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Review Article

Management of antithrombotic agents and current issues in patients undergoing endoscopic submucosal dissection

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ABSTRACT

Postoperative bleeding is a common adverse event in endoscopic submucosal dissection (ESD) and may be life-threatening. Postoperative bleeding occurs frequently in patients treated with antithrombotic agents, including aspirin, antiplatelet agents, warfarin, and non-vitamin K-dependent oral anticoagulants. Due to the aging population and the increase in the risk of thromboembolic disease, the number of patients who require antithrombotic therapy has increased. To date, several clinical studies have been conducted and several global guidelines have been updated. Nevertheless, determining the optimal use of antithrombotic agents in patients undergoing ESD is still challenging, and recommendations for the use of these agents vary slightly across different guidelines. In this review, I summarized the current guidelines and discussed several ongoing issues with the management of antithrombotic agents in patients undergoing ESD.

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Keywords: Anticoagulants; Antiplatelet agent; Antithrombotic agent; Aspirin; Endoscopic mucosal resection

Introduction

Endoscopic submucosal dissection (ESD) is a minimally invasive technique, that is widely used for the management of early gastrointestinal tumors, especially in Asia.^{1–3} It has the advantage of providing higher *en bloc* and complete resection rates compared to endoscopic mucosal resection (EMR).⁴ However, postoperative bleeding, which can be life-threatening, is a concern following ESD.^{5,6} The incidence of post-ESD bleeding ranges between 0% to 15.6% for gastric ESD,^{7,8} 1.5% to 6.6% for colorectal ESD,^{8–12} and 0% to 5.2% for esophageal ESD.^{8,13,14}

The concern for postoperative bleeding is even greater when patients taking antithrombotic agents require ESD. As the population ages and the risk of thromboembolic disease increases, the number of patients who require antithrombotic therapy also increases.^{15,16} Moreover, various antithrombotic medications, including aspirin, nonsteroidal anti-inflammatory drugs, adenosine diphosphate receptor/P2Y₁₂ inhibitors, glycoprotein IIb/IIIa inhibitors, prostacyclin, thromboxane inhibitors, phosphodiesterase inhibitors, vitamin K antagonists, heparin, and non-vitamin K-dependent oral anticoagulants (NOAC), are available.¹⁷ To cope with these changes, many clinical studies are being conducted and sev-

eral global guidelines are being updated.^{17–23} Additionally, a web-based application has recently been developed to help manage antithrombotic agents before endoscopy.²⁴ Nevertheless, the use of antithrombotic agents in patients undergoing endoscopy is still complex and recommendations for the use of these agents vary slightly across different guidelines. In this review, I summarize the recommendations from recent guidelines and discuss several issues with the management of antithrombotic agents in patients undergoing ESD.

Review of Recent Guidelines

The major statements on antithrombotic agents that focus on ESD in the recent guidelines are summarized in Table 1.^{17–23} Most guidelines recommend the management of antithrombotic therapy according to the risk of bleeding during endoscopic procedures. However, in the American Society for Gastrointestinal Endoscopy (ASGE) guidelines published in 2009, the risk of bleeding due to ESD had not been rated but polypectomy was considered a high-risk procedure.¹⁸ Thus, we applied the following statement to ESD: “When high-risk procedures are planned, clinicians may elect to discontinue aspirin and/or nonsteroidal anti-inflammatory drugs

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Table 1 Summary of Endoscopic Submucosal Dissection-Related Statements in the Recent Guidelines of Antithrombotic Agents

