

# A Critical Review of Post Endoscopic Sub-Mucosal Dissection (ESD) Delayed Bleeding Risk Factors

Bilal Khan<sup>1</sup>, Bilquis Nawabi<sup>2</sup>, Daniya Sivakumar<sup>3</sup>, Said Maisam Shuo<sup>4</sup>, Ruihua Shi<sup>5\*</sup>

<sup>1</sup>Gastroenterology Internal Medicine, Southeast University, Nanjing, China

<sup>2</sup>Institute Cure Hospital, Kabul, Afghanistan

<sup>3</sup>All Saints University College of Medicine, St Vincent

<sup>4</sup>Nanjing Medical University, Nanjing, China

<sup>5</sup>Gastroenterology Zhongda Hospital Affiliated with Southeast University, Nanjing, China

Email: \*ruihuashi@126.com

**How to cite this paper:** Khan, B., Nawabi, B., Sivakumar, D., Shuo, S.M. and Shi, R.H. (2020) A Critical Review of Post Endoscopic Sub-Mucosal Dissection (ESD) Delayed Bleeding Risk Factors. *Open Journal of Gastroenterology*, 10, 166-179.  
<https://doi.org/10.4236/ojgas.2020.106017>

**Received:** May 29, 2020

**Accepted:** June 25, 2020

**Published:** June 28, 2020

Copyright © 2020 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## Abstract

Endoscopic sub-mucosal dissection (ESD) has become a settled strategy for treatment of shallow neoplasms in the gastrointestinal tract. In three local areas, ESD was introduced to overcome traditional endoscopic mucosal resection (EMR) and inadequate resection of the EMR, combining mouth, stomach, and the colon, for early disruptive sores. ESD was grown first in Japan since that nation has the highest predominance of gastric malignant growth on the planet. Endoscopic sub-mucosal dissection causes enormous fake ulcers with more severe dangers of intra-usable and deferred postoperative draining. However, there is no agreement in regards to the ideal peri-usable administration for the anticipation of free draining and the advancement of ulcer mending. The hugeness of this investigation is to locate a superior procedure to bring down the hazard post ESD draining and to plan to defeat the confinements of regular EMR (endoscopic mucosal resection) and fragmented resection for early malignant injuries in the three districts which incorporate throat, stomach, and colon. However, it has considered a standard in Eastern Asian nations and Japan because of the incredible importance of ESD. The EMR and ESD approaches are discussed in this report. Thus, the warning factors for early gastric neoplasms of PPB after ESD were established, and a superior technique was created to mitigate the danger of ESD dying. EMR was already widely used for treating early neoplastic sores in the gastrointestinal tract; colon adenoma and colorectal tumors are widely acknowledged.

## Keywords

Post-Endoscopic Sub-Mucosal Bleeding, Risk Factor, Delayed Bleeding

## 1. Introduction

### 1.1. Background

The ESD (Endoscopic submucosal dissection) remained a prominent model for diagnosis of shallow neoplasms in the gastrointestinal tract [1]. The first advanced concept proposed in the 1990s was endoscopic sub-mucosal dissection (ESD). ESD was planned in three following regions—esophagus, stomach, and colone—to resolve the weakness of traditional endoscopic silver resection (EMR) and inadequate modern EMR resection in the following three regions [2]. Such therapies for gastric neoplasm are well-established. Bleeding is the most common ESD and EMR adverse case, with a range of 7.1% to 9.4% and 7.1% to 8.6%, respectively [3]. Right, 4.53% after ESD and 3.97% after EMR have been reported for post-procedural bleeding (PPB). The possibility of bleeding can influence both patient and lesion symptoms and medications and procedures [4]. Several experiments have, over time, answered this problem in an attempt to establish post-endoscopic submucosal dissection and impaired risk factors for bleeding [5].

ESD was first introduced extensively in Japan along with the more significant prevalence of gastric cancer. The findings of Japanese endoscopy were unsatisfactory in extracting early gastric cancer via EMR, primarily due to poor healing and high recurrence levels. They, therefore, began to investigate minimally invasive endoscopic alternatives to EMR. ESD has revolutionized the diagnosis of esophageal cancer, and has become the favored approach in the globe [6]. Endoscopic resection is a common treatment that includes all endoscopies of mucous resections (EMRs) and endoscopic submucosal dissections (ESDs) of gastric adenoma and upper gastrointestinal neurotoxin with a small risk of lymphatic node metastases [7]. ESD also allows cell prone en block resection, except for advanced disease, for precise histological analysis and eliminates the risk of complications. Endoscopic Submuscular Dissection (ESD) Operation to eliminate cancers that have not penetrated the muscle layer [8]. An outpatient procedure (ESD) has used to remove deep tumors from the gastrointestinal (GI) tract, which is curatively advantageous over EMR.

En block mode enables the decrease of local recurrence levels, independent of tumor scale, form, ulcer, or position. Also, the en block resection specimens allow for a detailed histological analysis of target lesions. EGC and gastric adenoma Endoscopic sub mucus dissection (ESD) demonstrated significantly greater en-block resection rate and a relatively lower resection rate than regular endoscope snare resection [9]. Long time complexity and ESD's bigger challenge, such as psychogenic fracturing and bleeding which hinder extensive use of ESD. For 4.5 - 5.7 percent of cases, there is post-SED bleeding (PEB). In addition, ESD has a relatively low risk of procedurally related adverse effects. Bleeding after ESD is amongst the worst side effects because bleeding after ESD could lead toward severe condition such as a hemorrhagic shock. [10]. Post-ESD bleeding can continue longer than other traumatic injuries, and more treatment can often arise after discharge. Delay in the blood is most significant endoscopic severe condition of submucosal dissection (ESD). ESD (Endoscopic Submolecular Dissection) has

become a popular treatment for unusually early gastrointestinal cancer in Asia. Different types of endoscopic operative cleats are added for ESD for the incision of mucus and portion during conventional endoscopic mucosal resection (EMR). This technique allows for better resection in patients with more extensive or ulcerated tumors and histological complete resection stages [9]. Early gastric neoplasms are treated with both the ESD and EMR. Efficacy of endoscopic resection is generally known [4].

