

## Open Access

## Endoscopically Diagnosed Gastric Cancers: Looking Alike, but Behave Differently

Won Hee Kim and Ki Baik Hahm

Digestive Disease Center, CHA Bundang Medical Center, CHA University, Seongnam, Korea

See "Early Gastric Cancer-Like Advanced Gastric Cancer versus Advanced Gastric Cancer-Like Early Gastric Cancer" by Hyun Sik Park, Sun-Young Lee, Sung Noh Hong, et al., on page 155-160

Gastric cancer remains the second leading cause of cancer mortality in the world, although the overall incidence is gradually declining.<sup>1</sup> Gastric cancers can be largely subdivided into early and advanced lesions in nature or intestinal and diffuse type in pathology. Early gastric cancer (EGC) is defined as a cancer that does not invade beyond the submucosa regardless of lymph node involvement, based on which endoscopic resection for EGC has become an established alternative effective treatment method through improved technology alongside with instrumental development.<sup>2</sup> Endoscopic resection for mucosal or minimal submucosal, small sized, and differentiated tumor is curative because lymph node metastases are rare in these tumors.<sup>3</sup> Of course, accurate staging especially prediction of the depth of tumor invasion is indispensable. On remote definition, the evaluation of depth of invasion was performed by gastroduodenoscopy based on the macroscopic appearance. Type 0 is superficial (T1, mucosal and submucosal invasion) tumors, and classified as EGC. Type 1 is polypoid tumors, type 2 is ulcerated tumors with raised margins surrounded by a thickened gastric wall with clear margins, type 3 is ulcerated tumors with raised margins surrounded by a thickened gastric wall without clear margins, type 4 tumors without marked ulceration or raised margins, the gastric wall is thickened and indurated and the margin is unclear, and type 5 is tumors that cannot be classified into any of the above types

4. Type 1 to 5 is classified as advanced gastric cancer (AGC).<sup>4</sup> With more detailed insights, type 0 was further classified into EGC as follows; EGC type I (elevated), EGC type II (flat, a, b, c), and EGC type III (excavated) based on endoscopic morphology by Japanese Society of Gastrointestinal Endoscopy.

Since bare-eye gastroscopic classification was imposed for gastric cancer, the accuracy of preoperative diagnosis of EGCs is limited, 5.9% to 22.2% of cases of clinically diagnosed EGCs are actually AGCs.<sup>5-8</sup> The endoscopic distinction between early and early-like advanced cancers was correctly made in 83.6% of the cases.<sup>9</sup> Misdiagnosed AGCs frequently have a macroscopic appearance like EGC, can be recognized as a subgroup of cancer, namely EGC-like AGC or AGC simulating EGCs. They showed different behavior as compared to conventional EGC or AGC. Most of these particular carcinomas were of the depressed type and frequently related to ulcer on gross inspection. Histologically, the tumors were of diffuse type in 60%, and the rate of the carcinomas restricted to within the muscularis propria was 48%. Some authors divided these particular cancers into four groups; small invasion type (type A) and ulcer-connected type (type B) having small percentage of lymph node metastasis and a good prognosis, whereas vessel permeation type (type C), and diffusely infiltrative type (type D), showing a high percentage and a poor prognosis accompanied with high-DNA ploidy.<sup>10</sup> The 5-year survival rate was favorable, 73% to 82.6%, in EGC-like AGC group, and about 60% in Bormann's criteria group.<sup>11</sup> Sun et al.<sup>12</sup> reported these EGC-like AGC have lymph node metastasis restricted to the perigastric lymph nodes and lymph nodes at stations of 7, 8a, and 9 for which cases gastrectomy with limited lymphadenectomy was sufficient.

In an article published in the *Clinical Endoscopy*, Park et al.<sup>13</sup> analyzed and characterized the EGC-like AGC and AGC like EGC in detail. Though this study was retrospective cohort

Received: February 13, 2013 Revised: February 27, 2013

Accepted: February 27, 2013

Correspondence: Ki Baik Hahm

Digestive Disease Center, CHA Bundang Medical Center, CHA University and CHA Cancer Prevention Research Center, CHA Cancer Institute, 59 Yatap-ro, Bundang-gu, Seongnam 463-712, Korea

Tel: +82-31-780-5220, Fax: +82-31-780-5219, E-mail: hahmkb@cha.ac.kr

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

study, a total of 14 (6.8%) cases among EGCs were finally diagnosed as EGC-like AGC, and 25 (14.9%) cases among 168 AGCs were finalized as AGC-like EGC. As results, AGC-like EGCs predominate in the distal part of the stomach (48% in antrum, 52% angle to lower body), 60% of them are moderately differentiated, 68% of them are intestinal type, whereas EGC-like AGCs predominate in the proximal part (50% mid to high body, 21% cardia and fundus), 64% of them are poorly differentiated, 71% of them are diffuse type.

