JGCA Gastric Cancer Treatment Guidelines
—A new trend in cancer treatment—

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Abstract: “General Rules for Gastric Cancer Study,” published by the Japanese Gastric Cancer Association (JGCA), has contributed greatly to advances in both the diagnosis and treatment of gastric cancer in Japan. In March 2001, the Association published a new book, “Gastric Cancer Treatment Guidelines,” a set of guidelines prepared by a committee of the Association. This is the first time in Japan that guidelines have been published for the treatment of cancer. These guidelines are expected to promote evidence-based medicine in the field of gastric cancer. In addition, an explanation of the guidelines for the patients and their families was published last December. This book provides clear, easy-to-understand information for the general public and may point to a new trend in the practice of cancer treatment.

Key words: Gastric cancer; Guidelines; EBM; Standard therapy; Japanese Gastric Cancer Association

Introduction

Gastric cancer is the most frequent type of cancer in Japan, with about 100,000 new cases occurring each year.1) Because of improved diagnostic techniques and more widespread screening, early gastric cancer has begun to account for a larger proportion of all gastric cancer cases, resulting in improved overall therapeutic results.

Standard gastrectomy, which involves resection of most of the stomach and extensive dissection of lymph nodes, was formerly a common procedure in the treatment of gastric cancer. However, as early cancers have increased relative to more advanced cases of gastric cancer, this treatment has begun to be reconsidered. Specifically, modified surgery involving limited resection of the stomach, preservation of the vagal nerve to avoid decreased postoperative function, and reduced dissection of lymph nodes have been tried. In addition, treatment by endoscopic mucosal resection (EMR) has been aggressively carried out in
patients with gastric cancer unlikely to be associated with lymph node metastasis. Laparoscopic gastrectomy, rather than open abdominal surgery, has also been used. On the other hand, for advanced gastric cancer, more extensive lymph node dissection including the para-aortic lymph nodes has been attempted. In addition to these modifications, chemotherapy, which previously had no substantial effect, has gradually become more beneficial because of new developments in dosing methods and improved drugs. In summary, the treatment of gastric cancer has been transformed from a conventional, fixed pattern of extensive resection and wide-ranging dissection to include increased variety and complexity.

These changes have created confusion among both doctors and patients as to the policies of treatment for gastric cancer. To clarify this confusion, the results of previous and current treatments need to be evaluated, and attempts to establish standard treatments appear necessary at this juncture. This paper provides an outline of the “Gastric Cancer Treatment Guidelines” issued by the Japanese Gastric Cancer Association (JGCA) in March 2001, and describes their significance.

Background

Although it is well accepted both within Japan and abroad that the treatment of gastric cancer in Japan ranks among the best in the world, treatment policies vary greatly among institutions. It is surprising to consider that no established policy of treatment exists for a disease that affects 100,000 persons per year. At a luncheon seminar of the Japan Surgical Society held in 1998, the author had the opportunity to give a presentation entitled “A Call for the Standard Treatment of Gastric Cancer.” On that occasion, the author offered the following three suggestions: first, that the “General Rules for Gastric Cancer Study,” which stipulate the staging of gastric cancer, not be altered frequently; second, that a questionnaire survey be administered to understand the present status of gastric cancer treatment; third, based on the understanding gained from the survey, that a standard treatment for gastric cancer be formulated on the basis of a thorough review of existing scientific evidence.

In addition, Dr. Toshifusa Nakajima, vice-president of the Cancer Institute Hospital, had evidenced great interest in formulating a standard treatment for gastric cancer, and, when he was installed as President of JGCA in June 1998, he organized a committee to formulate a standard treatment for gastric cancer and took action to develop guidelines for the treatment of gastric cancer.

Current Status in Japan and Guidelines in Other Countries

At present, there are almost no systematic guidelines for cancer treatment in Japan. One outstanding exception is the guidelines for breast-conserving therapy prepared by the Japanese Breast Cancer Society. However, these guidelines are restricted to breast-conserving therapy and do not cover the treatment of breast cancer as a whole. Nevertheless, this was a pioneering attempt in the preparation of guidelines for cancer treatment in Japan.

In other countries, particularly in the U.S., various guidelines are available and open to the public. Above all, the Physicians Data Query (PDQ), a database prepared and made available through the Internet by the National Cancer Institute, lists the treatments for all types of cancer according to stage.