ESD bleeding can occur within 24 hours to a month of diagnosis, manifesting as hematemesis or melena. This can happen in around 5 percent. Mainly it is rare. Post-ESD blood can lead to a severe blood transfusion reaction, immediate endoscopic care, or operation, which may contribute to significant hemorrhagic shock [11]. When the bleeding incident has occurred, endoscopic hemostasis or conservative management may typically be used to treat it. A scientifically relevant issue needs to be tackled to handle ESD better in gastric tumors, understanding of risk factors, careful management of post ESD bleeding, and avoidance of known-ESD bleeding. Big artificial ulcers have triggered by endoscopic submucosal dissection with increased potential for intraoperative and postoperative bleeding. However, there is no agreement on appropriate perioperative care for secondary bleeding prevention and ulcer healing promotion [12]. Several studies have addressed contributing factors, proper treatment, and prevention measures of bleeding during ESD. Strict training and professional improvement can enhance adverse incidents, such as perforation and bleeding intra-ESD. Instead, only clinical advancement will avoid the emergence of post-ESD [11]. However, there remain some concerns about significant factors of risk for post ESD bleeding; Cardiopathy, stroke diseases, antithrombic agents, tumor size, tumor size, hypertension, cirrhosis, ulceration, fibrosis/scarring must be identified. Identifying these risk factors is essential to quantify and stratify patients' bleeding risk in particular for ESD/EMR management.

## **1.2. Significance of the Study**

The significance of the study, to find a better strategy to lower the risk post ESD bleeding and also to intend Overcoming traditional endoscopic resection (EMR) limits and incomplete resection for early cancerous lesions in the three regions which include the esophagus, stomach, and colon. The most common adverse event is post-procedural bleeding (PPB), and is generally situation of any clinical bleeding symptoms such as hematemesis, melena, and requires endoscopic hemostasis. The occurrence rate of post ESD bleeding is 7.1% to 9.4% of the procedures, respectively. This bleeding can cause severe risks to the health of the patient. There are some controversies, and important post-EMR/ESD bleeding risk factors still to be identified, such as Cardiopathy, cerebrovascular diseases, Antithrombotic agents, tumor size, resection size, hypertension, cirrhosis, ulceration, and fibrosis/scarring. It is essential to define these risk factors to quantify and stratify the likelihood of bleeding. Managing ESD is beneficial. For potential paths, the current research is of great importance.

## 2. Literature Review

### 2.1. Review of Previous Studies

A study conducted by Goto [13] on Endoscopic Sub-Mucosal Dissection (ESD) demonstrated the widely documented curative surgical treatment of gastric epithelial neoplasms, and early gastric neoplasm. In another research, Libânio [3] reported prolonged potential risks for bleeding and found which bleeding is perhaps the most common consequence correlated with ESD and EMR, 7.1% to 9.4%, and 7.1% to 8.6%, accordingly, of medication. In particular, 4.53 percent after ESD and 3.97 percent after EMR post-procedural bleeding (PPB) have been recorded to occur [4]. Patient and lesion factors and drugs or surgical factors may determine the risk of bleeding. In the course of decades numerous work has discussed this problem to identify potential risks for PPB as identified in Lian's 2012 version, J. Eth *et al.* EMR (Endoscopic Mucosal Resection) has increased treatment opportunities for interventional endoscope and limits the number of cases referred to as surgical resection [2] [3]. It is essential to identify risk factors for evaluating the probability of bleeding and stratification of patients through the care of ESD/EMR. Kim JS had shown post-operative bleeding risk factors. It existed in 18 lesions based on severe bleeding (4.1 percent). The single serious consequence for rapid hemorrhage was the tumor's massive size (>20 mm). The odds of prolonged bleeding did not vary significantly between SLE patients (eight cases) and non-SLE patients (six cases,  $p = 0.787$ ). SLE also did not substantially minimize delayed bleeding ( $p = 0.670$ ) for lesions with elevated tumor scale. SLE demonstrates that SLE had little or no effect on protecting against delayed bleeding, regardless of risk factors. Endoscopy during endoscopic gastric submucosal dissection is not mandatory for all patients. On the other hand, Nomura [14] performed single-blind multicenter RCT in 2019, which offered an apparent response to endoscopic clamping [14]. The high frequency of overt bleeding following colorectal ESD could not be minimized by endoscopic clipping closure. In 1973 [15] demarcated fundamental definition of EMR/ESD. EMR was initially thought to be a dangerous process. However, in the 1980s, it became a globally common custom. EMR quickly kills certain minor adenoma and early cancers of the gastrointestinal tract. However, EMRs are not useful at times to ensure that large tumors are fully resected. Endoscopic submucosal (ESD) dissection was then established in Japan at the end of the 1990s. Often deemed to be too dangerous at the beginning because of the entirely uncommon endoscopic procedure and the chance of injuries, including perforation or bleeding, was higher. However, it has become a standard methodology in Japan and other East Asian nations, owing to the high value of ESD. The EMR and ESD methods are discussed in this report. This was thus aimed at determining the risk factors for early gastric neoplasms of PPB after ESD and at finding a better approach to reduce the risk of ESD bleeding. Early-stage Endoscopic neoplastic lesion resection (EMR) was conducted as endoscopic mucosal resection (**Table 1**).

