Table 3. Characteristics of clinical staging of MF/SS (2007–2011)

Clinical stage*	Total		Male	Female		Age at diagnosis (years)
	n	%	*n*	*n*	M/F	Median (range)
Total	774	100.0	459	314	1.46	62 (13–95)
IA	229	29.6	128	100	1.28	62 (16–92)
IB	303	39.1	177	126	1.40	62 (13–93)
IIA	33	4.3	19	14	1.36	61 (20–93)
IIB	86	11.1	51	35	1.46	61 (23–89)
IIIA	57	7.4	46	11	4.18	70 (33–95)
IIIB	7	0.9	5	2	2.50	61 (41–85)
IVA1	17	2.2	12	5	2.40	69 (37–83)
IVA2	28	3.6	12	16	0.75	64.5 (35–88)
IVB	14	1.8	9	5	1.80	64 (28–80)

*Clinical stage was identified using the International Society for Cutaneous Lymphomas/European Organization for Research and Treatment of Cancer proposal in 2007. MF, mycosis fungoides; SS, Sézary syndrome.

(62%) and the head/neck or the trunk in primary cutaneous $CD4^+$ small/medium T-cell lymphoma (52%). In pcFCL and MALT, the head and neck were commonly affected (84% and 56%, respectively). In contrast, the lower extremities were the most commonly affected sites in DLBCL, leg type (45%). BPDN preferentially arose on the trunk (83%).

DISCUSSION

In the present study, we aimed to reveal the distinct characteristics of the Japanese pattern of CL. After the initiation of the annual registry in 2007, 1733 newly diagnosed patients with CL have been registered from over 600 dermatological institutes throughout Japan. The present registry is not a "population-based" study in a precise sense. However, the data presented herein are believed to be representative of the Japanese CL. A possible limitation of the study includes uncertainty about the accuracy of the diagnostic procedure in each institute with lack of central pathology review. However, we believe this may not be a matter of great importance, because all enrolled institutes have residency programs for dermatologists to become board-certified by the JDA. By the present registry system, trends of overall incidence and disease distribution of CL in Japan will be evaluated continually.

We showed that the majority (85.7%) of CL cases were mature T-cell and NK-cell neoplasms, more or less similar to findings in previous studies from Japan and elsewhere.[7–15] However, in detail, the incidence rate of mature T-cell and NK-cell neoplasm in the present study was 8.7–14.4%, higher than in those of the USA and Europe. In contrast, the incidence of mature B-cell neoplasm (12.9%) was much lower: 10.1–15.6% lower than in the west (Table 4). It is noteworthy that the incidence rate of MALT in the present study was lower than in those of the USA and Europe. Occasionally, the distinction between B-cell pseudolymphoma and MALT can be very difficult in some patients.[19] Thus, one of the possible causes may include the diagnostic difficulty of MALT. The overall incidence pattern of CL in the present study was similar to that in previous studies from single centers of Japan and Korea (Table 4).[8,12] As compared with the incidence of CL in other countries or regions, MF/SS occurred at a similar frequency (45.2%) in Japan, while the incidence rates of ATLL and ENKL were observed to be 16.7% and 2.3%, respectively. The incidence rate of ENKL was higher than those of the USA and Europe, and lower than those of Korea and Taiwan.[11,12,20]

Adult T-cell leukemia/lymphoma is a distinct hematological neoplasm caused by the human T-cell lymphotropic virus type 1 (HTLV-1)-infected malignant $CD4^+$ T cells.[21–23] The endemic areas of ATLL include high-prevalence regions of HTLV-1, such as southwest Japan, various Caribbean countries, South America and Central Africa.[24–27] ATLL shows various clinical and prognostic features, and is classified into four categories according to the Shimoyama classification: acute, lymphoma, chronic and smoldering subtypes.[28] Cutaneous lesions are frequently observed in patients with ATLL, accounting for more than 50%.[21,29] Moreover, many types of ATLL-associated eruption have been reported to date.[30–32] The present study showed high prevalence of ATLL in Japan compared with other countries or regions including Korea (Table 4).

Extranodal NK/T-cell lymphoma, nasal type, is characterized by pleomorphic cell infiltration with NK-cell phenotype, which ordinarily demonstrates positivity to Epstein–Barr virus-encoded early small RNA by *in situ* hybridization.[2] Typically, pathological features include vascular damage and tissue necrosis by angiocentric infiltration of tumor cells. Frequently, ENKL affects the upper aerodigestive tract, followed by skin, soft tissue, the gastrointestinal tract and testes.[2] It is more prevalent in East Asia, Central America and South America than in Europe and the

Figure 1. The anatomical distribution sites of the primary skin lesion are shown in the graphic representation. (a) Primary cutaneous anaplastic large-cell lymphoma (pcALCL), (b) subcutaneous panniculitis-like T-cell lymphoma (SPTCL), (c) primary cutaneous $CD4^+$ small/medium T-cell lymphoma, (d) primary cutaneous follicle center lymphoma (pcFCL), (e) extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT), (f) primary cutaneous diffuse large-cell lymphoma, leg type (pcDLBCL, leg type) and (g) blastic plasmacytoid dendritic cell neoplasm (BPDN).