ASGE (2009) ¹⁸	
Overall assessment of ESD for risk of bleeding	Not done.
	Polypectomy is considered a high-risk procedure.
Major statements related to high-risk procedures	
Antiplatelet agent	Aspirin and/or NSAIDs may be continued for all endoscopic procedures.
	When high-risk procedures are planned, clinicians may elect to discontinue aspirin and/or NSAIDs for 5 to 7 days before the procedure, depending on the underlying indication for antiplatelet therapy.
ASGE (2016) ¹⁷	
Overall assessment of ESD for risk of bleeding	Higher-risk procedure
	EMR and polypectomy are considered as higher-risk procedures.
Major statements related to high-risk procedures	
Antiplatelet agent	We suggest that continuation of low doses of ASA and nonsteroidal anti-inflammatory drugs may be continued safely in the periendoscopic period.
	We recommend discontinuation of thienopyridines at least 5 to 7 days before high-risk endoscopic procedure or switching to ASA monotherapy and continuing until the thienopyridine can be safely resumed.
	We suggest that thienopyridines be withheld for at least 5 to 7 days (ticagrelor 3–5 days) before high-risk endoscopic procedures and that ASA be continued for patients requiring dual antiplatelet agent.
Anticoagulant	We suggest discontinuing anticoagulation (i.e., warfarin [Coumadin], NOACs) for the appropriate drug-specific interval in the periendoscopic period if high-risk.
	We suggest bridge therapy for patients undergoing high-risk endoscopic procedures who are at high risk for thromboembolic events.
	We suggest that warfarin (Coumadin) be restarted on the same day as the procedure in all patients who do not have ongoing bleeding.
	We suggest that the reinitiation of NOACs after high-risk endoscopic procedures be delayed until adequate hemostasis is ensured, given their rapid onset of action and lack of reversal agents. If therapeutic doses of NOACs cannot be restarted within 12 to 24 hours after a high-risk endoscopic procedure, thromboprophylaxis (i.e., UFH bridge) should be considered to decrease risk of thromboembolism, given the short half-life of the NOAC agent, in those with a high risk for thromboembolism.
ESGE (2011) ¹⁹	
Overall assessment of ESD for risk of bleeding	High-risk procedure
	EMR and colonic polypectomy > 1 cm are considered as high-risk procedures.
Major statements related to the high-risk procedures	
Antiplatelet agent	Both techniques (ESD and EMR) have always been performed after withholding antiplatelet agent; a short washout period has been associated with more post-procedure bleeding after gastric ESD. For EMR and ESD, discontinuation of all antiplatelet agent, including aspirin, is recommended provided the patient is not at high risk for a thrombotic event.
ESGE (2016) ²⁰	
Overall assessment of ESD for risk of bleeding	High-risk procedure
	EMR and endoscopic polypectomy are considered as high-risk procedures.
Major statements related to high-risk procedures	
Antiplatelet agent	For all endoscopic procedures we recommend continuing aspirin, with the exception of ESD, large colonic EMR (> 2 cm), upper gastrointestinal EMR and ampullectomy. In the latter cases, aspirin discontinuation should be considered on an individual patient basis depending on the risks of thrombosis versus haemorrhage.
	For high-risk endoscopic procedures in patients at low thrombotic risk, we recommend discontinuing P2Y ₁₂ receptor antagonists (e.g., clopidogrel) five days before the procedure. In patients on dual antiplatelet therapy, we suggest continuing aspirin.
	For high-risk endoscopic procedures in patients at high thrombotic risk, we recommend continuing aspirin and liaising with a cardiologist about the risk/benefit of discontinuing P2Y ₁₂ receptor antagonists (e.g., clopidogrel).

