



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

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Abstract

This editorial comments on the article "Efficacy of multi-slice spiral computed tomography in evaluating gastric cancer recurrence after endoscopic submucosal dissection". 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

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Core Tip: Post-endoscopic submucosal dissection (ESD) gastric cancer recurrence in patients with early gastric cancer 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 disease-free survival, recurrence-free survival, 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 HM[14].

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

FOOTNOTES

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REFERENCES

- Chen D, Chen G, Jiang W, Fu M, Liu W, Sui J, Xu S, Liu Z, Zheng X, Chi L, Lin D, Li K, Chen W, Zuo N, Lu J, Chen J, Li G, Zhuo S, Yan J. Association of the Collagen Signature in the Tumor Microenvironment With Lymph Node Metastasis in Early Gastric Cancer. *JAMA Surg* 2019; 154: e185249 [PMID: 30698615 DOI: 10.1001/jamasurg.2018.5249]

- 2 **Wang J**, Li SJ, Yan Y, Yuan P, Li WF, Cao CQ, Chen WG, Chen KN, Wu Q. Feasibility of same-day discharge following endoscopic submucosal dissection for esophageal or gastric early cancer. *World J Gastroenterol* 2022; **28**: 5957-5967 [PMID: [36405109](#) DOI: [10.3748/wjg.v28.i41.5957](#)]
- 3 **Jeon HK**, Kim GH, Lee BE, Park DY, Song GA, Kim DH, Jeon TY. Long-term outcome of endoscopic submucosal dissection is comparable to that of surgery for early gastric cancer: a propensity-matched analysis. *Gastric Cancer* 2018; **21**: 133-143 [PMID: [28397011](#) DOI: [10.1007/s10120-017-0719-4](#)]
- 4 **Yang HJ**, Kim JH, Kim NW, Choi IJ. Comparison of long-term outcomes of endoscopic submucosal dissection and surgery for undifferentiated-type early gastric cancer meeting the expanded criteria: a systematic review and meta-analysis. *Surg Endosc* 2022; **36**: 3686-3697 [PMID: [35194664](#) DOI: [10.1007/s00464-022-09126-9](#)]
- 5 **Yin JJ**, Hu X, Hu S, Sheng GH. Efficacy of multi-slice spiral computed tomography in evaluating gastric cancer recurrence after endoscopic submucosal dissection. *World J Gastrointest Oncol* 2023; **15**: 1636-1643 [PMID: [37746651](#) DOI: [10.4251/wjgo.v15.i9.1636](#)]
- 6 **Yamada S**, Hatta W, Shimosegawa T, Takizawa K, Oyama T, Kawata N, Takahashi A, Oka S, Hoteya S, Nakagawa M, Hirano M, Esaki M, Matsuda M, Nakaya N, Gotoda T. Different risk factors between early and late cancer recurrences in patients without additional surgery after noncurative endoscopic submucosal dissection for early gastric cancer. *Gastrointest Endosc* 2019; **89**: 950-960 [PMID: [30465769](#) DOI: [10.1016/j.gie.2018.11.015](#)]
- 7 **Smith JW**, Brennan MF, Botet JF, Gerdes H, Lightdale CJ. Preoperative endoscopic ultrasound can predict the risk of recurrence after operation for gastric carcinoma. *J Clin Oncol* 1993; **11**: 2380-2385 [PMID: [8246026](#) DOI: [10.1200/JCO.1993.11.12.2380](#)]
- 8 **Li JH**, Shen WZ, Gu XQ, Hong WK, Wang ZQ. Prognostic value of EUS combined with MSCT in predicting the recurrence and metastasis of patients with gastric cancer. *Jpn J Clin Oncol* 2017; **47**: 487-493 [PMID: [28334806](#) DOI: [10.1093/jjco/hyx024](#)]
- 9 **Takenaka R**, Kawahara Y, Okada H, Hori K, Inoue M, Kawano S, Tanioka D, Tsuchi T, Yagi S, Kato J, Uemura M, Ohara N, Yoshino T, Imagawa A, Fujiki S, Takata R, Yamamoto K. Risk factors associated with local recurrence of early gastric cancers after endoscopic submucosal dissection. *Gastrointest Endosc* 2008; **68**: 887-894 [PMID: [18565523](#) DOI: [10.1016/j.gie.2008.03.1089](#)]
- 10 **Lee JY**, Cho KB, Kim ES, Park KS, Lee YJ, Lee YS, Jang BK, Chung WJ, Hwang JS. Risk factors for local recurrence after en bloc endoscopic submucosal dissection for early gastric cancer. *World J Gastrointest Endosc* 2016; **8**: 330-337 [PMID: [27076871](#) DOI: [10.4253/wjge.v8.i7.330](#)]
- 11 **Japanese Gastric Cancer Association**. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). *Gastric Cancer* 2023; **26**: 1-25 [PMID: [36342574](#) DOI: [10.1007/s10120-022-01331-8](#)]
- 12 **Sekiguchi M**, Suzuki H, Oda I, Abe S, Nonaka S, Yoshinaga S, Taniguchi H, Sekine S, Kushima R, Saito Y. Risk of recurrent gastric cancer after endoscopic resection with a positive lateral margin. *Endoscopy* 2014; **46**: 273-278 [PMID: [24505020](#) DOI: [10.1055/s-0034-1364938](#)]