**Table 1.** Search strategy preferred reported items.

Study	Study Design	Country	Year of study	Resection Method	No. of cases	Overall PPB %	Risk Factors evaluated	Quality	Included studies
Park CH, <i>et al.</i>	Prospective Study	Korea	2015	ESD	459	5.4	Multiple	9	+
Choi CW, <i>et al.</i>	RCT	Korea	2015	ESD	273	8.4	Multiple	Low Risk	+
Kim JS, <i>et al.</i>	RCT	Korea	2014	ESD	446	5.2	Multiple	Low Risk	+
Choi CW, <i>et al.</i>	Retrospective studies	Korea	2014	ESD	616	5.6	Multiple	9	+
Koh R, <i>et al.</i>	RCT	Japan	2013	ESD	1166	5.3	Multiple	9	+
Tomita T, <i>et al.</i>	RCT	Japan	2012	ESD	156	5.7	Multiple	Low Risk	+
Nakamura M.	Retrospective studies	Japan	2012	ESD	544	6.9	Multiple	9	+
Goto O, <i>et al.</i>	Retrospective studies	Japan	2010	ESD	454	5.7	Multiple	7	+

## 2.2. Post-ESD Bleeding

The Post-ESD bleeding, malenas, hemodynamic breakdown or hémoglobin down-tick  $\geq 2$  g/dl are usually characterized by all symptoms of hematemesis. Post-ESD bleeding may be graded as rapid bleeding, early bleeding and late bleeding of red, in accordance with the timing of bleeding. Preventing bloating is more critical than persistent bloating soon or early, because it may have significant adverse effects like heart failure. The preparation in the next step following ESD is crucial to learning how to explain post-procedural bleeding.

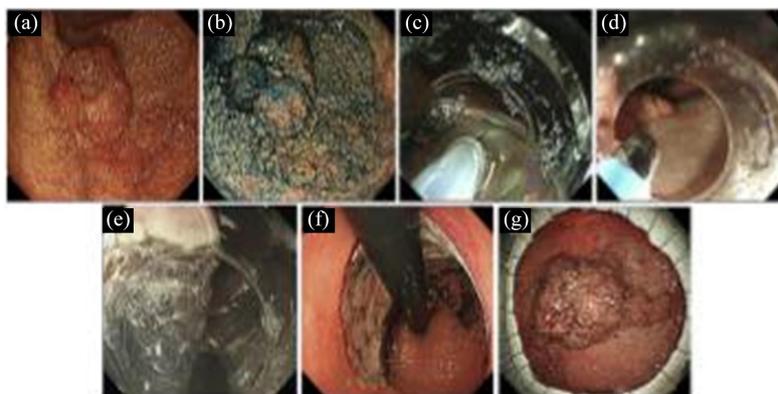
## 2.3. Techniques of Endoscopic Sub-Mucosal Dissection

ESD is a comprehensive procedure involving endoscopy for the extraction of gastrointestinal cancers that may not reach the striated appearance. ESD is an outpatient procedure for the detection of tumors with extreme GI (**Figure 1**).

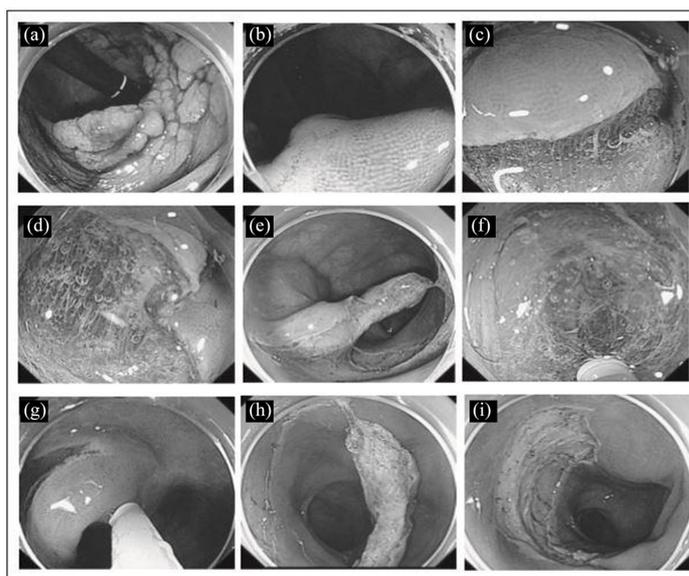
ESD tends to be correlated with a higher en block resection rate [8], with a lower probability of recurrence following resection, although this gain is partly balanced with higher risk of ESD perforation than EMR. Therefore, our comprehensive study is related to the higher en-block ESD resection, which is the least likely of a return. The new research supported the results of the analysis of these two methods from two historically identical studies. The main points in the ESD technique are listed (**Figure 2**). A mucosal incision is performed following submucosal injection. Therefore, our systemic research ties higher en-block ESD resection to a solid, least risk of recurrence therapeutic gain. The current work validates the findings of these two approaches study from two previously similar randomized control trials. Critical points in the ESD method (**Figure 2**) are identified. After submucosal injection, a mucosal incision is carried out.

