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SHORT COMMUNICATION

Design of Japanese multicenter prospective cohort study of endoscopic resection for early gastric cancer using Web registry (J-WEB/EGC)

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Abstract A Japanese multicenter prospective cohort study is currently being conducted on endoscopic resection (ER) for early gastric cancer (EGC) using a Web registry system developed to determine short-term and long-term outcomes based on the absolute and expanded indications. All consecutive patients with EGC or suspected EGC undergoing ER at the 41 participating institutions from July 2010 to June 2012 are being enrolled in the study cohort using the Web registry system, and each patient will be followed up for a minimum of 5 years. The study investigation includes baseline patient and lesion characteristics as well as short-term and long-term outcomes. A survey program to collect information on long-term outcomes is also being introduced for patients subsequently followed up in institutions other than their original participating institutions, as well as patients for whom the original participating institutions have been losing track of their follow-up. The primary endpoint is 5-year overall survival, with en bloc resection, curative resection, complication, local recurrence, distant metastasis, metachronous EGC, and recurrence-free survival being secondary endpoints in addition to the successful collection of long-term outcome data on enrolled patients utilizing the survey program.

Keywords Early gastric cancer · Endoscopic mucosal resection · Endoscopic submucosal dissection · Cancer registry

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Introduction

Endoscopic resection (ER) is accepted as a less-invasive method for local resection of early gastric cancer (EGC), with a negligible risk of lymph node metastasis [1]. Remarkable progress has been made during the past decade in making technical improvements and expanding the indications for ER. Endoscopic treatment methods vary from conventional endoscopic mucosal resection (EMR) to endoscopic submucosal dissection (ESD) [2–9]. According to the Japanese gastric cancer treatment guidelines for 2010, the absolute indications for ER of EGC consist of a lesion clinically diagnosed as a differentiated histological type intramucosal cancer $\leq$2 cm in diameter with no ulcer findings [10]. Based on a retrospective analysis of the

percentage of lymph node metastasis in a large number of surgical EGC cases, other groups of EGC patients with a negligible risk of lymph node metastasis have been identified to include patients with larger lesions and lesions with ulceration [11]. Such lesions were previously resected by surgery because of the difficulty in effectively using the EMR techniques then existing. Following the development of ESD, however, en bloc resections could be achieved even for larger and ulcerative lesions. As a result, the Japanese gastric cancer treatment guidelines for 2010 now include expanded indications for ER of EGC [10].

A number of reports have been published on the short-term and long-term outcomes of EMR and ESD for EGC based on the absolute and expanded indications, but most of the reports were retrospective studies from single centers [12–17]. One published multicenter retrospective study reported a favorable 3-year survival rate, although about 20 % of the patients were excluded from the long-term outcome analysis because their follow-up information was unavailable [12].

As a result, a Japanese multicenter prospective cohort study of ER for EGC using a Web registry system (J-WEB/EGC) was developed and introduced in July 2010.

J-WEB/EGC design

Purpose

Our purpose is to determine in a multicenter prospective cohort study the short-term and long-term outcomes of EMR and ESD for EGC based on the absolute and expanded indications.

Endpoints

The primary endpoint is 5-year overall survival. Secondary endpoints are en bloc resection, curative resection, complication, local recurrence, distant metastasis, metachronous EGC, and recurrence-free survival in addition to the successful collection of long-term outcome data on enrolled patients at 5 years utilizing the survey program.

Study cohort

We set the 41 participating institutions to cover nearly all regions of Japan (Table 1). All consecutive patients with EGC or suspected EGC undergoing ER at the participating institutions from July 2010 to June 2012 are included in this study. A patient is excluded only if written informed consent is not obtained. All enrolled patients are prospectively registered to the Web registry system, and each patient will be followed up for a minimum of 5 years. This study is being conducted with the approval of every institutional review board; written informed consent is being required for enrollment from each patient; and the

Table 1 Participating institutions from north to south in Japan

1	Tonan Hospital, Hokkaido
2	Kin-Ikyou Chuo Hospital, Hokkaido
3	Akita University Hospital, Akita
4	Iwate Medical University Hospital, Iwate
5	Yamagata Prefectural Central Hospital, Yamagata
6	Sendai City Medical Center, Miyagi
7	Fukushima Medical University Hospital, Fukushima
8	Niigata University Medical & Dental Hospital, Niigata
9	Niigata Prefectural Central Hospital, Niigata
10	Jichi Medical University Hospital, Tochigi
11	Tochigi Cancer Center, Tochigi
12	National Cancer Center Hospital East, Chiba
13	National Cancer Center Hospital, Tokyo
14	Cancer Institute Hospital, Tokyo
15	Toranomon Hospital, Tokyo
16	The University of Tokyo Hospital, Tokyo
17	National Center for Global Health and Medicine, Tokyo
18	Chofu Touzan Hospital, Tokyo
19	Kitasato University East Hospital, Kanagawa
20	Yokohama City University Medical Center, Kanagawa
21	Saku Central Hospital, Nagano
22	Shizuoka Cancer Center Hospital, Shizuoka
23	Toyama Prefectural Central Hospital, Toyama
24	Ogaki Municipal Hospital, Gifu
25	Aichi Cancer Center Hospital, Aichi
26	Ishikawa Prefectural Central Hospital, Ishikawa
27	University Hospital, Kyoto Prefectural University of Medicine, Kyoto
28	Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka
29	Osaka Koseinenkin Hospital, Osaka
30	Kobe University Hospital, Hyogo
31	Hyogo Cancer Center, Hyogo
32	Tottori Red Cross Hospital, Tottori
33	Okayama University Hospital, Okayama
34	Tsuyama Central Hospital, Okayama
35	Tokushima University Hospital, Tokushima
36	Hiroshima University Hospital, Hiroshima
37	Hiroshima City Hospital, Hiroshima
38	Shikoku Cancer Center, Ehime
39	Fukuoka University Chikushi Hospital, Fukuoka
40	Saga University Hospital, Saga
41	Nagasaki University Hospital, Nagasaki

study has been registered in the UMIN Clinical Trial Registry (UMIN000005871).