Table 1 Continued

Anticoagulant
For high-risk endoscopic procedures in patients at low thrombotic risk, we recommend discontinuing warfarin 5 days before the procedure. Check INR prior to the procedure to ensure < 1.5.
For high-risk endoscopic procedures in patients at high thrombotic risk, we recommend that warfarin should be temporarily discontinued and substituted with LMWH.
For high-risk endoscopic procedures in patients on NOACs, we recommend that the last dose of NOACs be taken at least 48 hr before the procedure. For patients on dabigatran with a creatinine clearance (or estimated glomerular filtration rate) of 30 to 50 mL/min we recommend that the last dose be taken 72 hr prior to the procedure. In any patient with rapidly deteriorating renal function a haematologist should be consulted.
JGES (2014) ²¹
Overall assessment of ESD for risk of bleeding
High-risk procedure
EMR and polypectomy are considered as high-risk procedures.
Major statements related to high-risk procedures
Antiplatelet agent
For gastroenterological endoscopic procedures that carry a high risk of bleeding, withdrawal of aspirin monotherapy is not required in patients who would be placed at high risk of thromboembolism by withdrawal. Aspirin can be withdrawn for 3 to 5 days in patients at low risk of thromboembolism.
Withdrawal of non-aspirin antiplatelet agents is required in gastroenterological endoscopic procedures that carry a high bleeding risk. Thienopyridine derivatives should be withdrawn for 5 to 7 days, but 1 day is sufficient for all other antiplatelet agents. Replacement with aspirin or cilostazol is required in patients at high risk of thromboembolism.
Anticoagulant
For gastroenterological endoscopic procedures that carry a high risk of bleeding, warfarin or dabigatran should be replaced with heparin.
General
After temporary withdrawal of antithrombotics, the same regimen should be re-established as soon as hemostasis has been confirmed. Ongoing monitoring for signs of bleeding is required after resumption.
JGES (2018) ²² – Appendix on anticoagulants including NOAC
Major statements related to high-risk procedures
Anticoagulant
For gastroenterological endoscopic procedures with a high risk of bleeding in patients on warfarin therapy, heparin replacement may increase the risk of postoperative bleeding. As an alternative to heparin replacement, continued warfarin treatment in patients where the INR falls within the therapeutic range, or a temporary switch to NOAC in those with non-valvular atrial fibrillation, should be considered during endoscopic procedures.
For gastroenterological endoscopic procedures with a high risk of bleeding, patients taking warfarin in combination with antiplatelet agents (aspirin and thienopyridine) should be handled with care depending on the individual patient's condition, and it is better to postpone the procedures until the antithrombotic withdrawal. If procedures with a high bleeding risk cannot be postponed, aspirin or cilostazol should be given in combination with continued warfarin treatment (maintaining the INR within the therapeutic range) or heparin replacement. In patients with non-valvular atrial fibrillation, a temporary switch from warfarin to NOAC is also permitted prior to the procedure.
For gastroenterological endoscopic procedures with a high risk of bleeding, patients receiving NOAC treatment should continue to receive NOAC orally until the day prior to the procedure and discontinue NOAC on the morning of the procedure. Oral administration of NOAC may be resumed on the morning after the procedure.
For gastroenterological endoscopic procedures with a high risk of bleeding, patients taking NOAC in combination with antiplatelet agents should be handled with care depending on the individual patient's condition. It is better to postpone procedures until antithrombotic withdrawal. According to need, procedures with a high bleeding risk can be carried out on antiplatelet monotherapy with aspirin or cilostazol. NOAC oral administration may be discontinued on the morning of the procedure and resumed on the morning after the procedure.
APAGE/APSDE (2018) ²³
Overall assessment of ESD for risk of bleeding
Ultrahigh-risk procedure
EMR of large (> 2 cm) polyps is considered as an ultra-high risk procedure; however, polypectomy is considered as a high-risk procedure.
Single antiplatelet therapy
We do not recommend discontinuation of aspirin except in ultra-high risk procedures.
We recommend withholding P2Y ₁₂ receptor inhibitor 5 days before the procedure.
We recommend resuming P2Y ₁₂ receptor inhibitor once adequate haemostasis has been achieved.
Dual antiplatelet therapy
Except for ultra-high risk procedures that may require stopping both antiplatelet agents, we recommend withholding P2Y ₁₂ receptor inhibitor for 5 days before the procedure while aspirin should be continued.
We recommend resuming P2Y ₁₂ receptor inhibitor once adequate haemostasis has been achieved.