Nevertheless, the remaining mucosa is often hard to remove. For ESD, it is essential to use distal fittings (transparent hood). The penetration in the exfoliating mucosa of a distal connection gives proper contracting of the submucosal layer and a clear vision of the surgical area. Repeated injections of submucosal should be provided to maintain submucosal elevation throughout the treatment. If hemorrhage is oozing from a tiny wound, coagulation is performed using kni-

feepoint. A haemostat forceps is necessary for hemorrhage from the large artery. Afterward, en-block resections of the tumor will continue with the prevention of perforation and hemorrhage.



**Figure 1.** Procedure for dissection of endoscopic submucosal membranes. A lesion in the lower rectum (a), (b) 70 mm 0-Is + IIa lesion (LST-G); (c) Submucosal injection (glycerol and sodium hyaluronate). (d) The circumferential incision were accomplished with a bipolar needle knife (jet B-Knife). (e) Submucosal dissection with a jet B knife as well as a nano knife (IT) separation tool. (f) En-block resected model of the Ulcer Surface (g) [8].



**Figure 2.** Colonic endoscopic sub-mucosal dissection. (a) 45 mm laterally spreading tumor non-granular type lesion was located at the splenic flexure. (b) The sub-mucosal injection was performed from the oral side. (c) The mucosal incision was made using DualKnifeJ. (d) Insertion of a distal attachment under the exfoliated mucosa provides good counter traction to the sub-mucosal layer. (e) The partial circumferential incision can maintain a higher elevation of the submucosa. (f) DualKnifeJ has a water-jet system that allows a rapid needle-free infusion into the submucosa. (g) It is easy to cut the residual mucosa because a little bit of the opposite mucosa was left uncut. (h) Gravity also provides the right concentration. (i) ESD was completed without any complication. Histopathological examination confirmed adenomas with severe dysplasia, and margin [11].

### 2.3.1. Stomach

In 2014, [16] study analyzed the ESD v. EMR for the diagnosis of early gastric cancer in a critical review. Ten studies have been included in the retrospective. Lower en block resection ratios (82.1% versus 42.2%) as opposed to EMR have associated with ESS and a lower local resection rates (0.6% versus 6.0%) than the ENR. ESD has also shown a higher EMR performance. Although there was little difference in the internal bleeding between the two techniques, ESD had connection to higher drilling levels (0.9 vs. 4.3 percent) than EMR. ESD's mean operational duration was greater than EMR. The long-term findings of ESD for early gastric cancer were evaluated in a retrospective analysis (2017) for Japan. There were reviews of 6456 total patient of ESD and 4202 patients who earned enhanced ESD confirmation. 0.22% of the absolute indicators were compared and 1.26% were aligned with the extended indicators. Most patients underwent endoscopic surgery as a further cure for recurrence. Recently, ESD gastric health and performance rates have risen to desirable conditions. Diagnostic ESD sometimes occurs when the pre-operative diagnosis is difficult for a full pathologic diagnosis. For the therapeutic strategies, this is most acceptable in the future.

### 2.3.2. Oesophagus

When more than 34<sup>th</sup> of the ring is extended as a circular or semicircular resection, postoperative stringency is sometimes observed. Although treating these lesions by endoscopic therapy is problematic, extreme dilatation may rescue them. An ESD versus EMR for diagnosis of superficial esophageal cancer was the latest study by Guo [17]. Increasing en-block resection (49.3% versus 97.1%), as well as a respective curative rate (92.3% versus 52.7%), were correlated with ESD as well as lower local recurrence risk (0.3% versus 11.5%) relative to EMR. During bleeding, ESD was associated with higher perforation rates of 4.0% vs. 1.3% than EMR, and postoperative esophageal rates were related.

### 2.3.3. Colon

A new meta-analysis of ESD vs. EMR have carried out [18] and was pre-operatically tested as not intrusive for colorectal lesions of more than 20 mm. The prevalence of ESD was higher than the EMR (89.9% versus 34.9%), the traditionally full incidence (77.6% versus 36.2%, respectively), and local recurrence rates (0.7% versus 12.7%) were smaller than that of EMR. While the perforation incidents of ESD were associated with higher (0.9 vs 4.9 percent) than EMR, the bleeding incidences of both techniques did not differ. At cost of a greater perforation risk, ESD achieves a higher en block rate and histologically complete resection than EMR. For prominent superficial lesions, piecemeal resection using EMR technology is commonly used, leading to successful clinical outcomes. The histopathological analysis is uncertain, and fragmentary resections have led to a high local recurrence risk (20%; 95% interval of trust: 16 - 25) [19].

For clear cancer tumors, thus, incomplete resection can be prevented. The European Society guidelines for endoscopical ESD enblock resection of colon or

rectal lesions of greatest significance were provided by the European Society for Gastrointestinal Endoscopy [20] [21].

Post-ESD bleeding was characterized as active bleeding from a post-ESD ulcer diagnosed with an emergency endoscopy or a scheduled endoscopy follow-up (**Figure 3**) [22].



**Figure 3.** Endoscopic presentation of excessive bleeding post-ESD ulcers have shown in figure. Paranormal bleeding was also referred to as post-ESD bleeding with such a significant chance of bleeding. They were cases of aggressive posterior ESD ulcer after water wash or a stream of water (Olympus) or uncovered arteries while a scheduled follow-up endoscopy was performed (**Figure 4**) [22].