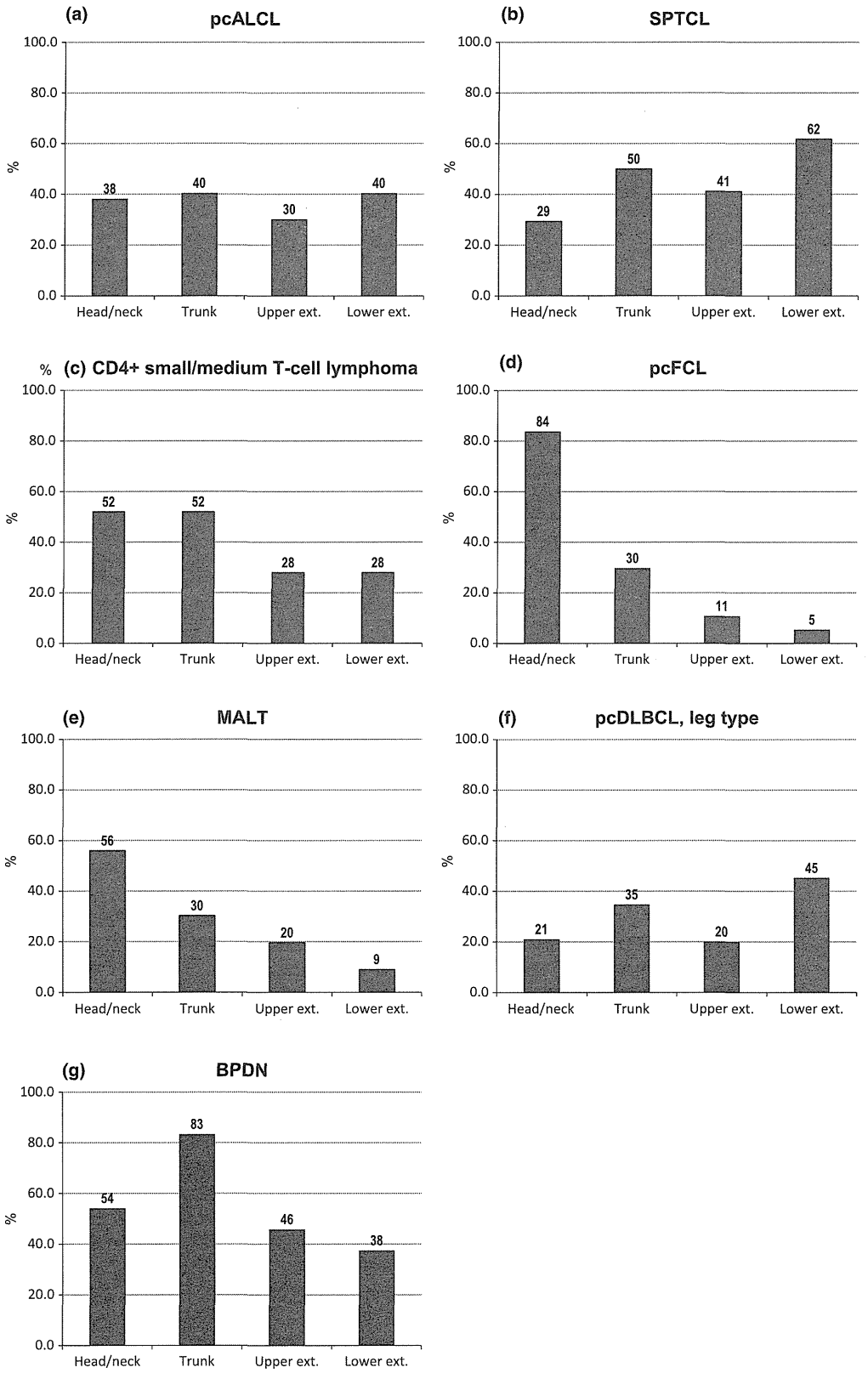

Table 4. Incidence patterns of cutaneous lymphomas from the present study and other cohorts

	Based on large-scale database			Survey from single medical centers			
Study group/registry or nation	JSCS	SEER16[15]	DACLG[13]	Switzerland[9]	France[7]	Korea[12]	Japan[8]
Total no.	1733	3884	1905	263	203	164	133
Surveillance period, year	5	5	17	20	7	16	14
Mature T-cell and NK-cell neoplasms	85.7	71.3	77	72	75.9	79.2	79.7
MF	43.3	38.3	47	43	43.3	14	41.4
SS	1.9	0.8	3	11	7.9	0.6	0.8
Primary cutaneous $CD30^+$ T-cell lymphoproliferative disorders	12.0	10.2		13			12.8
Primary cutaneous anaplastic large-cell lymphoma	7.8		8	8	3.5	14	6.8
Lymphomatoid papulosis	3.8		12	5	7.4	5.5	6.0
Subcutaneous panniculitis-like T-cell lymphoma	2.0	0.6	1		1	6.7	2.3
Peripheral T-cell lymphoma, NOS	5.8	20.8	2	2	1	4.9	3.8
Primary cutaneous $CD4^+$ small/medium T-cell lymphoma*	1.4		2	3	3	3	0.8
Primary cutaneous γδ T-cell lymphoma	0.3		<1		0.5	4.9	
Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma*	0.4				0.5		
Extranodal NK/T-cell lymphoma, nasal type	2.3	0.3	<1	<1	0	20.7	3.8
Adult T-cell leukemia/lymphoma	16.7	0.1				0.6	9.8
Mature B-cell neoplasms	12.9	28.5	23	28	24.1	16.5	18.0
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	4.2	7.1	7	14	4.9	8.5	5.3
Primary cutaneous follicle center lymphoma	2.1	8.5	11	8	17.7	0	0.0
Primary cutaneous diffuse large-cell lymphoma, leg type	5.5	2.6	4	4	1	1.2	
Intravascular large B-cell lymphoma	1.2		<1		0.5	1.2	0.8
Immature hematological neoplasms†	1.4	0.3					
Blastic plasmacytoid dendritic cell neoplasm	1.4	0.2					0.8

*Provisional. †Immature hematological neoplasms include "acute myeloid leukemia and related precursor neoplasms" and "precursor lymphoid neoplasms". JSCS, Japanese Skin Cancer Society; MF, mycosis fungoides; NK, natural killer; NOS, not otherwise specified; SD, standard deviation; SS, Sézary syndrome.

USA.[13,33–35] Also, the incidence of ENKL in CL was reported to be significantly higher in Korea (15% and 20.7%) than in Europe and the USA.[12,20] In three single-institution studies from Japan, the incidence rate of ENKL has ranged 3.8–8.8%.[8,36,37] In the present study, the incidence was somewhat lower (2.3%) than these previous studies. The difference may reflect the kind of selection bias specific to single-institution studies. Our results suggest that the high incidence rates of mature T-cell and NK-cell neoplasm are associated with the prevalence of ATLL in Japan, unlike that of ENKL in Korea.

Mycosis fungoides is the most common CL subtype in the present study as well as in almost all counties or ethnicities. In the past, staging of MF/SS was performed according to the previously proposed staging system.[38,39] Prior to the establishment of the new staging system, several clinical studies had been conducted on relatively large cohorts of cutaneous T-cell lymphoma for such a rare disease entity.[40–42] In 2007, the revised staging system for MF/SS was released by the ISCL/EORTC (which was in turn modified in 2011).[3,18] This system adopted a newly proposed classification of tumor–node–metastasis–blood rating. Since then, two clinical studies of MF/SS have been conducted in the UK and Japan.[5,6] In the present study, the proportion of patients with early stage (IA to IIA) was 73%, similar to that of the previous studies (70.7% and 78%) (Table 5). Stage IB accounted for 39.1% of the total MF/SS in the present study, making it the most prevalent clinical stage. This finding is similar to the results of previous studies (38.8% and 38%) (Table 5).[5,6] In addition, a predominance of males among MF/SS patients was shown in the present study, as in previous reports.[5,6,8,9,12–15,20,40–42] Notably, a male predominance was observed in erythrodermic MF or SS, with over twofold male predominance for stage IIIA (M : F ratio, 4.18), stage IIIB (M : F ratio, 2.50) and stage IVA1 (M : F ratio, 2.40).