Table 1 Continued

Warfarin
We recommend stopping warfarin 5 days before the procedure.
In patients with low thromboembolic risk, we recommend endoscopic procedures to be undertaken if INR is below 2.0.
In patients with high thromboembolic risk, we recommend bridging with heparin when INR is below 2.0 before endoscopic procedures.
We recommend resuming warfarin once adequate haemostasis has been achieved.
In patients with high thromboembolic risk, we recommend bridging with heparin after the procedure until INR reaches therapeutic range.
NOACs
We recommend withholding NOACs at least 48 hr before the procedure.
We do not recommend bridging anticoagulation.
We recommend resuming NOACs after adequate haemostasis has been achieved.
We recommend resuming DOACs after adequate haemostasis has been achieved.

ASGE, American Society for Gastrointestinal Endoscopy; ESD, endoscopic submucosal dissection; NSAID, nonsteroidal anti-inflammatory drug; ASA, acetylsalicylic acid; NOAC, non-vitamin K-dependent oral anticoagulant; UFH, unfractionated heparin; EMR, endoscopic mucosal resection; ESGE, European Society of Gastrointestinal Endoscopy; INR, international normalized ratio; LMWH, low molecular weight heparin; JGES, Japan Gastroenterological Endoscopy Society; APAGE, Asian Pacific Association of Gastroenterology; APSDE, Asian Pacific Society for Digestive Endoscopy.

for 5 to 7 days before the procedure, depending on the underlying indication for antiplatelet therapy.” In the ASGE guideline published in 2016, ESD was rated as a higher-risk procedure, similar to EMR and polypectomy.¹⁷ In this guideline many new statements were developed regarding the use of antiplatelet agents and anticoagulants. Summaries of the recommendations for the use of antiplatelet agents in high-risk procedures are: (1) low-dose aspirin may be continued during the perioperative period, (2) monotherapy with thienopyridine derivatives can be discontinued or switched to low-dose aspirin monotherapy during the perioperative period, and (3) dual antiplatelet therapy can be replaced with low-dose aspirin monotherapy during the perioperative period. Regarding anticoagulants, the guideline recommends that anticoagulants be discontinued during the perioperative period and replaced with heparin-bridge therapy in patients at a high risk of thromboembolic events. Compared to the previous version of the guideline, the 2016 ASGE guideline emphasized the continuation of low-dose aspirin during ESD.

In the European Society of Gastrointestinal Endoscopy (ESGE) guidelines published in 2011 and 2016, ESD, EMR, and polypectomy were considered high-risk procedures.^{19,20} In the 2011 ESGE guideline, discontinuation of all antiplatelet agents was recommended for both EMR and ESD if the patient was not at a high risk of thromboembolic events.¹⁹ In the 2016 ESGE guidelines, however, continuation of low-dose aspirin is recommended during ESD in patients undergoing dual antiplatelet therapy.²⁰ Low-dose aspirin or P2Y₁₂ receptor antagonist monotherapy can be discontinued during the perioperative period if patients are at a low risk of thromboembolic events. The recent guidelines also support the continuation of low-dose aspirin during ESD in patients at a high risk of thromboembolic events. For anticoagulation therapy, it is recommended that warfarin be discontinued in patients at a low risk of thromboembolic events and be replaced with low molecular weight heparin during the perioperative period in patients at a high risk of thromboembolic events.

The Japan Gastroenterological Endoscopy Society (JGES) guidelines published in 2014 also classified ESD, EMR, and polypectomy as high-risk procedures.²¹ The JGES guidelines support the continuation of low-dose aspirin during ESD in patients at a high risk of thromboembolic events. The discontinuation of thienopyridine derivatives is recommended during ESD. However, their replacement with aspirin or cilostazol is recommended in

