

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 83424

**Title:** Assessment of delayed bleeding after endoscopic submucosal dissection of early-stage gastrointestinal tumors in patients receiving direct oral anticoagulants

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06135791

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2023-01-24

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2023-02-23 01:19

**Reviewer performed review:** 2023-02-26 08:51

**Review time:** 3 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Endoscopic submucosal dissection (ESD) is a currently a most promising treatment for selected patients with early gastric cancer, however the management of postoperative bleeding remains a challenge. In this work, the post-ESD bleeding associated with anticoagulant(especially DOACs) was quietly reviewed, and the potential benefits of monitoring the anticoagulant effects of DOACs in clinical practice or endoscopic/surgical procedures were also discussed. I think it is a good work and worth of reading.

- 1、 The progress of ESD and the post-bleeding are the issues of great concern, since that delayed bleeding after ESD for gastrointestinal tumors has been discussed in some previous works, these parts can be briefly described or focus on recent developments.
- 2、 In section of Pharmacological characteristics of DOACs" Why should we monitor the anticoagulant effect of DOACs, this should be stated detailly. The clinical outcomes refer to the pharmacokinetic characteristics in special population or the genetic variations can be discussed.
- 3、 In section 7 Gastrointestinal bleeding after ESD in patients receiving DOACs , the heparin-bridging therapy refers to DOACs with heparin-bridging or any anticoagulants with heparin-bridging?
- 4、 DOACs is current

recommended for cancer patients due to prophylaxis of Venous thrombosis, the balance between the major bleeding(especially for high risk in gastrointestinal tumors) and VTE could be discussed in summary. 5、 As illustrated in section 6, there are subtle differences about the management of DOACs with ESD, the possible reasons could be discussed.

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**Reviewer's code:** 03881414

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Thailand

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2023-01-24

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-03-17 17:28

**Reviewer performed review:** 2023-03-19 14:18

**Review time:** 1 Day and 20 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="radio"/> Grade A: Excellent <input checked="" type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No creativity or innovation

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<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

This is a very nice review focusing specifically on the issue of delayed GI bleeding after endoscopic submucosal dissection (ESD) for early-stage gastrointestinal tumors in patients receiving direct oral anticoagulant (DOAC) therapy. Based on the available evidence, the authors demonstrate that there is possibly a lot of mechanisms contributing to delayed bleeding after ESD and provide evidence-based data regarding the prevalence of bleeding in each location, types of anticoagulant use and their related complications after ESD, as well as pharmacokinetic and pharmacodynamic related delayed bleeding of DOAC. The authors propose that the key underlying factor responsible for the bleeding is probably due mainly to the effect of direct oral anticoagulant therapy. They also point out that the serum level of DOAC at trough is positively related to the prevalence of bleeding. They emphasize that there is currently no strong evidence to guide management in this setting leading to differences in practice guideline among the country. The authors call for incorporating pharmacologic parameters of DOAC such as plasma DOAC level at trough, and Tmax and anti-factor Xa activity into the current scoring system to stratifying risk of post-ESD delayed

bleeding in each individual and encourage investigators to develop simple test for these pharmacologic parameters. I strongly agree with the authors and I think this review is worth to be published in terms of providing the beneficial information to the community and encouraging investigators to conduct the future research on the value of DOAC pharmacologic parameters on post-ESD GI bleeding.