**Figure 4.** Endoscopic appearance of post-ESD ulcers with apparently exposed vessels [22].

## 2.4. Adverse Events of Post ESD Bleeding

The most frequent adverse symptom associated with the ESD is post-ESD bleeding or bleeding during ESD. The blood rates following gastric ESD were found to range from 1.8% to 15.6%. Post-ESD bleeding typically requires endoscopic hemostasis of hemoglobin. A total of 76% of post-ESD bleeding occurred within 24 hours of ESD, even though it can occur at the nearest two weeks after a serious bleeding condition has been considered after post-ESD bleeding [5]. A study [23] suggested a stupid bleeding risk factor in the location of the tumor. Intermittent bleeding was more frequent in the upper third than those in the middle and bottom sections of the stomach mostly during the test. Independent research reported an increased risk of bleeding impaired during endoscopic mucosal resection [24]. Delayed hemorrhages, however, often vary from rapid hemorrhages, indicating that well-coagulated arteries never leak. Regularly scheduled use of medications that could be linked to gastrointestinal damage/hygiene in earlier studies is not a risk factor for post-ESD bleeding [23].

## 2.5. Risk Factors Associated with Delayed Bleeding

Many studies have been conducted with conflicting results for identifying risks to PPB after gastric EMR and endoscopic sub-mucosal (ESD). Lebanon [3] addressed risk factors in his analysis in 2016, which do not change for various designs, for example, the combined PPB average was 5.1 percent (95% trust, 4.5 - 5.7 percent). Significant complications have been reported including male, cardiopathic and anti-thrombotic drugs. There was no evidence of cirrhosis, renal dysfunction, tumor thickness, tissue resection, and curvature. PPB-related structural issues involve the system duration of 60 minutes and the usage of histamine-2 receptor antagonists. Nevertheless, a primary risk factor for heparin substitution was found, suggested after the elimination of oral anticoagulants. Post-operative bleeding was described as bleeding events, like h after an endoscopic hangover or decrease in hemoglobin rates of over 2 mg/dL relative to preoperative hemoglobin. Second-look PPB endoscopy (OR 1.34; 95% Confidence period, 85% to 2.12%) was not correlated with decreased PPB, and the study concluded that PPB risk factors were established, which may help to direct management following gastric ESD, namely to change more control. Endoscopy of the second look is not linked to reduced PPB [3]. Continuous treatment with antiplatelet agents was not a postoperative risk factor for bleeding after gastric ESD, according to recommendations, according to Shindo [5]. However, a major risk factor for heparin substitution has been reported, which is advised after eliminating oral anticoagulants. Postoperative bleeding was described as bleeding episodes, such as hematemesis and melena, after a treatment requiring endoscopy or a reduction in hemoglobin levels in excess in 2 mg/dL relative to preoperative hemoglobin. The study [24] that the beginner's coagulation tumor in the antrum and pharmacy constitute significant risk factors for post-ESD bleeding. The study [1] that ulcer margin bleeding frequently occurs with beginner operators.

## 2.6. Preventive Methods

The therapeutically selected interventional endoscopy (ESD) has been improved, decreasing the number of patients confirmed to have surgical resections [25] [26] [27], and the endoscopic sub-mucosal resections (ESD). (EMR) have been increased. Compared to an operating procedure, endoscopic resection offers a reduced cost of invasion, requiring small hospital and quick release [27] [28] [29]. For the therapy of colon colorectal tumors and adenomas, EMR is broadly acknowledged [30]-[39]. The resection (“en bloc”) rates in RMEs were 66.6% - 80% and were demonstrated as high with <20 mm tumor size [40]. In this case, resection is necessary, allowing the lateral tumor margins to be examined histologically. Sadly big lesions require resection by piecemeal, which increases the risk of recurrence. Recent results also shown that “piecemeal” has an incomplete resection rate slightly higher than “en-block” (18.9 vs. 12.6%),  $p = 0.01$  [41]. Scientific signs for ESDs are also lesions that would be quite challenging to resect from traditional EMR, which include abnormalities with underprivileged or pro-lifting conditions following submucosal injection, recurrent local infections following prior treatment, and relatively large outbreaks of [42] [43] [44] ESD endoscopic “en block” (en block) resection for the removal of the colon and rectal lesions with a strong suspicion of restricted submucosal invasion based on two significant parameters of stressed morphology and irregular or non-granular surface form, in specific, when the lesions are greater than 20 mm, or in terms of color, has recently suggested by the “European Society of Gastrointestinal Endoscopy” (ESGE) guidelines. This research is therefore intended to identify a suitable approach to reduce the chance of bleeding during ESD.

## 3. Conclusions

The aspect of a critical review of the post-endoscopic sub-mucosal dissection and delayed bleeding factors holds that a series of risks, such as a pooled blood pressure rate, was comparatively higher. Carcinoma and ulceration related histology can be termed a significant risk factor, which can be addressed by implementation of histamine-2 receptor antagonists instead of the proton pump. The use of antiplatelet agents as per guidelines can work on ensuring better health outcomes among the patients.