We evaluated the distinct anatomical distributions of the skin lesions in patients with several types of CL. In patients with pcFCL and MALT, the head and neck were the most commonly affected sites, as in previous reports from the USA and Asia.[15,43] By contrast, in Europe, the trunk was the most commonly affected site of pcFCL and MALT.[44–46] These results suggest that a difference in preferentially affected anatomical site in patients with pcFCL and MALT may exist, at least between Europe and the USA/Asia. By definition, the lower extremities are the most common site in patients with pcDLBCL, leg type. Primary cutaneous small/medium $CD4^+$ T-cell lymphoma is a rare CL entity with an indolent clinical course, which has been shown to preferentially affect the head and neck.[13,47,48] In the present study, the trunk in

Table 5. Incidence pattern of MF/SS by clinical staging

	Study group		
	JSCS	UK[5]	Japan[6]
Total no.	774	1502	100
Surveillance period, year	5	30	25
Clinical stage*			
IA	29.6	29.2	21
IB	39.1	38.8	38
IIA	4.3	2.7	19
IIB	11.1	11.1	8
IIIA	7.4	6.7	6
IIIB	0.9	3.7	0
IVA1	2.2	4.5	2
IVA2	3.6	2.5	3
IVB	1.8	0.9	3

*Clinical stage was identified using the International Society for Cutaneous Lymphomas/European Organization for Research and Treatment of Cancer proposal in 2007. JSCS, Japanese Skin Cancer Society.

addition to the head and neck was the most common site of primary cutaneous small/medium CD4$^+$ T-cell lymphoma. SPTCL is a distinct CL entity, characterized by primarily subcutaneous (mainly fat tissue) infiltration of malignant T lymphocytes with cytotoxic molecules. It predominantly affects the legs.[13,49] Also, we found that the lower extremities were the most commonly affected site in SPTCL (62%). In addition, a female predominance was demonstrated in Japan, as in a previous report.[49]

The present study was conducted to investigate the nationwide incidence patterns of Japanese CL patients, according to the WHO classification. It provides important data about trends in the overall incidence pattern of Japanese CL. In particular, the high prevalences of ATLL and ENKL in Japan are shown, with considerable accuracy. A male predominance was observed in most types of CL, except for SPTCL, ENKL, primary cutaneous CD4$^+$ small/medium T-cell lymphoma and LyP. The present study showed that the proportion of patients in each clinical stage of MF/SS was similar to that in previous studies. In the future, accumulated data from the present registry will allow us to investigate the etiology of varying CL subtypes, and to conduct targeted clinical research based on the characteristics of CL in Japan.

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SPECIAL ARTICLE

Japan Society of Gynecologic Oncology guidelines 2011 for the treatment of uterine cervical cancer

Yasuhiko Ebina · Nobuo Yaegashi · Hidetaka Katabuchi · Satoru Nagase · Yasuhiro Udagawa · Toru Hachisuga · Tsuyoshi Saito · Mikio Mikami · Yoichi Aoki · Hiroyuki Yoshikawa

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Abstract The second edition of the Japan Society of Gynecologic Oncology guidelines for the treatment of uterine cervical cancer was published in 2011. The guidelines comprise eight chapters and five algorithms. They were prepared by consensus among the members of the Japan Society of Gynecologic Oncology Guidelines Formulation Committee and Evaluation Committee and are based on a careful review of the evidence obtained from the literature, health insurance system, and actual clinical settings in Japan. The highlights of the 2011 revision are (1) the recommended grades have been changed to five stages—A, B, C1, C2, and D; (2) the revisions are consistent with the new International Federation of Gynecology and Obstetrics staging system; (3) the roles are shared between the 'Japanese classification of cervical cancer' and the new guidelines; (4) clinical questions related to adenocarcinoma have been revised; and (5) a clinical question regarding cervical cancer in pregnant patients has been added. Each chapter includes a clinical question, recommendations, background, objectives, explanations, and references. Each recommendation is accompanied by a classification of recommendation categories. The objective of these guidelines is to update the standard treatment strategies for cervical cancer, thus eliminating unnecessary and insufficient treatment.

Keywords Uterine cervical cancer · Clinical practice guidelines · Surgery · Chemotherapy · Irradiation · Recurrence

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Y. Ebina (✉)
Department of Obstetrics and Gynecology, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-Ku, Kobe 650-0017, Japan
e-mail: ebiyas@med.kobe-u.ac.jp

N. Yaegashi
Department of Obstetrics and Gynecology, Tohoku University Graduate School of Medicine, Sendai, Japan

H. Katabuchi
Department of Obstetrics and Gynecology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

S. Nagase
Department of Obstetrics and Gynecology, Faculty of Medicine, Yamagata University, Yamagata, Japan

Y. Udagawa
Department of Obstetrics and Gynecology, Fujita Health University School of Medicine, Toyoake, Japan

T. Hachisuga
Department of Obstetrics and Gynecology, University of Occupational and Environmental Health School of Medicine, Kitakyusyu, Japan

T. Saito
Department of Obstetrics and Gynecology, Sapporo Medical University School of Medicine, Sapporo, Japan

M. Mikami
Department of Obstetrics and Gynecology, Tokai University School of Medicine, Isehara, Japan

Y. Aoki
Department of Obstetrics and Gynecology, Graduate School of Medical Science, University of the Ryukyus, Nishihara, Japan

H. Yoshikawa
Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Introduction

An estimated 6,000 new cases of invasive cervical cancer were diagnosed in Japan in 2011 [1], and 2,737 women died of the disease [2]. The mortality rate associated with cervical cancer in Japan decreased from the 1960s until 1995; however, the incidence of cervical cancer has slightly increased [2].

The first edition of the Japan Society of Gynecologic Oncology (JSGO) guidelines for the treatment of uterine cervical cancer was published in 2007 [3]; however, some clinical questions (CQs) in the first edition remained unanswered. The second edition, published in 2011, was intended to represent an aggregation of domestic evidence while collecting up-to-date international evidence without providing a new section. For the first time, we accepted specialist physicians engaged in clinical practice in cancer centers or university hospitals as candidates for the committee. Radiation oncologists and pathologists were also members of the guideline committee.

The highlights of the 2011 revision are indicated below.

