ORIGINAL ARTICLE

Clinical predictors of histologic type of gastric cancer

Takashi Kanesaka, MD,[1] Takashi Nagahama, MD,[2] Noriya Uedo, MD,[1] Hisashi Doyama, MD,[3] Tetsuya Ueo, MD,[4] Kunihisa Uchita, MD,[5] Naohiro Yoshida, MD,[3] Yasuhito Takeda, MD,[3] Kentaro Imamura, MD,[2] Kurato Wada, MD,[4] Hideki Ishikawa, MD,[6] Kenshi Yao, MD[2]

Osaka, Chikushino, Kanazawa, Oita, Kochi, Kyoto, Japan

Background and Aims: Gastric cancer is classified into differentiated and undifferentiated types according to the degree of glandular differentiation. Undifferentiated-type early gastric cancer (EGC) carries a higher risk of lymph-node metastasis than differentiated type, and therefore the indication criteria for endoscopic resection differ. This study aimed to clarify the ability of clinical predictors to distinguish between differentiated-type and undifferentiated-type EGCs.

Methods: This was a post hoc study of a multicenter prospective trial carried out in 5 Japanese hospitals, including 343 patients with cT1 EGC of ≥10 mm. According to the protocol, age, sex, and endoscopic findings of cancer (diameter, location, macroscopic type, and invasion depth) were evaluated, and the final diagnosis was confirmed from resected specimens. We evaluated the associations between these clinical factors and the histologic type of cancer and calculated the ability of the factors to diagnose differentiated-type EGC. The diagnostic ability of forceps biopsy was also calculated as a reference.

Results: Multivariate analysis identified older age (≥72 years), male sex, larger tumor size (>30 mm), elevated type, and shallower invasion depth (cT1a) as independent significant predictors for differentiated-type EGC, with elevated type showing the highest positive likelihood ratio. The sensitivity, specificity, accuracy, and positive and negative likelihood ratios of elevated type for differentiated-type EGC were 24%, 99%, 38%, 15.7, and 0.77, respectively, compared with 96%, 86%, 95%, 7.0, and 0.04 for forceps biopsy.

Conclusions: Endoscopic elevated type is a significant predictor for differentiated-type EGC and may exclude undifferentiated-type EGC without the need for forceps biopsy. (Gastrointest Endosc 2017;■:1-9.)

INTRODUCTION

Gastric cancer is classified into differentiated and undifferentiated types according to the degree of glandular differentiation in the Japanese classification (Fig. 1).[1] These types correspond to intestinal and diffuse types, respectively, as identified in Lauren's classification.[2] The risk of lymph-node metastasis is higher in patients with undifferentiated-type early gastric cancer (EGC) compared with differentiated type,[3-5] and the indication criteria for endoscopic resection are therefore more restricted in undifferentiated-type compared with differentiated-type EGC.[2] Distinguishing between these histologic types is thus essential for making decisions regarding endoscopic resection of EGC. Nevertheless, no clinical predictors concerned with the histologic types of EGC have yet been fully verified. This study aimed to clarify the diagnostic ability of major

Abbreviations: CI, confidence interval; EGC, early gastric cancer; M, mucosa; M-NBI, magnifying narrow-band imaging; ROC, receiver operating characteristic; SM, submucosa.

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Current affiliations: Department of Gastrointestinal Oncology, Osaka International Cancer Institute, Osaka (1); Department of Endoscopy, Fukuoka University Chikushi Hospital, Chikushino (2); Department of Gastroenterology, Ishikawa Prefectural Central Hospital, Kanazawa (3); Department of Gastroenterology, Oita Red Cross Hospital, Oita (4); Department of Gastroenterology, Kochi Red Cross Hospital, Kochi (5); Department of Molecular Targeting Cancer Prevention, Kyoto Prefectural University of Medicine, Kyoto, Japan (6).

Reprint requests: Takashi Kanesaka, MD, Department of Gastrointestinal Oncology, Osaka International Cancer Institute, 3-1-69, Otemae, Chuo-ku, Osaka 541-8567, Japan.

If you would like to chat with an author of this article, you may contact Dr Kanesaka at kanesaka-ta@mc.pref.osaka.jp.