The PDQ is an excellent resource for several reasons. First, because it is updated at regular intervals, the literature cited is also updated frequently. Regular review of guidelines requires enormous effort, but, unless such effort is put forth, the guidelines may become more harmful than useful. Another important feature of the PDQ is that an edition of the guidelines devoid of technical terms is available to the general public, in addition to the technical
Preparation of “Gastric Cancer Treatment Guidelines”

1. Scientific review

To establish a standard treatment for gastric cancer, it is necessary to submit evidence that it is indeed standard. Namely, a treatment policy with a scientific basis, i.e., evidence-based medicine, should be formulated. The best evidence for this purpose is that derived from prospective randomized studies carried out under strictly defined conditions. In actuality, however, such studies are rare in the field of surgical treatment in Japan. Most studies have drawn conclusions on the basis of experience with a limited number of subjects from a limited number of institutions. Typically, reports of these studies end with a phrase something like “further investigation in a greater number of patients is warranted.”

Therefore, in the absence of clear, strong evidence to the contrary, the most common treatment for gastric cancer employed by Japanese doctors was adopted as the standard treatment. In order to determine the most common treatment, the committee in charge of formulating a standard treatment for gastric cancer concluded that the status quo of gastric cancer treatment should be surveyed by questionnaire. The committee prepared a questionnaire and conducted a survey that covered member institutions of the JGCA in the autumn of 1998. From the results, it became apparent that almost all institutions had similar policies regarding some treatments, while completely opposing opinions were held with regard to other treatments. Of course, a consensus of institutions was firm grounds for recommending a treatment as standard.

2. Principles used in formulation of the guidelines

From the results of this questionnaire survey, a symposium entitled “Establishing Treatment Standards for Gastric Cancer” was held at the 71st general meeting of JGCA in 1999. This symposium was intended to show the current status of gastric cancer treatment in Japan as it emerged from the results of the questionnaire survey. At the same time, the symposium attempted to clarify for the members of JGCA the importance of standard gastric treatment, because the significance of such treatment had not been fully comprehended, leaving room for misunderstandings to arise.

In general, doctors do not like to have restrictions placed on their treatment strategies, and they were considered likely to resist the standard treatment policies prescribed by the Association as being meaningless or even harmful and as placing restrictions on their practice of medicine. At this symposium, not only the advantages but also the possible disadvantages of developing standard treatment policies were open for discussion. As a result of the open discussion, it was pointed out that the term “standard treatment” was not appropriate, and it was changed to “guidelines” for treatment. As a consequence, doctors’ understanding and acceptance of the guidelines were greatly enhanced.

The committee then proceeded to a discussion of gastric cancer treatment including endoscopic treatments such as endoscopic mucosal resection (EMR), modified surgery, and function-conserving surgery for early gastric cancer; surgical treatment for advanced gastric cancer; and chemotherapy. Next, treatment policies were set forth as guidelines according to the stage of the disease.

In formulating the guidelines, treatments that were considered to be current standards
based on a survey of available evidence were recommended for daily clinical practice (Table 1). On the other hand, controversial treatments were recommended for further clinical investigation (Table 2). Controversial treatments were considered to be those undergoing a process of clinical evaluation to determine their efficacy. For example, there was some controversy as to the indication of EMR for early gastric cancer; some doctors were of the opinion that it can be indicated for histologically undifferentiated cancers, whereas others disagreed. Based on its review, the committee decided that EMR for undifferentiated cancer is not a current standard because there is no clear evidence supporting this indication of EMR. This does not mean that EMR for undifferentiated cancer should be avoided. If EMR is used for undifferentiated cancer, it should be employed with well-defined indications, and the results should be reported to provide scientific evidence.

The same attitude was held toward adjuvant chemotherapy associated with surgery for gastric cancer. Although many institutions use chemotherapy for advanced cancer, there is a great deal of difference in its content, and documentation of data supporting its usefulness is insufficient. Therefore, the committee came to the conclusion that all types of adjuvant chemotherapy should be performed as part of clinical research rather than as options for daily clinical practice. It was noted that the usefulness of adjuvant chemotherapy associated with surgery should be evaluated in clinical trials in comparison with surgery without adjuvant chemotherapy. This conclusion is expected to promote clinical trials rather than to discourage them. Naturally, the guidelines would be altered if ongoing clinical trials demonstrated unequivocal results.
3. Evaluation of the guidelines

A draft of the guidelines was completed in the autumn of 1999, and was distributed to all members of JGCA. A consensus meeting then was held at the 72nd general meeting of JGCA in February 2000 in Niigata. At this meeting, committee members were to reply to criticisms presented on each aspect of the guidelines, including EMR, surgery, and chemotherapy. The hall was filled to overflowing, reflecting the strong interest of the members in the guidelines. Because of limited time, in-depth discussion of each aspect was not possible. However, opinions tended not to be critical of the guidelines themselves but were concerned more with their content. There was almost no objection to the preparation of guidelines. At that point, the committee considered the preparation of guidelines to have been approved by the members of the association, and proceeded with its elaboration of their content.