- 13 **Yang HJ**, Lee WS, Lee BE, Ahn JY, Jang JY, Lim JH, Nam SY, Kim JH, Min BH, Joo MK, Park JM, Shin WG, Lee HL, Gweon TG, Park MI, Choi J, Tae CH, Kim YI, Choi IJ. Long-term Outcomes of Undifferentiated-Type Early Gastric Cancer with Positive Horizontal Margins after Endoscopic Resection. *Gut Liver* 2021; **15**: 723-731 [PMID: [33790056](#) DOI: [10.5009/gnl20291](#)]
- 14 **Figueiredo PC**, Pimentel-Nunes P, Libanio D, Dinis-Ribeiro M. A systematic review and meta-analysis on outcomes after Rx or R1 endoscopic resection of superficial gastric cancer. *Eur J Gastroenterol Hepatol* 2015; **27**: 1249-1258 [PMID: [26225870](#) DOI: [10.1097/MEG.0000000000000440](#)]
- 15 **Chung CS**, Woo HS, Chung JW, Jeong SH, Kwon KA, Kim YJ, Kim KO, Park DK. Risk Factors for Metachronous Recurrence after Endoscopic Submucosal Dissection of Early Gastric Cancer. *J Korean Med Sci* 2017; **32**: 421-426 [PMID: [28145644](#) DOI: [10.3346/jkms.2017.32.3.421](#)]
- 16 **Bang CS**, Baik GH, Shin IS, Kim JB, Suk KT, Yoon JH, Kim YS, Kim DJ. Helicobacter pylori Eradication for Prevention of Metachronous Recurrence after Endoscopic Resection of Early Gastric Cancer. *J Korean Med Sci* 2015; **30**: 749-756 [PMID: [26028928](#) DOI: [10.3346/jkms.2015.30.6.749](#)]
- 17 **Zhang J**, Bai J, Zhu H, Li W, An Q, Wang D. The upregulation of circFNDC3B aggravates the recurrence after endoscopic submucosal dissection (ESD) in early gastric cancer (EGC) patients. *Sci Rep* 2022; **12**: 6178 [PMID: [35418175](#) DOI: [10.1038/s41598-022-07154-y](#)]
- 18 **Choi KS**, Kim SH, Kim SG, Han JK. Early Gastric Cancers: Is CT Surveillance Necessary after Curative Endoscopic Submucosal Resection for Cancers That Meet the Expanded Criteria? *Radiology* 2016; **281**: 444-453 [PMID: [27243549](#) DOI: [10.1148/radiol.2016152866](#)]
- 19 **Kawabata H**, Kawakatsu Y, Yamaguchi K, Ueda Y, Okazaki Y, Hitomi M, Miyata M, Motoi S, Enoki Y, Minamikawa S. A Rare Case of Local Recurrence Following Curative Endoscopic Submucosal Dissection of Intramucosal Differentiated-Type Gastric Cancer. *Gastroenterology Res* 2019; **12**: 103-106 [PMID: [31019622](#) DOI: [10.14740/gr1159](#)]
- 20 **Radenkovic D**, Keogh SB, Maruthappu M. Data science in modern evidence-based medicine. *J R Soc Med* 2019; **112**: 493-494 [PMID: [31526210](#) DOI: [10.1177/0141076819871055](#)]
- 21 **Yun HR**, Huh CW, Jung DH, Lee G, Son NH, Kim JH, Youn YH, Park JC, Shin SK, Lee SK, Lee YC. Machine Learning Improves the Prediction Rate of Non-Curative Resection of Endoscopic Submucosal Dissection in Patients with Early Gastric Cancer. *Cancers (Basel)* 2022; **14** [PMID: [35954406](#) DOI: [10.3390/cancers14153742](#)]
- 22 **Na JE**, Lee YC, Kim TJ, Lee H, Won HH, Min YW, Min BH, Lee JH, Rhee PL, Kim JJ. Utility of a deep learning model and a clinical model for predicting bleeding after endoscopic submucosal dissection in patients with early gastric cancer. *World J Gastroenterol* 2022; **28**: 2721-2732 [PMID: [35979158](#) DOI: [10.3748/wjg.v28.i24.2721](#)]
- 23 **Zhou C**, Hu J, Wang Y, Ji MH, Tong J, Yang JJ, Xia H. A machine learning-based predictor for the identification of the recurrence of patients with gastric cancer after operation. *Sci Rep* 2021; **11**: 1571 [PMID: [33452440](#) DOI: [10.1038/s41598-021-81188-6](#)]
- 24 **Xie B**, Xia Y, Wang X, Xiong Y, Chen SB, Zhang J, He WW. Factors associated with heterochronic gastric cancer development post-endoscopic mucosal dissection in early gastric cancer patients. *World J Gastrointest Oncol* 2023; **15**: 1644-1652 [PMID: [37746653](#) DOI: [10.4251/wjgo.v15.i9.1644](#)]
- 25 **Jiang XC**, Yao XB, Xia HB, Su YZ, Luo PQ, Sun JR, Song ED, Wei ZJ, Xu AM, Zhang LX, Lan YH. Nomogram established using risk factors of early gastric cancer for predicting the lymph node metastasis. *World J Gastrointest Oncol* 2023; **15**: 665-676 [PMID: [37123061](#) DOI: [10.4251/wjgo.v15.i4.665](#)]
- 26 **Sano T**, Sasako M, Kinoshita T, Maruyama K. Recurrence of early gastric cancer. Follow-up of 1475 patients and review of the Japanese literature. *Cancer* 1993; **72**: 3174-3178 [PMID: [8242540](#) DOI: [10.1002/1097-0142\(19931201\)72:11<3174::AID-CNCR2820721107>3.0.CO;2-H](#)]
- 27 **Min BH**, Kim ER, Kim KM, Park CK, Lee JH, Rhee PL, Kim JJ. Surveillance strategy based on the incidence and patterns of recurrence after curative endoscopic submucosal dissection for early gastric cancer. *Endoscopy* 2015; **47**: 784-793 [PMID: [26111362](#) DOI: [10.1055/s-0034-1364938](#)]