The events related to bleeding at ulcer margins are a few risk factors. However, the proactive steps to manage the existing range of problems. Furthermore, it can be conclusively stated that there needs to be an immense series of modern medical interventions that must be appropriately guided and managed to ensure better health outcomes. The current study proposed further studies in regards to the current scenario promising better medical procedures.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- [1] Sumiyoshi, T., Kondo, H., Minagawa, T., Fujii, R., Sakata, K., Inaba, K. and Oyamada, Y. (2017) Risk Factors and Management for Gastric Stenosis after Endoscopic Submucosal Dissection for Gastric Epithelial Neoplasm. *Gastric Cancer*, **20**, 690-698. <https://doi.org/10.1007/s10120-016-0673-6>
- [2] Lian, J., Chen, S., Zhang, Y. and Qiu, F. (2012) A Meta-Analysis of Endoscopic Submucosal Dissection and EMR for Early Gastric Cancer. *Gastrointestinal Endoscopy*, **76**, 763-770. <https://doi.org/10.1016/j.gie.2012.06.014>
- [3] Libânio, D., Costa, M.N., Pimentel-Nunes, P. and Dinis-Ribeiro, M. (2016) Risk Factors for Bleeding after Gastric Endoscopic Submucosal Dissection: A Systematic Review and Meta-Analysis. *Gastrointestinal Endoscopy*, **84**, 572-586. <https://doi.org/10.1016/j.gie.2016.06.033>
- [4] Park, Y.M., Cho, E., Kang, H.Y. and Kim, J.M. (2011) The Effectiveness and Safety of Endoscopic Submucosal Dissection Compared with Endoscopic Mucosal Resection for Early Gastric Cancer: A Systematic Review and Meta-Analysis. *Surgical Endoscopy*, **25**, 2666-2677. <https://doi.org/10.1007/s00464-011-1627-z>
- [5] Shindo, Y., Matsumoto, S., Miyatani, H., Yoshida, Y. and Mashima, H. (2016) Risk Factors for Postoperative Bleeding after Gastric Endoscopic Submucosal Dissection in Patients under Antithrombotics. *World Journal of Gastrointestinal Endoscopy*, **8**, 349. <https://doi.org/10.4253/wjge.v8.i7.349>
- [6] Shiga, H., Kuroha, M., Endo, K., Kimura, T., Kakuta, Y., Kinouchi, Y., Shimosegawa, T., et al. (2015) Colorectal Endoscopic Submucosal Dissection (ESD) Performed by Experienced Endoscopists with Limited Experience in Gastric ESD. *International Journal of Colorectal Disease*, **30**, 1645-1652. <https://doi.org/10.1007/s00384-015-2334-3>
- [7] Nishizawa, T. and Yahagi, N. (2017) Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection: Technique and New Directions. *Current Opinion in Gastroenterology*, **33**, 315-319. <https://doi.org/10.1097/MOG.0000000000000388>
- [8] De Ceglie, A., Hassan, C., Mangiavillano, B., Matsuda, T., Saito, Y., Ridola, L. and Conio, M. (2016) Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection for Colorectal Lesions: A Systematic Review. *Critical Reviews in Oncology Hematology*, **104**, 138-155. <https://doi.org/10.1016/j.critrevonc.2016.06.008>
- [9] Arimoto, J., Higurashi, T., Kato, S., Fuyuki, A., Ohkubo, H., Nonaka, T. and Taguri, M. (2018) Risk Factors for Post-Colorectal Endoscopic Submucosal Dissection (ESD) Coagulation Syndrome: A Multicenter, Prospective, Observational Study. *Endoscopy International Open*, **6**, E342-E349. <https://doi.org/10.1055/s-0044-101451>
- [10] Choi, C.W., Kang, D.H., Kim, H.W., Hong, J.B., Park, S.B., Kim, S.J. and Cho, M. (2015) High Dose Proton Pump Inhibitor Infusion versus Bolus Injection for the Prevention of Bleeding after Endoscopic Submucosal Dissection: A Prospective Randomized Controlled Study. *Digestive Diseases and Sciences*, **60**, 2088-2096. <https://doi.org/10.1007/s10620-015-3560-9>
- [11] Koh, R., Hirasawa, K., Yahara, S., Oka, H., Sugimori, K., Morimoto, M., Taguri, M., et al. (2013) Antithrombotic Drugs Are Risk Factors for Delayed Postoperative Bleeding after Endoscopic Submucosal Dissection for Gastric Neoplasms. *Gastrointestinal Endoscopy*, **78**, 476-483. <https://doi.org/10.1016/j.gie.2013.03.008>
- [12] Tomita, T., Kim, Y., Yamasaki, T., Okugawa, T., Kondo, T., Toyoshima, F. and Fukui, H. (2012) A Prospective Randomized Controlled Trial to Compare the Effects of Omeprazole and Famotidine in Preventing Delayed Bleeding and Promoting Ulcer Healing after Endoscopic Submucosal Dissection. *Journal of Gastroenterology and Hepatology*, **27**, 1441-1446. <https://doi.org/10.1111/j.1440-1746.2012.07144.x>