Although preparation of the guidelines was intended to be evidence-based, the possibility of bias could not be eliminated because their

Table 2  Indications of Treatments Recommended for Clinical Research According to Clinical Stage
(reproduced from “Gastric Cancer Treatment Guidelines: For Doctors,” March 2001 edition)

<table>
<thead>
<tr>
<th>Stage</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (M) &gt;2.0 cm</td>
<td>IA EMR (fractionated resection) EMR→local/segmental resection Laser radiation for incomplete EMR cases</td>
<td>IB Laparoscopic-assisted resection</td>
<td>II</td>
<td>IV Extended gastrectomy (combined resection, D3 dissection) Volume-reduction surgery Chemotherapy (systemic, local) Hyperthermo-chemotherapy</td>
</tr>
<tr>
<td>T1 (SM)</td>
<td>IA Local/segmental resection Laparoscopic local resection Laparoscopic-assisted resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>IB Laparoscopic-assisted resection II Postoperative adjuvant chemotherapy</td>
<td>IIIA Postoperative adjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>II Postoperative adjuvant chemotherapy Preoperative chemotherapy IIIA Extended gastrectomy (D3 dissection) Postoperative adjuvant chemotherapy Preoperative chemotherapy</td>
<td>IIB Extended gastrectomy (D3 dissection) Postoperative adjuvant chemotherapy Preoperative chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>IIIA Chemotherapy Preoperative chemotherapy Postoperative adjuvant chemotherapy Radiotherapy</td>
<td>IIIB Extended gastrectomy (combined resection, D3 dissection) Chemotherapy Preoperative chemotherapy Postoperative adjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H1, P1, CY1, M1</td>
<td></td>
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</tbody>
</table>
preparation was entrusted to a limited number of committee members. Therefore, to determine whether any extreme bias was present, the Guidelines Review Committee, comprised of members completely different from those of the Guidelines Preparation Committee (Chair: Dr. Nakajima), was formed. The draft guidelines proposed by the preparation committee were submitted to the review committee for careful consideration, and the opinions of the review committee were then presented to the preparation committee. Based on the results of the review, the draft guidelines were again deliberated in the preparation committee, and submitted for approval by the Board of Trustees of the Association. The final proposed guidelines were distributed to all members of JGCA, and were published following the “Gastric Cancer Treatment Guidelines” forum of the 73rd general meeting of JGCA held in Kanazawa in March 2001.

Prior to publication, this set of guidelines was examined in a special program, “Consideration of Cancer Guidelines: Using the Gastric Cancer Treatment Guidelines,” of the 38th annual meeting of the Japan Society of Clinical Oncology held in October 2000. On that occasion, opinions of specialists in treating other cancers such as breast and lung cancers and those of medical journalists outside JGCA were solicited. A generally favorable evaluation of the Gastric Cancer Treatment Guidelines was obtained, and most participants were of the opinion that similar guidelines were desirable for cancers of other organs.

“Gastric Cancer Treatment Guidelines” was published by Kanehara & Co., Ltd., and is currently in its third printing. The guidelines provide an explanation of currently available treatment modalities and present them in relation to the stage of gastric cancer according to the classifications used in daily clinical practice and those used in clinical investigations. The data and documents that served as the basis for these treatment policies are also presented. Copies of the guidelines (in Japanese) are available for 800 yen each.

4. Explanation of the Gastric Cancer Treatment Guidelines:

Guidelines for the General Public

Inspired by the PDQ model in the U.S., “Explanation of the Gastric Cancer Treatment Guidelines” (Guidelines for the General Public) was prepared. To obtain feedback about the “Guidelines for the General Public” in the process of preparation, the draft was distributed to the members of JGCA, together with the draft of the guidelines for doctors as a reference. In response, various comments and suggestions from the members were obtained. Comments on the draft “Guidelines for the General Public” were also collected from patients and other health care professionals such as nurses. The “Guidelines for the General Public” were published in autumn 2001 after a process of review by the review committee, in the same manner as that for the “Guidelines for Doctors,” and deliberation based on the results of such review.