1. The recommended grades have been changed to five stages—A, B, C1, C2, and D.
2. The revisions are consistent with the new International Federation of Gynecology and Obstetrics (FIGO) staging system. The new FIGO staging system was revised during the creation of these updated guidelines. The new FIGO classification excludes stage 0 carcinoma in situ; however, stage 0 still has high importance in the guidelines because many people, especially young people, have stage 0 disease. Therefore, stage 0 is present in the guidelines. Additionally, stage IIA has been reclassified to stage IIA1 and stage IIA2 in the new FIGO classification. This revision from the Japan Society of Obstetrics and Gynecology 'Japanese classification of cervical cancer' has been adopted, and the reclassification to stage IIA1 and IIA2 is present in the new guidelines.
3. Roles are shared between the 'Japanese classification of cervical cancer' and the new guidelines. A specific radiotherapy technique is detailed in the guidelines.
4. CQs related to adenocarcinoma have been revised. Few clinical trials on adenocarcinoma alone have been conducted; thus, the chapter on adenocarcinoma was deleted and a CQ related to adenocarcinoma is described in each chapter.
5. A CQ regarding cervical cancer in pregnant patients has been added. Because of the increasing incidence of cervical cancer in younger patients and of pregnancy in older patients, the treatment of cervical cancer and its complications owing to pregnancy should be addressed. Therefore, these treatment guidelines are described in detail by increasing the CQs relevant to this topic.

Treatment guidelines for cervical cancer

Chapter 1: Overview of guidelines

1. How to use these guidelines

These guidelines are intended for doctors (general practitioners and specialists) who provide medical care for patients with cervical cancer. The guidelines aim to provide useful treatment methods by integrating previous evidence of treatment benefits. However, the guidelines are not intended to be limited to the therapies listed. Their main purposes are (1) to indicate the current cervical cancer treatments that are considered appropriate, (2) to reduce differences in therapy among various institutions, (3) to improve the prognosis and safety of treatments, (4) to reduce the economic and psychosomatic burden on patients by performing appropriate treatment, and (5) to promote mutual understanding between healthcare professionals and patients.

The JSGO bears the responsibility for the content and descriptions of these guidelines. However, the final decision to use these guidelines should be made by the individual user. Thus, the physicians in charge of treatment are responsible for the outcome of treatment.

2. Method used to prepare these guidelines

To create these guidelines, the Guidelines Formulation Committee and Evaluation Committee were established independently from the Committee for the Treatment Guidelines for Cervical Cancer. The initial draft was created by thoroughly evaluating the various opinions from within and outside the JSGO prior to incorporating them into the final draft. The guidelines were published after approval by the JSGO.

(1) Classification of evidence

1. The guidelines were created in accordance with the international standard procedures of evidence-based medicine used for the creation of clinical practice guidelines.
2. In principle, searches of data and published literature were performed prior to December 2009 in Japan and overseas, and evidence was collected.
3. This collected evidence was evaluated for quality using the criteria of the Japan Society of Clinical Oncology and its Formulation Committee on clinical practice guidelines for the use of anticancer agents [4, 5]; however, it was modified to allow some of it to fit into the guidelines (Table 1).

Table 1 Classification of evaluation criteria for evidence quality

Level I Evidence from multiple randomized controlled trials or meta-analyses of multiple randomized controlled trials
Level II Evidence from at least one randomized controlled trial or multiple well-designed controlled studies without randomization
Level III Evidence from at least one other type of well-designed quasi-experimental study or from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, or case studies
Level IV Expert committee reports, or opinions and/or clinical experiences of respected authorities

Table 2 Classification of recommendation categories

Grade A The treatment is strongly recommended if at least one level I evidence indicates validity
Grade B The treatment is recommended if at least one level II evidence indicates validity
Grade C1 The treatment can be considered, but the evidence is insufficient; for example, there are several reports of level III evidence that show validity with generally consistent results
Grade C2 The treatment is not recommended without sufficient scientific evidence
Grade D The treatment is not recommended because neither utility nor effectiveness has been shown and because the treatment may be harmful

(2) Clinical questions and classification of recommendation categories

As a result of the discussions held by the Guideline Committee, controversial issues were selected as CQs and associated recommendations were made. Each recommendation in response to a CQ is accompanied by a classification of the evidence and a classification of the recommendation categories based on the consensus reached by the Guideline Committee members.

The strengths of the recommendations in our guidelines were also determined by the recommendation criteria of the Japan Society of Clinical Oncology and its Formulation Committee of Clinical Practice Guidelines for the Use of Anticancer Agents [6]. These were modified while referring to the 'Guide 2007 Minds practice guidelines' (Tables 2, 3).

Chapter 2: Primary treatment for stage 0 to IA cervical cancer (Fig. 1)

CQ01. What treatments are recommended for carcinoma in situ?

Recommendations A cervical cone biopsy is recommended (grade B).

Table 3 Classification of risk of postoperative recurrence of cervical cancer

Low-risk group: patients who meet all of the following criteria
Small cervical tumor
Negative pelvic nodes
Negative parametrical invasion
Shallow cervical stromal invasion
No venous or lymphatic infiltration
Intermediate-risk group: patients with negative pelvic nodes and negative parametrical invasion but who meet one of the following criteria
Large cervical tumor
Deep cervical stromal invasion
Positive venous or lymphatic infiltration
High-risk group: patients who meet one of the following criteria
Positive pelvic nodes
Positive parametrical invasion

CQ02. What treatments are recommended for recurrence following conservative treatment?

Recommendations (1) For recurrence following laser cone biopsy or the loop electrosurgical excision procedure, the same procedure should be repeated or a total hysterectomy considered, depending on the patient (grade B). (2) For recurrence following laser ablation or cryotherapy, either a cone biopsy or total hysterectomy is recommended (grade B).

CQ03. What treatments are recommended for stage IA1 disease?

Recommendations (1) It is possible to preserve the uterus by performing a cervical cone biopsy in patients who strongly desire fertility preservation; however, these patients must have no vascular or lymphatic infiltration, negative resection margins, and negative histological results from endocervical curettage (grade B). (2) A total hysterectomy without pelvic lymphadenectomy is recommended for patients with no evidence of vascular or lymphatic infiltration (grade B). (3) Both a modified radical hysterectomy and pelvic lymphadenectomy are sometimes performed for patients with vascular or lymphatic infiltration (grade C1).

CQ04. What treatments are recommended for stage IA2 disease?