- [13] Goto, O., Fujishiro, M., Kodashima, S., Ono, S., Niimi, K., Hirano, K., Koike, K., *et al.* (2010) A Second-Look Endoscopy after Endoscopic Submucosal Dissection for Gastric Epithelial Neoplasm May Be Unnecessary: A Retrospective Analysis of Postendoscopic Submucosal Dissection Bleeding. *Gastrointestinal Endoscopy*, **71**, 241-248. <https://doi.org/10.1016/j.gie.2009.08.030>
- [14] Nomura, M., Fujita, N., Matsunaga, A., Uchimi, K., Noda, Y., Yuki, T. and Utsunomiya, K. (2001) Scratch-Stick-Method for Endoscopic Mucosal Resection of Colorectal Tumors. *Gastroenterological Endoscopy*, **43**, 1821-1827.
- [15] Deyhle, P., Largiader, F., Jenny, S. and Fumagalli, I. (1973) A Method for Endoscopic Electroresection of Sessile Colonic Polyps. *Endoscopy*, **5**, 38-40. <https://doi.org/10.1055/s-0028-1098209>
- [16] Facciorusso, A., Antonino, M., Di Maso, M. and Muscatiello, N. (2014) Endoscopic Submucosal Dissection vs Endoscopic Mucosal Resection for Early Gastric Cancer: A Meta-Analysis. *World Journal of Gastrointestinal Endoscopy*, **6**, 555. <https://doi.org/10.4253/wjge.v6.i11.555>
- [17] Guo, H.M., Zhang, X.Q., Chen, M., Huang, S.L. and Zou, X.P. (2014) Endoscopic Submucosal Dissection vs Endoscopic Mucosal Resection for Superficial Esophageal Cancer. *World Journal of Gastroenterology: WJG*, **20**, 5540. <https://doi.org/10.3748/wjg.v20.i18.5540>
- [18] Arezzo, A., Passera, R., Marchese, N., Galloro, G., Manta, R. and Cirocchi, R. (2016) Systematic Review and Meta-Analysis of Endoscopic Submucosal Dissection vs Endoscopic Mucosal Resection for Colorectal Lesions. *United European Gastroenterology Journal*, **4**, 18-29. <https://doi.org/10.1177/2050640615585470>
- [19] Belderbos, T.D., Leenders, M., Moons, L.M. and Siersema, P.D. (2014) Local Recurrence after Endoscopic Mucosal Resection of Nonpedunculated Colorectal Lesions: Systematic Review and Meta-Analysis. *Endoscopy*, **46**, 388-402. <https://doi.org/10.1055/s-0034-1364970>
- [20] Pimentel-Nunes, P., Dinis-Ribeiro, M., Ponchon, T., Repici, A., Vieth, M., De Ceglie, A. and Conio, M. (2015) Endoscopic Submucosal Dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*, **47**, 829-854. <https://doi.org/10.1055/s-0034-1392882>
- [21] Yahagi, N. and Nishizawa, T. (2017) Mucosal Endoscopic Resection and Submucosal Endoscopy: Science and New Paths. *Gastroenterology Opinion*, **33**, 315-319. <https://doi.org/10.1097/MOG.0000000000000388>
- [22] Mukai, S., Cho, S., Kotachi, T., Shimizu, A., Matuura, G., Nonaka, M., Nakanishi, T., *et al.* (2012) Analysis of Delayed Bleeding after Endoscopic Submucosal Dissection for Gastric Epithelial Neoplasms. *Gastroenterology Research and Practice*, **2012**, Article ID: 875323. <https://doi.org/10.1155/2012/875323>
- [23] Takizawa, K., Oda, I., Gotoda, T., Yokoi, C., Matsuda, T., Saito, Y. and Ono, H. (2008) Routine Coagulation of Visible Vessels May Prevent Delayed Bleeding after Endoscopic Submucosal Dissection—An Analysis of Risk Factors. *Endoscopy*, **40**, 179-183. <https://doi.org/10.1055/s-2007-995530>
- [24] Okano, A., Hajiro, K., Takakuwa, H., Nishio, A. and Matsushita, M. (2003) Predictors of Bleeding after Endoscopic Mucosal Resection of Gastric Tumors. *Gastrointestinal Endoscopy*, **57**, 687-690. <https://doi.org/10.1067/mge.2003.192>
- [25] Kaltenbach, T., Binmoeller, K., Kalindindi, V. and Soetikno, R. (2008) Endoscopic Resection of Large Colorectal Lesions in the United States in a Referral Center Is a Dominant Strategy-Long-Term Efficacy and Cost Analysis Results: 533. *American Journal of Gastroenterology*, **103**, S206. <https://doi.org/10.14309/0000434-200809001-00533>

