

**Original contribution**

# Prognostication of superficial Barrett's carcinoma: a Japanese multicenter study<sup>☆</sup>



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Received 23 October 2017; revised 23 February 2018; accepted 1 March 2018

**Key Words:**

Superficial Barrett's carcinoma;  
Risk factor;  
Lymph node metastasis;  
Prognostication;  
Endoscopic resection;  
Surgical resection

**Summary** Endoscopic resection (ER) has become the standard therapy for superficial Barrett's carcinoma (BC) in Japan and other countries. Patients undergoing ER sometimes require additional treatment because of recurrence of lymph node metastasis (LNM). We attempted to clarify the histopathologic risk factors for LNM, and the difference between these risk factors for Japanese patients and the conventional risk factors documented for Western patients. This multi-center study included 12 leading institutions belonging to the Japan Research Society for Early Esophageal Cancer and Chromoendoscopy, and was based on a questionnaire designed to gather data on the features of superficial BC cases, except for high-grade intraepithelial neoplasia, treated at those institutions. These features were assessed using the standardized pathologic approach employed in Japan, whereby surgically and endoscopically resected specimens are cut into parallel slices 4–5 mm and 2 mm thick, respectively. Seventy-four surgically resected (SR) and 201 ER specimens were analyzed separately. Significant risk factors for LNM were almost the same as conventional risk factors, such as tumor size (cut-off value; 17.5 mm) and depth, vessel infiltration, presence of poorly differentiated components, and the depth (cut-off value; 990 μm) and width (cut-off value; 4300 μm) of the submucosal component, in addition to growth pattern (a protruding or flat elevated pattern) and the presence of infiltrative growth. Histopathologic examination revealed that BC cases without invasion to the deep muscularis mucosae (DMM) had almost no risk of LNM. Detailed histopathologic evaluation of thin-slice preparations of ER specimens is considered highly important for prognostication.

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<sup>☆</sup> Conflicts of interest and source of funding: This study was supported by Tokyo Metropolitan Institute of Gerontology. The authors and our institution did not receive payment or services from a third party for any aspect of the submitted work. This manuscript represents no conflicts of interest, none of the content has been published previously, and the manuscript is not under consideration by any other journal.

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<https://doi.org/10.1016/j.humpath.2018.03.001>

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## 1. Introduction

Although Barrett's carcinoma (BC) is less frequent in Japan than in European countries or the USA [1], gastroesophageal reflux disease and Barrett's esophagus and carcinomas have recently been increasing in Japan. Endoscopic resection (ER) for mucosal BC has become the standard therapy in Japan, and also in Western countries. Histopathologic evaluation of ER specimens is considered critical for prognostication, and many studies of the risk factors for poor outcome of BC have reported from Western countries. However, few studies have investigated the factors that are important for prognostication of superficial BC in Japan.

We attempted to clarify the risk factors for lymph node metastasis (LNM) and the difference between such risk factors in Japanese cases and those in Western cases. We collected data that had been recorded in a uniform manner: all data were based on materials that had been resected en bloc endoscopically or surgically, and diagnosed as superficial BC using the same criteria. We then ascertained the elements that were of prognostic relevance, especially the depth of tumor invasion, along with conventional risk factors. We also attempted to assess whether any differences might have arisen due to the preparation methods employed.

This multi-center study included leading institutions specializing in the diagnosis and therapy of superficial BC belonging to the Japanese Research Society for Early Esophageal Cancer and Chromoendoscopy (JRSEEC; 72nd organizer: Junko Aida, Conference President: Tatsuyuki Kawano, <http://sikiso.kenkyuukai.jp/about/>).

The JRSEEC was established in 1978 for the analytical study and popularization of chromoendoscopy by iodine mucosal staining, which is useful for diagnosis of early squamous cell carcinoma of the esophagus. Thereafter, official meetings have been held biannually to discuss timely topics related to esophageal endoscopy. The Society has been active in contributing to (1) consolidation of methods for early diagnosis of

esophageal cancer, and (2) conceptualization of early esophageal cancer and development of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). At all of the participating institutions, pathologic examination of resected specimens is based on the Japanese Classification of Esophageal Cancer (JCEC) [2,3]. Preparations and diagnoses based on the JCEC criteria are always required at the JRSEEC study meetings. For this, whole step sections are prepared from surgically (SR) and endoscopically resected superficial cancers, and the entire resected specimen is cut into slices 4-5 mm and 2 mm thick, respectively [2,4]. Although the many gastroenterology-related societies in Japan hold regular meetings, we consider that the JRSEEC provides a forum for the most specialized and detailed discussions regarding superficial esophageal cancers (pT1NXMX) [3,5]. All individuals (surgeons, endoscopists, and pathologists) involved in the present study are members of the JRSEEC and have considerable experience in esophageal cancers, all being experts in diagnosis and therapy for esophageal diseases.

Therefore, we considered that inclusion of cases handled by JRSEEC members would be an optimal approach to ensure reliable standardization of specimens and diagnosis.

## 2. Materials and methods

### 2.1. Case collection by questionnaire

We attempted to clarify the risk factors for LNM and local recurrence, and the importance of evaluating superficial (T1) BC. The participating institutions are shown in Table 1. The first author (J.A.) had prepared the questionnaire; each practitioner at the collaborating institutions entered details about the features of pT1 BC cases they had treated in the period 2000-2014, except for high-grade intraepithelial neoplasia (HGIN) (considered as BC in situ in Japan) and cases without any preoperative therapy.

**Table 1** Coauthors at the participating institutions and the numbers of cases

| Institution (participants)  | SR | ER  |
|---|----|-----|
| Naoko Inoshita, Pathology; Kei Matsui, GI Med., Toranomon Hosp.   | 16 | 47  |
| Akiko Takahashi, Tsuneo Oyama; GI Med., Saku Center of Hospital, Advanced Care Center                   | 0  | 39  |
| Soji Ozawa, Takayuki Nishi; GI Surg., Tokai Univ.   | 31 | 1   |
| Manabu Takeuchi; GI Med., Niigata Univ.   | 0  | 31  |
| Mika Tsunomiya, Miwako Arima; GI Med., Saitama Pref. Cancer Center                                      | 9  | 18  |
| Kenro Kawada; Surg., Tokyo Med. Dent. Univ.   | 9  | 18  |
| Yuki Maeda; GI Med., Sendai Open Hosp.  | 1  | 20  |
| Ryu Ishihara; GI Med., Osaka Med. Center, Cancer and Cardiovascular Dis.                                | 6  | 12  |
| Yoichiro Ono; GI Med., Fukuoka Univ.  | 1  | 10  |
| Shinshichi Hamada; Pathology, Otsu Municipal Hosp.  | 1  | 2   |
| Junko Aida, Kaiyo Takubo, Geriat. Pathology; Makoto Nishimura, GI Med., Tokyo Met. Geriat. Hosp & Inst. | 0  | 2   |
| Kenji Kobayashi; Surg., Hyogo Pref. Nishinomiya Hosp.   | 0  | 1   |
| Total   | 74 | 201 |

Abbreviations: SR, surgically resected specimens; ER, endoscopically resected specimens.

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