Recommendations (1) A modified radical hysterectomy or a more extensive procedure with lymphadenectomy should be considered for stage IA2 disease (grade C1). (2) After thorough histopathological examination of a specimen obtained by diagnostic conization, omission of

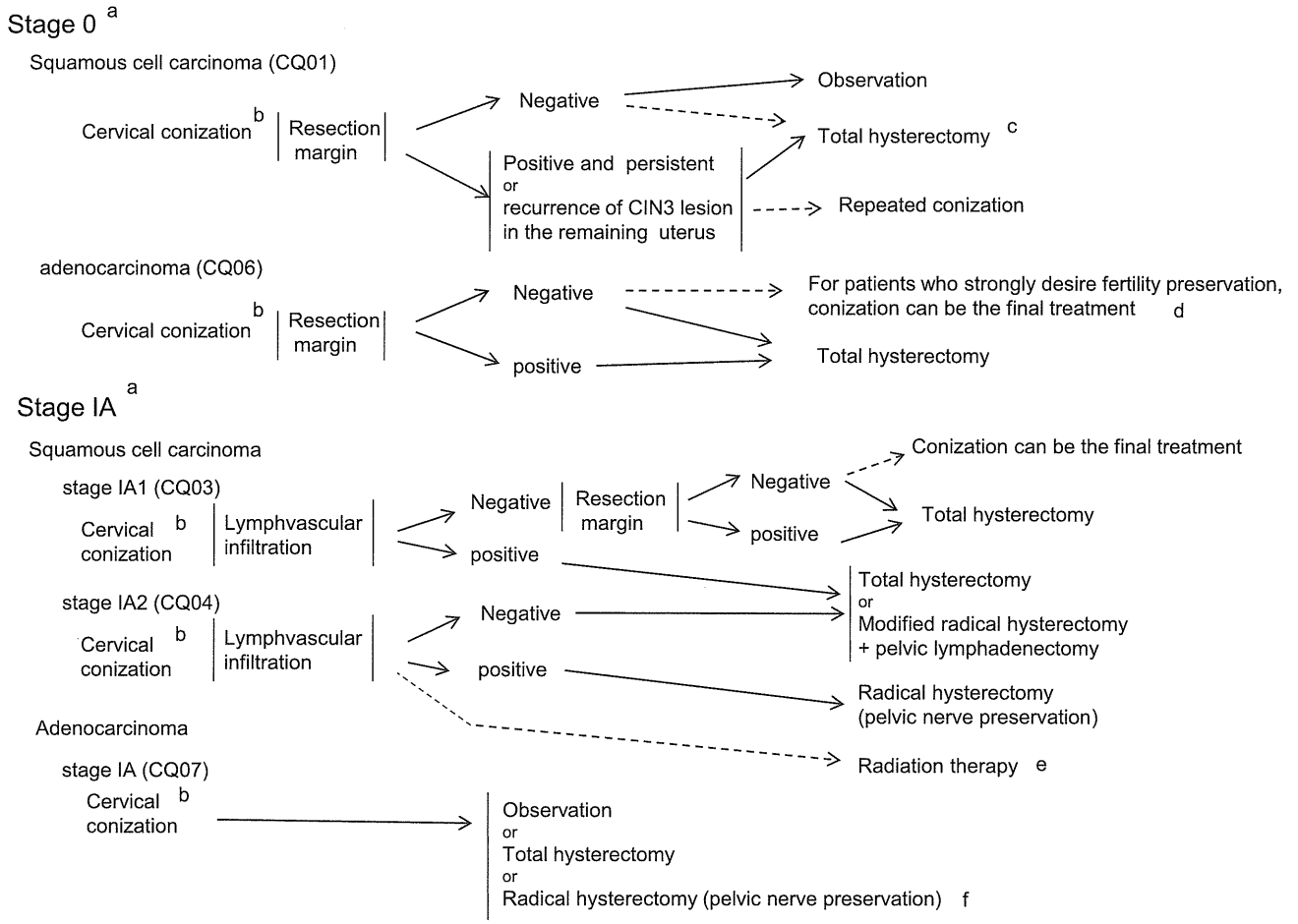

Fig. 1 Primary treatment for stage 0 to IA cervical cancer. **a** If cervical conization is difficult because of atrophy of the cervix, such as in older patients, omission of the conization may be considered. However, prior to surgery, it is necessary to carefully review the cytology, colposcopy, and biopsy tissue findings; this allows for the performance of a hysterectomy suitable for the estimated lesion. **b** Cervical canal curettage should be performed at the time of cervical conization. If cervical curettage is positive, the patient should be treated as if they have positive margins. **c** Hysterectomy may be considered if the patient does not wish to preserve her fertility. **d** Residual lesions are reportedly found in about 20 % of cases involving negative margins. Careful inspection is required to preserve the uterus. **e** In the NCCN clinical practice guidelines in oncology, radiation therapy is also an option for patients with cervical cancer. **f** Operative procedures should be individualized according to the histopathological findings of the conization specimens, namely the extent of invasion and the presence or absence of lymphovascular infiltration

lymphadenectomy in patients with no vascular or lymphatic infiltration can be considered (grade C1).

CQ05. What treatments are recommended if the disease is upstaged to stage IB or higher following total hysterectomy?

Recommendations Adjuvant radiotherapy or concurrent chemoradiotherapy (CCRT) should be considered (grade C1).

CQ06. What treatments are recommended for adenocarcinoma in situ?

Recommendations (1) A total hysterectomy is recommended (grade B). (2) Uterus preservation can be considered with cervical cone biopsy in patients who strongly desire fertility preservation. However, careful management is required (grade C1).

CQ07. What treatments are recommended for stage IA adenocarcinoma?

Recommendations (1) In cases involving deep invasion, a radical hysterectomy or modified radical hysterectomy with pelvic lymphadenectomy should be considered (grade C1). (2) In cases involving shallow invasion, a hysterectomy without pelvic lymphadenectomy (total hysterectomy or modified radical hysterectomy) can also be considered (grade C1). (3) If the patient strongly desires fertility preservation, a cervical cone biopsy can be performed

to preserve the uterus. Careful case selection is required (grade C1).

Chapter 3: Primary treatment for stage IB to II cervical cancer (Fig. 2)

CQ08. What treatments are recommended for stage IB1 and IIA1 squamous cell carcinoma?

Recommendations A radical hysterectomy or radiation therapy is recommended (grade B).

CQ09. What treatments are recommended for stage IB2 and IIA2 squamous cell carcinoma?

Recommendations A radical hysterectomy (+ adjuvant therapy) or CCRT is recommended (grade B).

CQ10. What treatments are recommended for stage IIB squamous cell carcinoma?

Recommendations A radical hysterectomy (+adjuvant therapy) or CCRT is recommended (grade B).

CQ11. Is neoadjuvant chemotherapy recommended for stage IB and II squamous cell carcinoma?

Recommendations Neoadjuvant chemotherapy can be considered depending on the extent and size of the tumor (grade C1).

CQ12. Is pelvic nerve preservation recommended in radical hysterectomy?

Recommendations Pelvic nerve preservation can be considered when curability is not impaired (grade C1).

CQ13. Is ovary preservation possible in radical hysterectomy?

Recommendations (1) Ovary preservation is possible without compromising curability if appropriate case selection is performed by considering the patient's histological type or stage (grade B). (2) If the ovaries are to be preserved, ovarian transposition and fixation outside of the pelvic radiation field can be considered (grade C1).

CQ14. Is para-aortic lymphadenectomy recommended in radical hysterectomy?

Recommendations If diagnostically useful, para-aortic lymphadenectomy can be considered to search for metastasis or determine the irradiation field (grade C1).