- [26] Soetikno, R. and Gotoda, T. (2009) Con: Colonoscopic Resection of Large Neoplastic Lesions Is Appropriate and Safe. *American Journal of Gastroenterology*, **104**, 272-275. <https://doi.org/10.1038/ajg.2009.75>
- [27] Longcroft-Wheaton, G., Duku, M., Mead, R., Basford, P. and Bhandari, P. (2013) Risk Stratification System for Evaluation of Complex Polyps Can Predict Outcomes of Endoscopic Mucosal Resection. *Diseases of the Colon & Rectum*, **56**, 960-966. <https://doi.org/10.1097/DCR.0b013e31829193e0>
- [28] Repici, A., Pellicano, R., Strangio, G., Danese, S., Fagoonee, S. and Malesci, A. (2009) Endoscopic Mucosal Resection for Early Colorectal Neoplasia: Pathologic Basis, Procedures, and Outcomes. *Diseases of the Colon & Rectum*, **52**, 1502-1515. <https://doi.org/10.1007/DCR.0b013e3181a74d9b>
- [29] Swan, M.P., Bourke, M.J., Alexander, S., Moss, A. and Williams, S.J. (2009) Large Refractory Colonic Polyps: Is It Time to Change Our Practice? A Prospective Study of the Clinical and Economic Impact of a Tertiary Referral Colonic Mucosal Resection and Polypectomy Service (with Videos). *Gastrointestinal Endoscopy*, **70**, 1128-1136. <https://doi.org/10.1016/j.gie.2009.05.039>
- [30] Wang, J., Zhang, X.H., Ge, J., Yang, C.M., Liu, J.Y. and Zhao, S.L. (2014) Endoscopic Submucosal Dissection vs Endoscopic Mucosal Resection for Colorectal Tumors: A Meta-Analysis. *World Journal of Gastroenterology: WJG*, **20**, 8282. <https://doi.org/10.3748/wjg.v20.i25.8282>
- [31] Belle, S., Haase, L., Pilz, L.R., Post, S., Ebert, M. and Kaehler, G. (2014) Recurrence after Endoscopic Mucosal Resection—Therapy Failure? *International Journal of Colorectal Disease*, **29**, 209-215. <https://doi.org/10.1007/s00384-013-1783-9>
- [32] Kim, H.S.E. and Cho, E.J. (2014) What Can Be the Criteria of Outpatient-Based Endoscopic Resection for Colon Polyp? *World Journal of Gastrointestinal Endoscopy*, **6**, 493. <https://doi.org/10.4253/wjge.v6.i10.493>
- [33] Knabe, M., Pohl, J., Gerges, C., Ell, C., Neuhaus, H. and Schumacher, B. (2014) Standardized Long-Term Follow-Up after Endoscopic Resection of Large, Nonpedunculated Colorectal Lesions: A Prospective Two-Center Study. *American Journal of Gastroenterology*, **109**, 183-189. <https://doi.org/10.1038/ajg.2013.419>
- [34] Hong, Y.M., Kim, H.W., Park, S.B., Choi, C.W. and Kang, D.H. (2015) Endoscopic Mucosal Resection with Circumferential Incision for the Treatment of Large Sessile Polyps and Laterally Spreading Tumors of the Colorectum. *Clinical Endoscopy*, **48**, 52. <https://doi.org/10.5946/ce.2015.48.1.52>
- [35] Kashani, A., Lo, S.K. and Jamil, L.H. (2016) Cap-Assisted Endoscopic Mucosal Resection Is Highly Effective for Nonpedunculated Colorectal Lesions. *Journal of Clinical Gastroenterology*, **50**, 163-168. <https://doi.org/10.1097/MCG.0000000000000315>
- [36] Oka, S., Tanaka, S., Saito, Y., Iishi, H., Kudo, S.E., Ikematsu, H., Hisabe, T., *et al.* (2015) Local Recurrence after Endoscopic Resection for Large Colorectal Neoplasia: A Multicenter Prospective Study in Japan. *The American Journal of Gastroenterology*, **110**, 697-707. <https://doi.org/10.1038/ajg.2015.96>
- [37] Curcio, G., Granata, A., Ligresti, D., Tarantino, I., Barresi, L., Liotta, R. and Traina, M. (2015) Underwater Colorectal EMR: Remodeling Endoscopic Mucosal Resection. *Gastrointestinal Endoscopy*, **81**, 1238-1242. <https://doi.org/10.1016/j.gie.2014.12.055>
- [38] Voudoukis, E., Tribonias, G., Tavernaraki, A., Theodoropoulou, A., Vardas, E., Paraskeva, K., Paspatis, G.A., *et al.* (2015) Use of a Double-Channel Gastroscope Reduces Procedural Time in Large Left-Sided Colonic Endoscopic Mucosal Resections. *Clinical Endoscopy*, **48**, 136. <https://doi.org/10.5946/ce.2015.48.2.136>

- [39] Binmoeller, K.F., Hamerski, C.M., Shah, J.N., Bhat, Y.M., Kane, S.D. and Garcia-Kennedy, R. (2015) Attempted Underwater En Block Resection for Large (2-4 cm) Colorectal Laterally Spreading Tumors (with Video). *Gastrointestinal Endoscopy*, **81**, 713-718. <https://doi.org/10.1016/j.gie.2014.10.044>
- [40] Nakajima, T., Saito, Y., Tanaka, S., Iishi, H., Kudo, S.E., Ikematsu, H., Hisasbe, T., *et al.* (2013) Current Status of Endoscopic Resection Strategy for Large, Early Colorectal Neoplasia in Japan. *Surgical Endoscopy*, **27**, 3262-3270. <https://doi.org/10.1007/s00464-013-2903-x>
- [41] Cipolletta, L., Rotondano, G., Bianco, M.A., Buffoli, F., Gizzi, G. and Tessari, F. (2014) Endoscopic Resection for Superficial Colorectal Neoplasia in Italy: A Prospective Multicentre Study. *Digestive and Liver Disease*, **46**, 146-151. <https://doi.org/10.1016/j.dld.2013.09.019>
- [42] Rahmi, G., Hotayt, B., Chaussade, S., Lepilliez, V., Giovannini, M., Coumaros, D., Prat, F., *et al.* (2014) Endoscopic Submucosal Dissection for Superficial Rectal Tumors: Prospective Evaluation in France. *Endoscopy*, **46**, 670-676. <https://doi.org/10.1055/s-0034-1365810>
- [43] Bialek, A., Pertkiewicz, J., Karpinska, K., Marlicz, W., Bielicki, D. and Starzynska, T. (2014) Treatment of Large Colorectal Neoplasms by Endoscopic Submucosal Dissection: A European Single-Center Study. *European Journal of Gastroenterology & Hepatology*, **26**, 607-615. <https://doi.org/10.1097/MEG.000000000000079>
- [44] Agapov, M. and Dvoynikova, E. (2014) Factors Predicting Clinical Outcomes of Endoscopic Submucosal Dissection in the Rectum and Sigmoid Colon during the Learning Curve. *Endoscopy International Open*, **2**, E235-E240. <https://doi.org/10.1055/s-0034-1377613>