- 10.1055/s-0034-1392249]
- 28 **Na HK**, Choi KD, Ahn JY, Lee JH, Kim do H, Song HJ, Lee GH, Jung HY, Kim JH. Endoscopic prediction of recurrence in patients with early gastric cancer after margin-negative endoscopic resection. *J Gastroenterol Hepatol* 2016; **31**: 1284-1290 [PMID: 26820101 DOI: 10.1111/jgh.13301]
- 29 **Ryu DG**, Kim SJ, Choi CW, Park SB, Nam HS, Lee SH, Hwang SH. Local Recurrence after Endoscopic Submucosal Dissection of Early Gastric Cancer. *J Clin Med* 2023; **12** [PMID: 36902804 DOI: 10.3390/jcm12052018]
- 30 **Nishizawa T**, Yahagi N. Long-Term Outcomes of Using Endoscopic Submucosal Dissection to Treat Early Gastric Cancer. *Gut Liver* 2018; **12**: 119-124 [PMID: 28673068 DOI: 10.5009/gnl17095]
- 31 **Moon HS**, Yun GY, Kim JS, Eun HS, Kang SH, Sung JK, Jeong HY, Song KS. Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia: Retrospective, single-center study. *World J Gastroenterol* 2017; **23**: 4407-4415 [PMID: 28706423 DOI: 10.3748/wjg.v23.i24.4407]



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