Several limitations of this study should be considered. Since the study was retrospective study, there might be high selection bias. Furthermore, the number of study subject was small, AGC like EGC was only 14 and EGC-like AGC was 25. Therefore, the analysis of mucin phenotype or microsatellite instability could not reach statistical significance. Moreover, as the authors mentioned in discussion, they did not apply endoscopic ultrasonography (EUS), magnifying endoscopy, or narrow band image which may helpful for further accurate assessment of tumor depth. In a study of EGC, high-frequency EUS was found to have 90% accuracy for differentiating between mucosal and submucosal tumor invasion<sup>14</sup> and magnifying endoscopy with narrow band image accurately predicted depth of invasion in 95%.<sup>15</sup> Also, there was no information about patients prognosis, difference of lymph node metastasis. The authors just compare EGC-like AGC with AGC-like EGC, and they did not compare to Bormann's type AGC. Also, only one examiner determined macroscopic classification. Despite of those limitations, the study confirmed that AGC-like EGC and EGC-like AGC were different in clinical feature, and when evaluating the depth of a gastric cancer, more care should be taken not to underestimate measurements in proximal gastric cancers. Importantly, care should be taken not to overestimate measurements the cancers locating in stomach antrum. Though looking similar, they imparts quite different clinical impacts in spite of looking alike on endoscopy. Though looking similar, but behave quite differently in gastric cancer.

#### Conflicts of Interest

The authors have no financial conflicts of interest.

#### REFERENCES

- Shibuya K, Mathers CD, Boschi-Pinto C, Lopez AD, Murray CJ. Global and regional estimates of cancer mortality and incidence by site: II. Results for the global burden of disease 2000. *BMC Cancer* 2002;2:37.
- Chung IK, Lee JH, Lee SH, et al. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. *Gastrointest Endosc* 2009;69:1228-1235.
- Gotoda T, Yanagisawa A, Sasako M, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. *Gastric Cancer* 2000;3:219-225.
- Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer* 2011;14:101-112.
- Baek YH, Yoo HS, Yoon HA, et al. The usefulness of the endoscopic findings for predicting depth of invasion in early gastric cancer. *Korean J Gastrointest Endosc* 2007;35:297-303.
- Kim SG. Estimation by gross findings in early gastric cancer. *Clin Endosc* 2012;45:245-247.
- Choi J, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Endoscopic prediction of tumor invasion depth in early gastric cancer. *Gastrointest Endosc* 2011;73:917-927.
- Choi J, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Comparison of endoscopic ultrasonography and conventional endoscopy for prediction of depth of tumor invasion in early gastric cancer. *Endoscopy* 2010;42:705-713.
- Sano T, Okuyama Y, Kobori O, Shimizu T, Morioka Y. Early gastric cancer. Endoscopic diagnosis of depth of invasion. *Dig Dis Sci* 1990;35:1340-1344.
- Mori M, Adachi Y, Nakamura K, Kuroiwa S, Enjoji M, Sugimachi K. Advanced gastric carcinoma simulating early gastric carcinoma. *Cancer* 1990;65:1033-1040.
- Maehara Y, Anai H, Moriguchi S, Watanabe A, Tsujitani S, Sugimachi K. Gastric carcinoma invading muscularis propria and macroscopic appearance. *Eur J Surg Oncol* 1992;18:131-134.
- Sun Z, Wang ZN, Zhu GL, et al. Advanced gastric cancer with early cancer macroscopic appearance: is it worthy of D2 lymphadenectomy? *Ann Surg Oncol* 2010;17:1278-1290.
- Park HS, Lee SY, Hong SN, et al. Early gastric cancer-like advanced gastric cancer versus advanced gastric cancer-like early gastric cancer. *Clin Endosc* 2013;46:155-160.
- Yoshida S, Tanaka S, Kunihiro K, et al. Diagnostic ability of high-frequency ultrasound probe sonography in staging early gastric cancer, especially for submucosal invasion. *Abdom Imaging* 2005;30:518-523.
- Li HY, Dai J, Xue HB, et al. Application of magnifying endoscopy with narrow-band imaging in diagnosing gastric lesions: a prospective study. *Gastrointest Endosc* 2012;76:1124-1132.