Study methods

The study investigation is divided into baseline patient and lesion characteristics as well as short-term and long-term outcomes. Baseline patient and lesion characteristics are entered using the Web registry system by each of the 41 participating institutions before ER. Baseline patient characteristics include age, gender, performance status, body weight, body height, medical history, concomitant disease, regular use of anticoagulant and/or antiplatelet drugs, and information on *Helicobacter pylori* infection/eradication. Other personal identification information, such as name, date of birth, and institutional reference number for each patient, is not entered in the Web registry system database, but a conversion code is instead used, based on the applicable institutional reference number, to ensure patient confidentiality. Baseline lesion characteristics include endoscopic determinations on tumor location, size, and depth, macroscopic type, ulcer findings, and the histological diagnosis of any biopsy specimen.

Short-term outcomes are entered using the Web registry system by each of the participating institutions for 6 months following ER. Short-term outcomes include the day and method of ER, primary instrument used during ESD, type of anesthesia, procedure time, number of resected specimens, complications, histological findings from ER specimens, and any additional treatment. Histological findings include tumor histological type, size, depth, macroscopic type, ulcer finding, lymphatic involvement, vascular involvement, lateral margin, and vertical margin.

Long-term outcomes are entered using the Web registry system by each of the participating institutions at 1, 3, and 5 years following ER. Long-term outcomes include follow-up status, local recurrence, metastasis, metachronous EGC, information on *Helicobacter pylori* infection/eradication, and mortality. Follow-up status includes follow-up in the original participating institution, subsequent follow-up at another institution, and losing track of appropriate follow-up.

According to the Japanese gastric cancer treatment guidelines 2010, it is recommended each patient be followed up with an esophagogastroduodenoscopy at least annually for 5 years following ER. In the case of a histologically curative resection for EGC based on the expanded indications, an abdominal computed tomography or ultrasonography examination is also recommended at least annually.

Survey program for patients subsequently followed up at other institutions and patients whose follow-up has been lost

To collect information on the long-term outcomes for a patient subsequently followed up at an institution other than the original participating institution, a questionnaire survey is sent to such institution. For a patient for whom the original participating institution has lost track of their follow-up, and for whom there has been no response to the questionnaire survey from such other institution, a questionnaire survey is sent directly to the patient. If there is still no response, we refer to the patient's residential register for information on whether the patient has moved or is no longer living. For any patient who has moved, a questionnaire survey is sent to the new address provided by such patient's residential register. If it becomes necessary to identify a patient's cause of death, cause of death is confirmed by contacting the institution where the patient died, hospital-based cancer registries, the Ministry of Justice, or using mortality data from the Ministry of Health, Labour and Welfare.

The coordinating center for the J-WEB/EGC conducts these follow-up surveys as necessary after requesting the original participating institution for personal identification information on a particular patient, except for two participating institutions that conduct their own follow-up surveys without sending personal identification information on such a patient to the coordinating center as recommended by the institutional review boards of those two institutions. Long-term outcome data obtained from any follow-up survey for a particular patient are made available to the original participating institution through the Web registry system.

Discussion

J-WEB/EGC is a Japanese multicenter prospective cohort study of ER for EGC using a Web registry system that has several unique features. First, the follow-up survey program will be conducted for patients followed up at other institutions and patients whose follow-up has been lost. It can be quite difficult to follow up all consecutive patients in each participating institution for a lengthy period. Although a nationwide population-based cancer registry is currently being developed in Japan that will provide data on patient prognosis to hospital-based cancer registries, it may not be completed by the end of this study's initial 5-year follow-up period [18]. In this study, the patient is informed that the follow-up survey program will be conducted only when the patient is followed up in another institution or the original participating institution loses

track of the follow-up, and written informed consent is obtained from each patient before enrollment.

Second, the participating institutions cover nearly all regions of Japan for evaluating a large number of consecutive ER patients with EGC. Approximately 5,000 patients have already been enrolled during the first year from July 2010 (data not shown), so both short-term outcomes and long-term outcomes based on an expected high patient follow-up rate will become available from a very large number of cases as a result of this study.

Third, the Web registry system is being utilized in this study so each of the 41 participating institutions and the coordinating center can adequately handle an enormous amount of data from a very large number of EGC cases. The Web registry system is equipped with a number of security measures including a firewall, intrusion detection, antivirus program, secure socket layer, and access restriction. In addition, specific personal identification information such as name, date of birth, and institutional reference number for each patient is not entered in the Web registry system database; a conversion code based on a patient's institutional reference number being used instead to further protect patient confidentiality. The security of the Web registry system was also confirmed in a pilot study conducted before this study, and there have been no security-related problems since J-WEB/EGC was introduced in July 2010.

In summary, J-WEB/EGC became fully operational in July 2010. Short-term outcomes and long-term outcomes of ER for EGC based on a high patient follow-up rate will become available in a few years from a very large number of cases as a result of this comprehensive study.

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