope endoclips for small perforations and over-the-scope clips (OTSC) for larger ones[19]. Also, electrocautery injury may induce colon perforations, which can be closed by endoscopic clipping, particularly during endoscopic submucosal dissection (ESD)[20,21]. According to systematic reviews, the OTSC method is effective for treating diagnostic and therapeutic colon perforations[22,23]. Also, endoscopic band ligation is a salvage technique for the treatment of iatrogenic colonic perforation after failure of endo-clipping[24].

3. Post polypectomy syndrome was not adequately mentioned in this review.

Please add this part.

Answer: We agree. We have added discussion of post-polypectomy syndrome as below.

Post-polypectomy syndrome (PPS) is defined as the progress of abdominal pain, leukocytosis, fever, and localized peritonitis without radiographic evidence of colonic perforation[53]. PPS arises after colonoscopic polypectomy with electrocoagulation. The incidence of PPS is reported to vary from 0.003% to 0.1%[54]. However, PPS after ESD occurs in about 9% of cases, which is higher than that after polypectomy or endoscopic mucosal resection[55]. The risk factors for PPS are hypertension, large lesion, and non-polypoid lesion[56]. The protective effect of submucosal injection against PPS is unclear[57]. Generally, PPS should be managed conservatively with medical therapy (NPO status, IV fluids, and broad-spectrum antibiotics), because the prognosis is good in the majority of cases. However, in rare cases, surgical treatment may be necessary if there is a clear perforation with diffuse peritoneal signs[55].

4. Post polypectomy bleeding has many perceivable risk factors, please review and discuss and put these risk factors as a table.

Response: We agree. We have reviewed and discussed the risk factors for post-polypectomy bleeding (see text below), and listed them in Table 2.

Bleeding after a polypectomy is known to occur more frequently and can be divided into immediate bleeding and delayed bleeding according to the time of onset[35,36]. The post-polypectomy bleeding rate (0.98%) is significantly higher compared with when a polypectomy is not performed (0.06%) ($P < 0.001$)[5]. The mechanism of post-polypectomy bleeding varies depending on polyp morphology. In the case of pedunculated polyps, a large feeding vessel usually passes through the stalk. Insufficient electrocoagulation during stalk cutting with a snare may cause pulsatile bleeding[40]. In the case of sessile polyps, the polypectomy section is usually deep and wide, which may result in insufficient

electrocoagulation of the interior, resulting in bleeding from the internal margin of the section. In addition, exposed vessels are often located in the submucosal layer, which may increase the risk of delayed bleeding[41,42]. The number, size, morphology, and histology of polyps, and cardiovascular disease, are risk factors for post-polypectomy bleeding[8]. Shalman et al[43] reported that use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) does not increase the risk of post-polypectomy bleeding. A recent meta-analysis showed that aspirin and NSAIDs are risk factors for delayed, but not immediate, post-polypectomy bleeding[44]. Table 2 summarizes the risk factors associated with post-polypectomy bleeding.

Table 2. The summarizes of related risk factors for post-polypectomy bleeding[36,41,51,80-84].

Patient related factors	*Polyp related factors*	*Procedure related factors*
Older age	*Polyp size*	*Cutting mode*
Anticoagulants	*Morphology of polyps*	*Bowel preparation*
Cardiovascular disease	*Histology*	*Inadvertent cold polypectomy*
Chronic vascular disease	*Number of resected polyps*	*Endoscopist's experience*
Clopidogrel and concomitant aspirin/nonsteroidal anti-inflammatory drugs		*Resection method*
		Use of prophylactic hemostasis

5. Miscellaneous and rare complications have been reported in curtained group of patients such as bacteremia and peritonitis in cirrhotic patients or patients who have peritoneal dialysis, renal or heart failure and hyperphosphatemia developed after bowel preparation, etc. Please add this part as another paragraph.

Response: We have added descriptions of miscellaneous and rare complications of colonoscopy to the manuscript, as below.

The rate of bacteremia related to colonoscopy was 0–25%, and it was not associated with

infectious complications[58]. Only one study has evaluated the risk of bacteremia after colonoscopy in non-bleeding cirrhotic patients[59]. Llach et al[60] reported that 6 of 58 cirrhotic patients who underwent colonoscopy were culture positive. All detected organisms were members of the normal skin flora and all patients were asymptomatic. This result demonstrates that colonoscopy does not induce bacteremia in cirrhotic patients and that routine use of prophylactic antibiotics is not required[60]. Very rarely, continuous ambulatory peritoneal dialysis (CAPD) after colonoscopy with or without polypectomy may occur[61,62]. The International Society for Peritoneal Dialysis (ISPD) guidelines suggest antibiotic prophylaxis prior to colonoscopy; however, this recommendation is not supported by randomized controlled studies[63]. Bowel preparation (particularly with oral sodium phosphate [OSP]) may induce disorders of renal function and electrolytes[64]. In a large nationwide study, the adjusted OR for acute renal failure associated with use of OSP was 3.7 (95% CI 2.37–5.67) within 1 week. Other studies have also reported that hyperphosphatemia occurs in small individuals (including low-risk and well-hydrated patients) after administration of standard dose of OSP, and that this is related to body weight[65,66]. In South Korea, prescribing OSP for bowel preparation is illegal; therefore, we strongly recommend that OSP not be used for the purpose of bowel preparation.

I would like to confirm again that there is nothing to be declared and all authors have approved the revised manuscript. I hope that our revised manuscript will better meet the requirement of the *'World Journal of Gastroenterology'* for publication. And I thank you for valuable comments by reviewers.

Sincerely,

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