patients at a high risk of thromboembolic events. Additionally, it is recommended that warfarin and dabigatran be replaced with heparin during the perioperative period. In 2018, the JGES published further statements concerning anticoagulants including NOAC.²² Recommendations different from those in other guidelines were presented. These recommendations are: “For gastroenterological endoscopic procedures with a high risk of bleeding in patients on warfarin therapy, heparin replacement may increase the risk of postoperative bleeding. As an alternative to heparin replacement, continued warfarin treatment in patients where the international normalized ratio falls within the therapeutic range, or a temporary switch to NOAC in those with non-valvular atrial fibrillation, should be considered during endoscopic procedures.”²² These statements are notable because the existing guidelines recommend either the discontinuation of warfarin or heparin-bridge therapy according to the risk of thromboembolic events. On the contrary, the 2018 JGES guidelines suggest that the continuation of warfarin may be better than heparin-bridge therapy in patients at a high risk of thromboembolic events.

The joint Asian Pacific Association of Gastroenterology (APAGE) and Asian Pacific Society for Digestive Endoscopy (APSDE) guidelines were published in 2018.²³ The most important difference between these and other guidelines is that ESD was rated as an ultrahigh-risk procedure. A category for ultrahigh-risk procedures was added to the APAGE/APSDE guidelines because: (1) ESD is frequently performed in this area of the world, (2) many relevant studies were conducted in Asia, and (3) the opinions and clinical practice patterns for the management of antithrombotic agents significantly differ between Eastern and Western endoscopists.^{23,25,26} For high-risk procedures such as polypectomy, it is recommended that low-dose aspirin be continued in patients undergoing low-dose aspirin monotherapy or dual anti-platelet therapy. However, this recommendation does not apply to an ultrahigh-risk procedure such as ESD. In other words, the discontinuation of low-dose aspirin in patients who are scheduled for ESD may be considered. For anticoagulation therapy, heparin-bridge therapy is recommended for patients who are undergoing treatment with warfarin, but not those being treated with NOAC.

The recent guidelines have two concepts in common: (1) the risk of bleeding following ESD is high or ultrahigh and (2) antithrombotic agents should be discontinued based on the risk of thromboembolic events. However, there are issues with differ-

ences in the guidelines around the management of antithrombotic agents. These issues are: (1) the continuation of low-dose aspirin in patients at a high risk of thromboembolic events (such as those with dual antiplatelet therapy), (2) differences in the risk of bleeding or thromboembolic events between patients in Eastern and Western countries, and (3) the recommendation of heparin-bridge therapy during ESD in patients at a high risk of thromboembolic events. These issues will be discussed in the subsequent sections.

Continuation of Low-Dose Aspirin Therapy during ESD

Although the APAGE/APSDE guidelines do not recommend the continuation of low-dose aspirin therapy during ultrahigh-risk procedures such as ESD, most guidelines suggest that low-dose aspirin therapy can be continued even during ESD. Such a recommendation is based on the results of several studies that showed that low-dose aspirin did not increase the post-ESD bleeding rate.^{27–29} A meta-analysis found that aspirin did not significantly increase post-ESD bleeding (odds ratio [95% confidence interval]: 1.81 [0.85–3.83]).³⁰ Considering that thromboembolic events usually result in more serious sequelae than post-ESD bleeding, the continuation of low-dose aspirin therapy during ESD is reasonable for patients at a high thromboembolic risk.

Given that a meta-analysis showed that low-dose aspirin had a tendency of increasing post-ESD bleeding in patients, the continued use of low-dose aspirin may be of concern in patients at a higher risk of bleeding, such as those undergoing dual antiplatelet therapy. In a study by Cho et al,³¹ which was included in the abovementioned meta-analysis, the post-ESD bleeding rate was 3.4% in aspirin non-users, 3.6% in aspirin users who discontinued the use of aspirin, and 21.1% in aspirin users who continued using aspirin. The authors concluded that aspirin should be discontinued in patients at a low risk for thromboembolic diseases to minimize bleeding complications.³¹ However, the findings of the aforementioned study should be interpreted with caution because 36.8% of patients in the group that continued using aspirin compared to only 5.4% of patients in the group that discontinued the use of aspirin underwent dual antiplatelet therapy. Although the administration of antiplatelet agents other than aspirin was discontinued at least seven days before ESD and was resumed seven days after the ESD, the high post-ESD bleeding rate in the group that continued using aspirin might be due to other antiplatelet agents. In a study by Sanomura et al,²⁷ similar numbers of patients who were taking either antiplatelet agents or anticoagulants were included in the low-dose aspirin continuation and discontinuation groups (32% in each group). In the aforementioned study, the post-ESD bleeding rate did not differ between the groups (continuation 3.6% vs discontinuation 4.8%, $P > 0.999$). When the impact of dual antiplatelet therapy is excluded, the continuation of low-dose aspirin therapy alone may not significantly increase the risk of post-ESD bleeding.