In the “Guidelines for the General Public,” technical terms have been replaced by words that are easier to understand, and the stomach and stomach cancer are explained clearly using illustrations. In daily clinical practice, the “Guidelines for the General Public,” rather than those for doctors, may occupy a central role.

Critique of the Guidelines

Some doctors have expressed concern that publication of the guidelines may be associated with certain problems. Examples of their concerns include use of the guidelines to initiate medical lawsuits and possible restrictions on treatment policies that should be left to the doctors. However, doctors should abandon the idea that they can perform whatever treatment they wish simply because they have a medical license.

In regard to medical lawsuits, the guidelines may allow doctors to better fulfill their respon-
sibilities by providing clearer explanations to the patients and being able to offer them the “Guidelines for the General Public.” According to experts on similar guidelines in the U.S., lawsuits related to certain diseases have actually decreased rather than increased after the formulation of guidelines. Therefore, the doctors should assume a positive attitude with regard to use of the guidelines. To this end, the doctors should regard the guidelines as a matter of their own interest and should indicate points that need to be improved by carefully reviewing the contents of the guidelines. This process would result in better guidelines.

With regard to restrictions on treatment policies, it should be recognized that the absence of restrictions is unusual. If a doctor wishes to use a treatment other than that recommended for daily clinical practice, he or she should provide the patient with the rationale for the decision as well as information about the treatment that is considered standard. If a doctor were to perform an investigational treatment while allowing the patient to believe the treatment was commonly used in clinical practice, it could result in a lawsuit if the outcome were unfavorable. In contrast, if the doctor provided accurate information, it could lead to an increase in the number of patients wishing to participate in clinical trials, since such patients would understand the significance of the investigational treatment. Therefore, the guidelines are expected to promote rapid progress in clinical research.

The Ministry of Health, Labor and Welfare has been encouraging the preparation of guidelines for various diseases, and actually has organized investigations by various study groups. However, these governmental guidelines highlight the government’s intentions based on state interests although they may also focus on the benefits to the patients. In this regard, it seems ideal that an independent academic society, like JGCA, develops relevant guidelines independently while observing proper procedures. The preparation of this set of guidelines is of great significance in that it is independent of support from the Ministry of Health, Labor and Welfare and from health care and pharmaceutical companies. It is expected that the publication of “Gastric Cancer Treatment Guidelines” will provide an impetus for other academic societies to prepare their own guidelines.

**Future of the Guidelines: Conclusions**

The contents of the guidelines should not be preserved without alteration; rather, they should be improved by frequent reviews to reflect advances in treatment. To this end, it is essential that the doctors accumulate findings and report them accurately, and that the results of studies be evaluated fairly and rigorously by the committees, to update and improve the guidelines. Thus, the Preparation Committee and Review Committee have a great obligation to the future. There are a number of issues left untouched in the current guidelines. For example, policies in postoperative follow-up have hardly been touched. Such issues should be discussed straight away.

In April 2001, Dr. Nakajima, the chair of the Guidelines Preparation Committee, gave a special lecture, “Gastric Cancer Treatment Guidelines in Japan,” at the 4th International Gastric Cancer Congress, attracting the attention of attendees from various countries. Since a call for publication of the contents of the guidelines via the Internet was put forth by the audience, JGCA is now preparing for future publication of the guidelines in both Japanese and English at its URL. Readers of this document are encouraged to examine the “Gastric Cancer Treatment Guidelines” and submit candid comments and criticisms to JGCA.

**REFERENCE**


6) Committee for Formulating the Standard Treatment of Gastric Cancer, Japanese Gastric Cancer Association: *Status of Today’s Gastric Cancer Treatment: Results of the Questionnaire Survey by the Japanese Gastric Cancer Association,* 1999. (in Japanese)


**World Wide Web reference sites**

1) http://www.jgca.jp
(website of the Japanese Gastric Cancer Association; a summary of the “Gastric Cancer Treatment Guidelines” is available at this URL.)

2) http://cancernet.nci.nih.gov/pdq/pdq_treatment.shtml
(PDQ is available here.)