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Name of Journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 89511

Manuscript Type: EDITORIAL

Early gastric cancer recurrence after endoscopic submucosal dissection: Not to be ignored!

Zeng Y *et al.* Non-ignorable EGC recurrence after ESD

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Abstract

This editorial comments on the article by Yin JJ *et al.* published in a recent issue of the *World Journal of Gastrointestinal Oncology* 2023; 15(9):1636-1643. We focus on the importance of paying more attention to post-endoscopic submucosal dissection (ESD) gastric cancer recurrence in patients with early gastric cancer (EGC) and how to manage it effectively. ESD has been a well-known treatment and the mainstay for EGC, with the advantages of less invasion and fewer complications when compared with traditional surgical procedures. Despite a lower local recurrence rate after ESD, the problem of postoperative recurrence in patients with EGC has become increasingly non-ignorable with the global popularization of ESD technology and the increasing number of post-ESD patients.

Key Words: Early gastric cancer; Recurrence; Endoscopic submucosal dissection; Postoperative; Prediction

Zeng Y, Zhang JW, Yang J. Early gastric cancer recurrence after endoscopic submucosal dissection: Not to be ignored!. *World J Gastrointest Oncol* 2023; In press

Core Tip: Post-endoscopic submucosal dissection (ESD) gastric cancer recurrence in patients with early gastric cancer (EGC) has become increasingly non-ignorable with the global popularization of ESD technology and the increasing number of post-ESD patients. A combination approach, including endoscopic techniques, radiographic examinations, predictive biological markers, and machine learning-based prediction models, should be recommended in the individualized surveillance and management of gastric cancer recurrence after ESD.

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INTRODUCTION

Early gastric cancer (EGC) is defined as gastric cancer (GC) confined to the mucosa or submucosa with or without nodal involvement^[1]. Endoscopic submucosal dissection

(ESD) is considered an effective treatment for EGC and is recommended worldwide due to its safer and more cost-effective advantages^[2]. Although the recurrence rate after ESD for EGC is relatively low, the problem of post-ESD recurrence in EGC patients has grasped momentous attention in recent years due to the popularization of ESD technology and the increase of post-ESD patients worldwide. In particular, published studies have pointed out that ESD had inferior ³ disease-free survival (DFS), recurrence-free survival (RFS), and higher recurrence when compared with surgery^[3,4], which has also sounded the alarm for paying more attention to GC recurrence after ESD.

We are very interested in the original article by Yin *et al.*^[5] published in the September 2023 issue of the World Journal of Gastrointestinal Oncology. We consider this a qualified and enlightening study, as the authors explore a practical approach to monitoring post-ESD GC recurrence in patients with EGC based on the urgent need to simplify follow-up procedures and reduce operational risks. In addition, by comparing with tissue pathology, the gold standard, the authors found that the inadequacy of multi-slice spiral computed tomography (MSCT) lay in the inferior accuracy in predicting GC recurrence. We thank Yin *et al.* ^[5] for their study, which has been instrumental in raising attention to GC recurrence after ESD and developing recurrence risk monitoring programs.

FACTORS ASSOCIATED WITH GC RECURRENCE AFTER ESD

The factors affecting EC recurrence after ESD in EGC patients may be split into three main sections, including several preoperative, intraoperative, and postoperative risk factors.

First of all, preoperative assessment focuses on the evaluation of the invasion depth and lymphatic metastasis, not only because multicenter studies with a large cohort found that lymphatic infiltration would significantly affect early cancer recurrence^[6] but also because the recurrence rate of patients judged by preoperative endoscopic ultrasonography (EUS) to be of higher grade T stage would be significantly higher than that of patients with T1 stage^[7]. Based on these results, EUS combined with MSCT has

been recommended in assessing preoperative EGC patients^[8]. In addition, the primary location of EGC is also considered to have a significant relationship with the local GC recurrence^[9, 10].

Second, intraoperative risk factors mainly concentrate on whether complete resection of primary GC has been achieved^[11]. Previous research found that a cancer-positive horizontal margin (HM) more significant than 6 mm had been identified as an independent risk factor in the local GC recurrence^[12]. However, subsequent studies have also shown that, without additional treatment, positive HM patients still have a comparable long-term prognosis and a low risk of lymphatic metastasis despite a non-low recurrence rate^[13]. Furthermore, published research has found a higher GC recurrence risk in post-ESD patients with unevaluable or positive vertical margins than those with unevaluable or positive horizontal margins^[14].

Third, postoperative risk factors may involve multiple elements. Among them, it is worth mentioning that helicobacter pylori (Hp) ² has been identified as an independent risk factor for metachronous GC recurrence after ESD^[15]. Thus, Hp eradication after ESD in EGC patients has been recommended to reduce metachronous GC recurrence^[16]. Furthermore, recent studies have found that Hp eradication can reduce GC cell migration and invasion by blocking circFNDC3B expression, which also supports Hp detection and treatment in EGC patients after ESD^[17].

SURVEILLANCE STRATEGIES FOR POST-ESD RECURRENCE

MSCT, follow-up endoscopy, and tissue pathology are the three main methods for GC recurrence surveillance. Although MSCT is convenient and non-invasive, its most significant and non-negligible inadequacy is still its unsatisfactory accuracy. The sensitivity, specificity, and negative and positive predictive values of MSCT in Yin's study were all below 50%^[5], while an even lower CT diagnostic accuracy was reported in another study^[18]. Meanwhile, despite the increasing application of EUS and magnifying chromoendoscopy^[19], follow-up endoscopy and tissue pathology

applications are still restricted by scarce medical resources and potential operational risks.

Are there any practical suggestions for these seemingly unsolvable contradictions mentioned above? Combining the above three follow-up methods may be one attempt, but it may also increase total medical costs and cause an unnecessary waste of medical resources. Another promising solution may rely on the rapidly evolving field of data science. Big data and machine learning (ML) have opened up a new era for medical research and clinical practice, such as predicting risks and facilitating personalized clinical decision-making^[20]. ML-based prediction models have been reported to predict non-radical resection rates and post-ESD bleeding risks in EGC patients^[21, 22]. Also, an ML-based predictor has been confirmed to identify post-surgery gastric cancer recurrence^[23]. Therefore, we believe that the recurrence risk prediction, recurrence identification, and individualized follow-up management of EGC patients after ESD interventions through ML-based prediction models is of research significance and application prospect in the current situation of increasing post-ESD patients.

CURRENT RESEARCH FOR POST-ESD RECURRENCE

Reference Citation Analysis (RCA, <https://www.referencecitationanalysis.com/>) is a unique artificial intelligence system for citation evaluation of biomedical literature. RCA has been employed to analyze previous studies of EGC patients with post-ESD up to December 2023. Published studies on post-ESD GC recurrence focus mainly on risk identification and assessment model creation, imaging and endoscopy, molecular markers, and integrated treatment strategies after recurrence^[24, 25].

Several deficiencies exist in the current study of GC recurrence in post-ESD patients, including widely varied recurrence rates in different studies^[26-28], inconsistent follow-up periods after ESD^[5, 29, 30], the absence of standardized treatment protocols for postoperative GC recurrence, and lack of large-scale, multicenter, and prospective clinical data^[31]. Research in these areas could be of interest in the future.

CONCLUSION

In conclusion, the recurrence and follow-up management of EGC patients after ESD should not be ignored, and further research is needed to assess the recurrence risk better and develop individualized management plans.

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