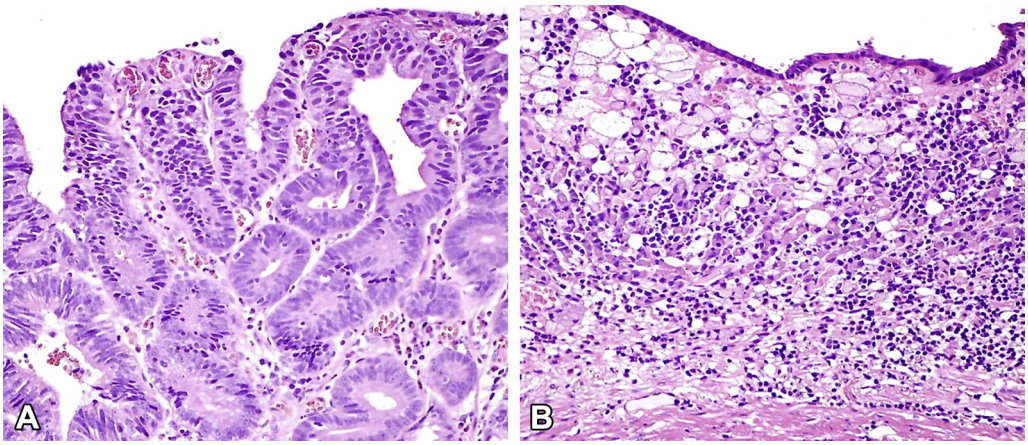

Figure 1. Histopathologic images of early gastric cancer with hematoxylin and eosin staining. **A**, Differentiated type (well-differentiated tubular adenocarcinoma). **B**, Undifferentiated type (signet ring cell carcinoma).

clinical findings to distinguish between differentiated-type and undifferentiated-type EGC.

METHODS

Study design and participants

This was a post hoc study of a multicenter prospective trial carried out in 5 hospitals in Japan (clinical trial registration number: UMIN000014628) (Nagahama T, Yao K, Uedo N, et al., unpublished data). The protocol of the trial was approved by the Ethics Committee of Fukuoka University Chikushi Hospital on May 9, 2014, and by the ethics committees in each participating institution. The trial was conducted according to the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) initiative and followed the Declaration of Helsinki.[6] Written informed consent was obtained from all patients.

The prospective trial recruited patients aged ≥20 years with an EGC ≥10 mm in diameter, between August 2014 and April 2016. Patients with a history of gastric resection, severe organ failure, or anticoagulant medication were excluded. The primary endpoint of the trial was a comparison of the diagnostic ability of margin delineation between chromoendoscopy using indigo carmine and magnifying narrow-band imaging (M-NBI). Narrow-band imaging is an image-enhanced technology generally used in combination with magnifying endoscopy for the diagnosis of EGC. A total of 384 patients were enrolled and assigned randomly to undergo chromoendoscopy (n = 191) or M-NBI (n = 193). If more than 2 EGCs were detected in a patient, the one located in the most proximal part of the stomach was chosen for evaluation to ensure independence of the analytical units. Biopsy specimens were taken from the lesions after completion of all endoscopic diagnoses. The lesions were then removed by endoscopic or surgical resection for the final histologic diagnosis. Forty-one patients were excluded and 343 were finally analyzed in the prospective trial (Fig. 2).

Participating endoscopists

All examinations were performed by 38 endoscopists in 5 Japanese hospitals, with a median length of experience of upper endoscopy of 8.5 years (range, 1-25 years).

Endoscopy system and setting

The procedure was carried out using an endoscope (GIF-Q240Z, GIF-H260Z, GIF-FQ260Z, or GIF-H290Z; Olympus, Tokyo, Japan). The endoscopy system consisted of a video processor (CV-290; Olympus) and a light source (CLV-290SL; Olympus) that worked in high-resolution white-light imaging. Structural enhancement of the endoscopic video processor was set to B-mode level 4-6 for white-light endoscopy and to B-mode level 8 for M-NBI. The color mode was set at level 1.

Evaluation of the clinicopathologic findings

In the prospective trial, the location and histologic type of cancer, as evaluated in previous examinations, as well as patient age and sex, were recorded in the first case report form when the patients were enrolled. In addition to evaluating the primary endpoint (margin delineation), the diameter, macroscopic type, and invasion depth of the target lesion were also evaluated by an endoscopist during gastroscopy and recorded in the second case report form. After endoscopic or surgical resection, the final histologic diagnosis of the cancer and its histologic classification, diameter, macroscopic type, and invasion depth were recorded in the third case report form. All data in the present study were evaluated before the final diagnosis.

Endoscopic evaluation of cancer

Endoscopic findings of cancer were defined based on the Japanese gastric cancer treatment guidelines and the Japanese Classification of Gastric Carcinoma.[2,7] The