CQ15. What treatments are recommended for stage IB and II adenocarcinoma?

Recommendations In principle, surgery should be considered for stage IB and II disease (grade C1).

Chapter 4: Postoperative therapy for stage IB to II cervical cancer (Fig. 3)

CQ16. What is the recommended postoperative adjuvant therapy?

Recommendations (1) CCRT is recommended for patients at high risk of recurrence (grade B). (2) Radiation therapy is recommended for patients at intermediate risk of recurrence. However, CCRT can be considered depending on the number and extent of risk factors (grade C1).

CQ17. What irradiation methods are recommended when performing postoperative adjuvant radiotherapy for a patient at high risk of relapse?

Recommendations (1) Whole-pelvis irradiation is recommended (grade B). (2) Three-dimensional treatment planning is recommended (grade B). (3) The addition of intracavitary irradiation is not recommended with the exception of cases involving positive margins (grade C2).

CQ18. For whom is prophylactic para-aortic irradiation indicated?

Recommendations Para-aortic irradiation can be considered for patients with a high risk of recurrence in the para-aortic lymph nodes (grade C1).

CQ19. Are oral anticancer drugs and immunotherapy recommended as maintenance therapies?

Recommendations (1) Oral anticancer agents are not recommended because their usefulness is unclear (grade C2). (2) Immunotherapy is not recommended because its usefulness has not been fully verified (grade C2).

Chapter 5: Primary therapy for stage III to IV cervical cancer (Fig. 4)

CQ20. Which is the recommended radiotherapy for stage III and IVA disease: definitive radiotherapy or CCRT?

Recommendations CCRT is recommended rather than radiation monotherapy (grade B).

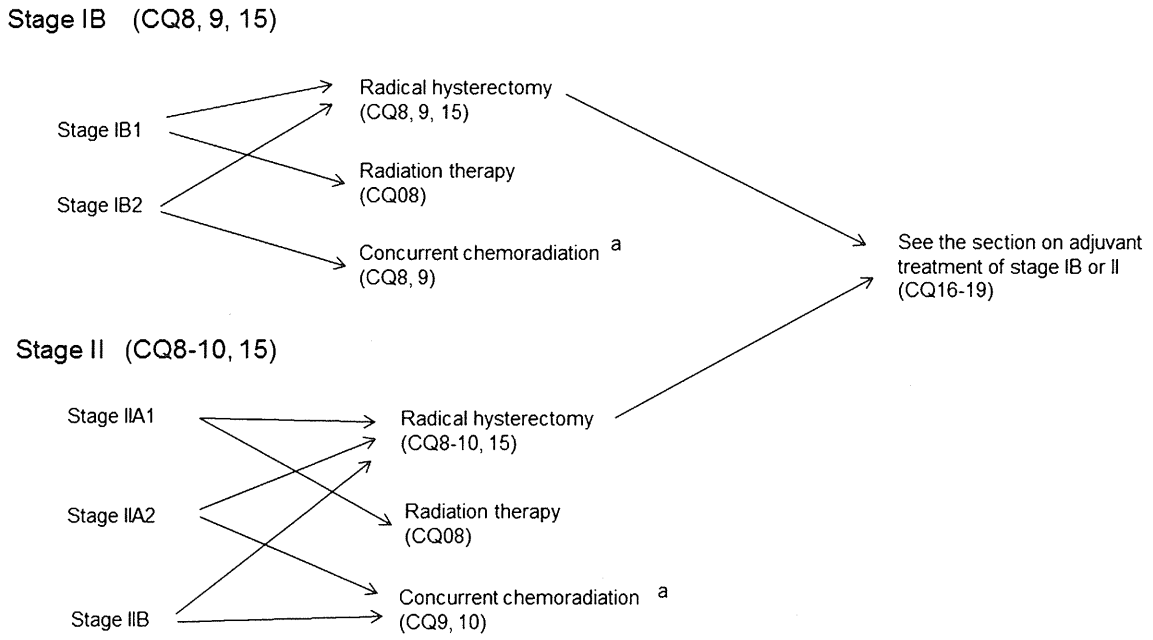

Fig. 2 Primary treatment for stage IB to II cervical cancer (including squamous cell carcinoma and adenocarcinoma). **a** Primary treatment for stage IB to II cervical cancer should be performed with caution because the tolerability of concurrent chemoradiation therapy among Japanese women has not been sufficiently tested

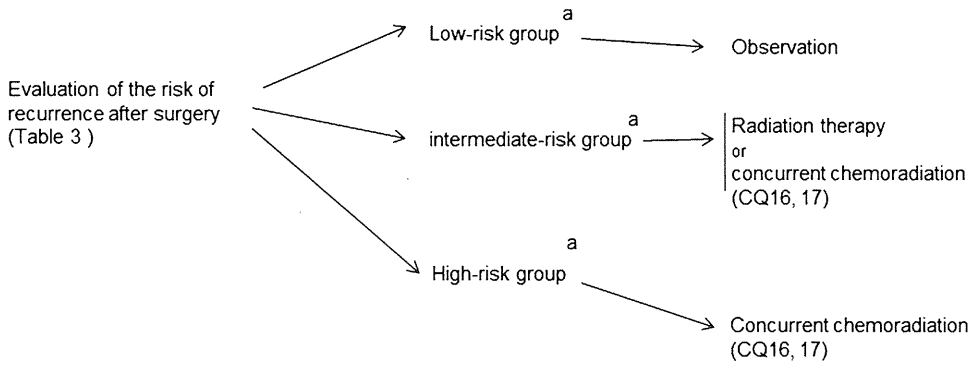

Fig. 3 Postoperative therapy for stage IB to II cervical cancer (including squamous cell carcinoma and adenocarcinoma). **a** There are many discussions and various reports on risk assessment for postoperative recurrence. Postoperative therapy must be considered according to the individual case

CQ21. What CCRT regimens are recommended for stage III and IVA disease?

Recommendations Regimens that include cisplatin are recommended (grade A).

CQ22. Is chemotherapy recommended prior to principal treatment for stage III and IVA disease?

Recommendations (1) Chemotherapy is not recommended before radiotherapy (grade D). (2) Chemotherapy is not recommended before surgery (grade C2). (3) For adenocarcinoma, chemotherapy is not recommended before primary treatment (grade C2).

CQ23. Is surgery recommended for stage III and IVA disease?

Recommendations Surgery is not recommended (grade C2).

CQ24. What treatments are recommended for stage IVB disease?