Harada et al,³² in a recent study, evaluated the impact of low-dose aspirin continuation during ESD according to the dual antiplatelet therapy. In their study, the continuation of low-dose aspirin did not increase post-ESD bleeding (continuation 10.7% vs discontinuation 10.3%, $P > 0.99$) in patients undergoing single low-dose aspirin therapy. In patients who were undergoing dual antiplatelet therapy, the post-ESD bleeding rate tended to be higher in the low-dose aspirin continuation group than in the discontinuation group (23.1% vs 5.0%, $P = 0.141$). Although the statistical power was low in the study, the study findings implied that concerns about low-dose aspirin continuation remain among patients at a high thromboembolic risk, such as those undergoing

dual antiplatelet therapy.

Difference in Bleeding or Thromboembolic Risk between Patients of Different Ethnicities

Concerns that the continuation of aspirin may increase the risk of post-ESD bleeding have been noted in the APAGE/APSDE guidelines. The guidelines recommends the interruption of all antithrombotic agents during ultrahigh-risk procedures provided that the perceived benefits of the procedure outweigh the patient's thromboembolic risk.²³ As mentioned earlier, ultrahigh-risk procedures were defined in the APAGE/APSDE guidelines for several reasons, including the difference in clinical practices between Eastern and Western endoscopists during the management of antithrombotic agents. Lee et al²⁵ conducted a study on this issue, which involved 105 Eastern and 106 Western endoscopists. In the study, Eastern endoscopists usually discontinued aspirin more than seven days before polypectomy (76.3%), while 39.6% of Western endoscopists did not stop the use of aspirin before polypectomy. Additionally, Eastern endoscopists resumed aspirin administration one to three days after polypectomy (44.8%), while Western endoscopists resumed aspirin administration on the day of polypectomy (35.9%). Interestingly, more Eastern than Western endoscopists (22.4% vs 8.1%, $P = 0.006$) agreed that the risk of bleeding is higher in Asians than in other ethnic groups. Additionally, more Eastern endoscopists agreed that the risk of thromboembolism is higher in whites than in other ethnic groups (39.4% vs 21.0%, $P = 0.007$). Eastern endoscopists seem to believe that following Western guidelines is dangerous because it leads to an increased risk of bleeding in Asian patients.²⁶ Although differences in bleeding or thromboembolic risk among patients of different ethnicities have not been well documented, either the threshold for antiplatelet therapy or the metabolism of warfarin differs between Easterners and Westerners.^{33–36} Taking into consideration the current evidence and perspective, it is necessary to refer to both Eastern and Western guidelines during the management of antithrombotic agents for Asian patients who undergo ESD.