Recommendations (1) Systemic chemotherapy can be considered for patients with a good performance status and preserved organ function (grade C1). (2) Surgery, radiotherapy, chemotherapy, or a combination of these treatments can be selected for patients with distant metastatic lesions, such as resectable lung metastases, or with lymph

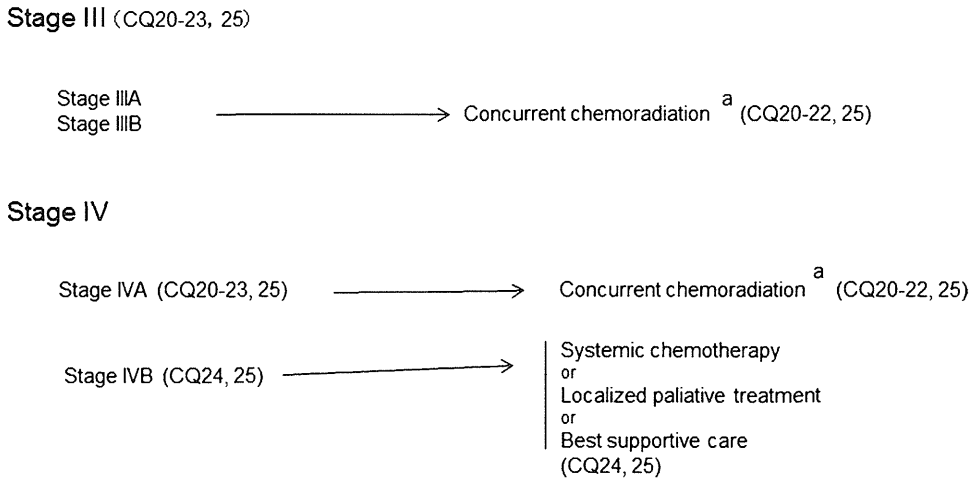

Fig. 4 Primary treatment for stage III to IV cervical cancer (including squamous cell carcinoma and adenocarcinoma). **a** Primary treatment for stage III to IV cervical cancer should be performed with caution because the tolerability of concurrent chemoradiation therapy among Japanese women has not been sufficiently tested

node metastases only (grade C1). (3) If the patient has severe symptoms accompanying oncological complications, palliative radiotherapy of the causal lesion is recommended (grade B).

CQ25. What treatments are recommended for stage III and IV adenocarcinoma?

Recommendations CCRT involving external irradiation and intracavitary irradiation is recommended for stage III or VIA adenocarcinoma (grade B). (2) A platinum-based agent other than cisplatin, either as monotherapy or as part of combination chemotherapy, can also be considered for patients with stage IVB adenocarcinoma with preserved organ function (grade C1).

Chapter 6: Therapies for relapsed cervical cancer (Fig. 5)

CQ26. What treatment methods are recommended for recurrence confined to the pelvis if radiotherapy has not been previously performed?

Recommendations (1) Radiotherapy is recommended (grade B). (2) CCRT can also be considered (grade C1).

CQ27. What treatments are recommended for recurrence within the radiation field?

Recommendations (1) Palliative treatment for symptomatic relief is the general rule for treatment (grade C1). (2) Chemotherapy can also be considered, keeping in mind that the response rate is low for recurrence within the radiation field (grade C1). (3) Localized radiotherapy or pelvic exenteration can also be considered for central recurrence in the vaginal stump after a thorough preoperative evaluation (grade C1). (4) Re-irradiation is not recommended (grade C2).

CQ28. What treatments are recommended for recurrence outside the radiation field or for extrapelvic recurrence if radiotherapy has not been previously performed?

Recommendations (1) Para-aortic metastasis: radiation therapy or CCRT can be considered for solitary metastasis (grade C1). (2) Brain metastasis: (a) stereotaxic radiosurgery along with whole-brain radiation therapy (WBRT) or WBRT alone is recommended for metastases of up to three sites (grade B). (b) WBRT is recommended for more than four metastases (grade B). (3) Bone metastasis: (a) single-fraction or multi-fraction radiotherapy is recommended for pain relief (grade B). (b) Bisphosphonates are recommended for symptom relief (grade B). (c) Strontium chloride can be considered for multiple bone metastases if medical therapy is ineffective (grade C1). (4) Lung metastasis: resection or stereotactic body radiotherapy can be considered for one to three localized metastases (grade C1).

CQ29. Is systemic chemotherapy recommended for recurrence?

Recommendations Systemic chemotherapy is recommended for patients with disease that is difficult to control by surgery or radiotherapy as well as for patients with a good performance status and preserved organ function (grade B).

CQ30. What systemic chemotherapy regimens are recommended to treat recurrent disease?

Recommendations (1) Cisplatin as either monotherapy or part of two-drug combination chemotherapy is