Heparin-Bridge Therapy in Patients at a High Risk of Thromboembolic Events

Traditionally, heparin-bridge therapy during the perioperative period was thought to be necessary to minimize thromboembolic risk due to the discontinuation of warfarin during this period. Most of the current guidelines, including the APAGE/APSDE guidelines, recommend heparin-bridge therapy during the period of warfarin discontinuation if patients have a high thromboembolic risk.^{17,20,23} However, heparin-bridge therapy increases the risk of post-ESD bleeding from 4.2 to 34.4 times.^{37–39} Additionally, there is no consensus on whether heparin-bridge therapy is an effective strategy. Recently, an interesting prospective observational study on this issue was conducted by Harada et al⁴⁰ They investigated the differences in clinical outcomes, including post-ESD bleeding, operation time, and length of hospital stay, between the continuous use of low-dose warfarin and heparin-bridge therapy in patients. Although the post-ESD bleeding rate did not differ between the groups, it tended to be lower in the continuous use of low-dose warfarin group than in the heparin-bridge therapy group (9.1% vs 21.7%, $P = 0.414$). The operation time and length of hospital stay were significantly shorter in the continuous use of low-dose warfarin group than in the heparin-bridge therapy group. Although a large-scale study is required to reach a definitive conclusion, the continuous use of warfarin may be another

treatment option for patients at a high thromboembolic risk.

The effect of the continuous use of warfarin was also investigated in the field of cardiology. In a randomized-controlled trial performed by Birnie et al,⁴¹ the continuous use of warfarin during pacemaker or implantable cardioverter-defibrillator surgery markedly reduced the incidence of clinically significant device-pocket hematoma compared to heparin-bridge therapy (16.0% vs 3.5%, $P < 0.001$). The number of days of hospitalization due to hematoma in the continuous use of warfarin group was shorter than that in the heparin-bridge therapy group (1.2% vs 4.7%, $P = 0.006$). The rate of interruption of anticoagulation therapy due to hematoma was also lower in the continuous use of warfarin group than in the heparin-bridge therapy group (14.2% vs 3.2%, $P < 0.001$). The concept of an “anticoagulant stress test” may provide an explanation for these findings.^{41,42} If patients undergo surgery while receiving full-dose anticoagulation therapy, every minor bleed will be detected and appropriately treated while the wound is still open.⁴¹ On the contrary, in patients undergoing heparin-bridge therapy, some minor bleeds may not be identified during the operation, which will then cause bleeding after surgery when full-dose anticoagulation therapy is restarted. This hypothesis may apply to patients who undergo heparin-bridge therapy during ESD. Although the continuous use of warfarin may increase the incidence of bleeding during ESD, potential bleeds on the iatrogenic ulcer bed can be detected and appropriately coagulated. If ESD was successfully performed despite the continuous use of warfarin, the risk of post-ESD bleeding may decrease compared to if the patient underwent heparin-bridge therapy. In this respect, the recently updated JGES guidelines, which emphasize the continued use of warfarin as an alternative treatment to heparin-bridge therapy, is worth considering.

Management of Antithrombotic Agents in Esophageal or Colorectal ESD

Although current guidelines cover esophageal, gastric, and colorectal ESD, the most studied type is gastric ESD. Few studies are available on colorectal ESD and there is no study on esophageal ESD and the use of antithrombotic agents.^{12,20,43} Presently, antithrombotic agents in esophageal or colorectal ESD should be selected based on the results of studies on gastric ESD.

Summary and Conclusion

In this review, guideline recommendations for the management of antithrombotic agents in patients who undergo ESD were discussed. Because ESD is a high-risk procedure, thienopyridine derivatives may be discontinued to reduce the risk of post-ESD bleeding. However, in patients undergoing dual antiplatelet therapy, switching to a single low-dose aspirin therapy can be considered when thienopyridine derivatives are discontinued during the perioperative period. Most of the recent guidelines support the continuous use of low-dose aspirin even in patients who undergo ESD. However, there is still a concern about the increased risk of bleeding with the use of low-dose aspirin in patients undergoing dual antiplatelet therapy, especially in the Asian population.

In patients receiving anticoagulants, either warfarin or NOAC can be discontinued depending on the risk of thromboembolic events. For patients at a high risk of thromboembolic events, most current guidelines recommend the discontinuation of warfarin and heparin-bridge therapy. However, the continuous use of warfarin can also be considered in patients who undergo ESD, as recommended in the JGES guidelines.²²

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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