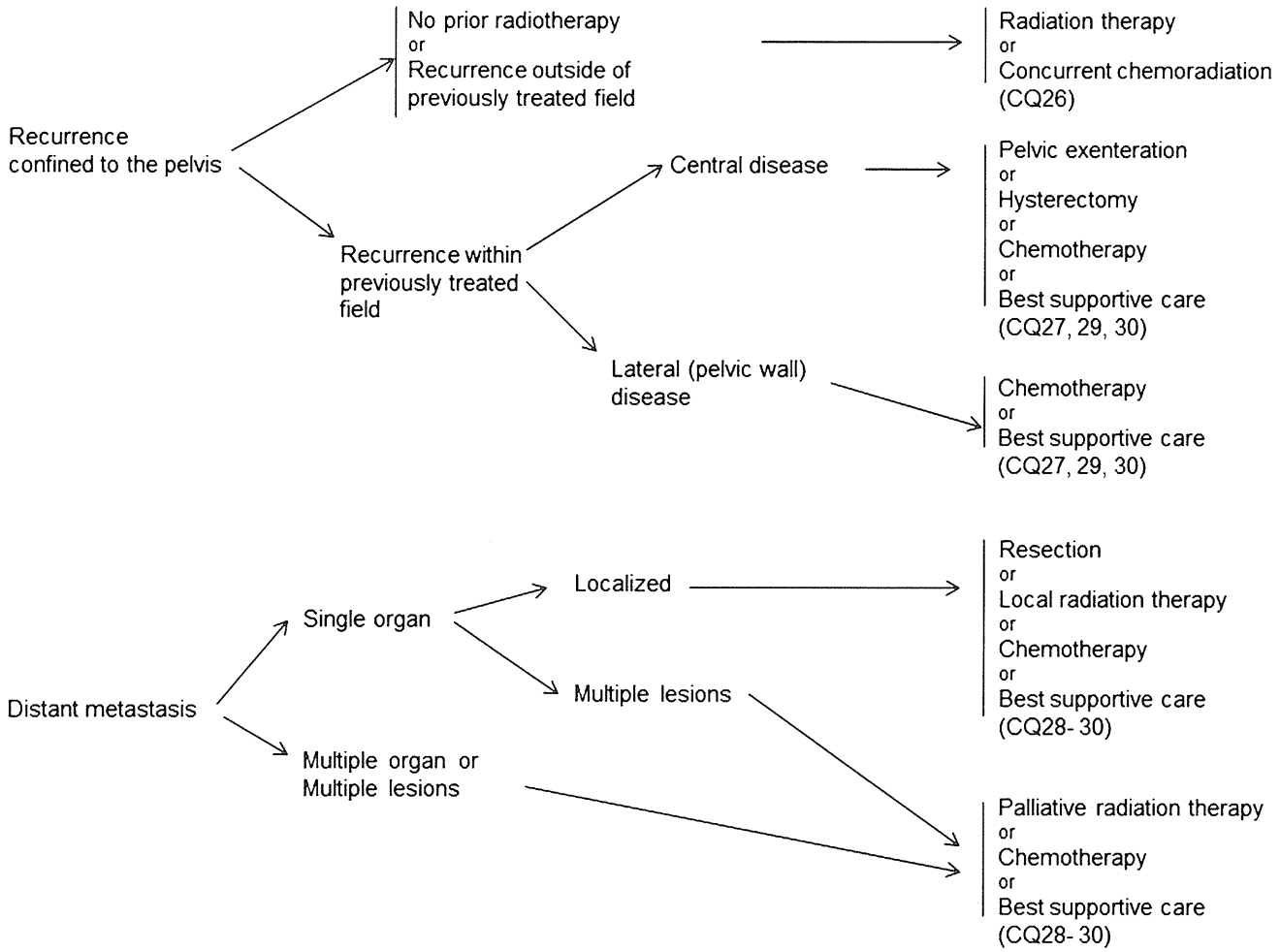

Fig. 5 Therapy for relapsed cervical cancer (including squamous cell carcinoma and adenocarcinoma)

recommended (grade B). (2) A platinum-based agent other than cisplatin, as either monotherapy or part of two-drug combination chemotherapy, can also be recommended (grade B). (3) Cisplatin as either monotherapy or part of two-drug combination chemotherapy is preferable for recurrent adenocarcinoma (grade C1).

Chapter 7: Management of cervical cancer during pregnancy

CQ31. What treatments are recommended for stage 0 disease during pregnancy?

Recommendations (1) Cone biopsy may be delayed until after delivery as long as the diagnosis is stage 0 disease based on consistent cytology, colposcopy, or biopsy analysis results (grade C1). (2) If adenocarcinoma in situ is suspected, a cone biopsy should be performed to determine the diagnosis during pregnancy (grade C1).

CQ32. What treatments are recommended for stage IA disease during pregnancy?

Recommendations If stage IA or higher disease is suspected, a cervical cone biopsy should be considered to determine the diagnosis during pregnancy (grade C1).

CQ33. What treatments are recommended for invasive cancer during pregnancy?

Recommendations If the diagnosis made during the gestational period (usually during the 3rd trimester) indicates that the fetus can survive outside the uterus, standard treatment after delivery can be considered (grade C1).

Chapter 8: Surveillance after treatment for cervical cancer

CQ34. What intervals are recommended for post-treatment surveillance?

Recommendations The following intervals are recommended for standard surveillance (grade C1):

For the first 1–2 years: every 1–3 months
For the 3rd year: every 3–6 months
For the 4th and 5th years: every 6 months
From the 6th year: every 12 months

CQ35. What investigations and examinations should be performed during post-treatment surveillance?

Recommendations (1) A physical examination (including pelvic and rectal examination), cytological examination, chest radiography, measurement of tumor markers, and diagnostic imaging should be performed (grade C1). (2) Any complications associated with surgery, radiotherapy, or chemotherapy should be noted (grade C1).

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Conflicts of interest None of the members of the committee in charge of the preparation of these guidelines has any conflict of interest with entities such as a specific profit or nonprofit organization. The board of the Society Conflict of Interest Committee confirmed the self-reported absence of any conflicts of interest by the Guideline Committee members.

Members of guidelines formulation committee (alphabetical order)

Yoichi Aoki, Yasuhiko Ebina, Takayuki Enomoto, Hisaya Fujiwara, Toru Hachisuga, Yasuyuki Hasuo, Atsushi Hongo, Seiryu Kamoi, Takahiro Kasamatsu, Hidetaka Katabuchi, Naoki Kawamura, Hiroaki Kobayashi, Yoichi Kobayashi, Takeshi Kodaira, Junichi Kodama, Kaneyuki Kubushiro, Masaki Mandai, Mikio Mikami, Yoshiki Mikami, Etsuko Miyagi, Toshinari Muramatsu, Tetsuro Nagasaka, Satoru Nagase, Toru Nakanishi, Kaei Nasu, Hideyuki Ohtake, Tsuyoshi Saito, Toshiaki Saito, Masaru Sakamoto, Muneaki Shimada, Nao Suzuki, Tsutomu Tabata, Masashi Takano, Nobuhiro Takeshima, Takafumi Toita, Yasuhiro Udagawa, Takashi Uno, Yoh Watanabe, Nobuo Yaegashi, Masanori Yasuda, Yoshihito Yokoyama

Members of guidelines evaluation committee (alphabetical order)

Daisuke Aoki, Masaki Fujimura, Keiichi Fujiwara, Masayuki Hatae, Masamichi Hiura, Yoshiki Inoue, Kiyoshi Ito, Hisao Ito, Tsuyoshi Iwasaka, Toshiko Jobo, Tsunehisa Kaku, Toshiharu Kamura, Noriyuki Katsumata, Junzo Kigawa, Eizo Kimura, Tsunekazu Kita, Hiroyuki Kuramoto, Yoshinari Matsumoto, Takashi Nishida, Kazunori Ochiai, Yujiro Ota, Aikou Okamoto, Isao Otsuka, Satoru Sagae, Noriaki Sakuragi, Mayumi Sugiura, Toru Sugiyama, Mitsuaki Suzuki, Hironori Tashiro, Hiroshi Tsuda, Masatsugu Ueda, Naohiko Umesaki, Masato Yamasaki, Hiroyuki Yoshikawa

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資料

AYA世代のがん登録の問題点

瀧本哲也
Tetsuya Takimoto
国立成育医療研究センター臨床研究開発センターデータ管理部小児がん登録室室長

Key word
●小児がん
●AYA世代
●がん登録

要　旨
AYA世代(15歳以上30歳未満)には胎児性の腫瘍はほとんどみられなくなり，成人に多いがんが増加してくるとされているが，その実態を知ることができる登録システムは存在しない。一方で，この世代であっても小児に特徴的ながん種については，小児の治療方式の成績のほうが良好なことが示唆されている。AYA世代のがん罹患の実態を把握できる登録のみならず，治療から長期フォローアップにつなげるシステムの確立が急務である。

わが国における小児がん登録の現状

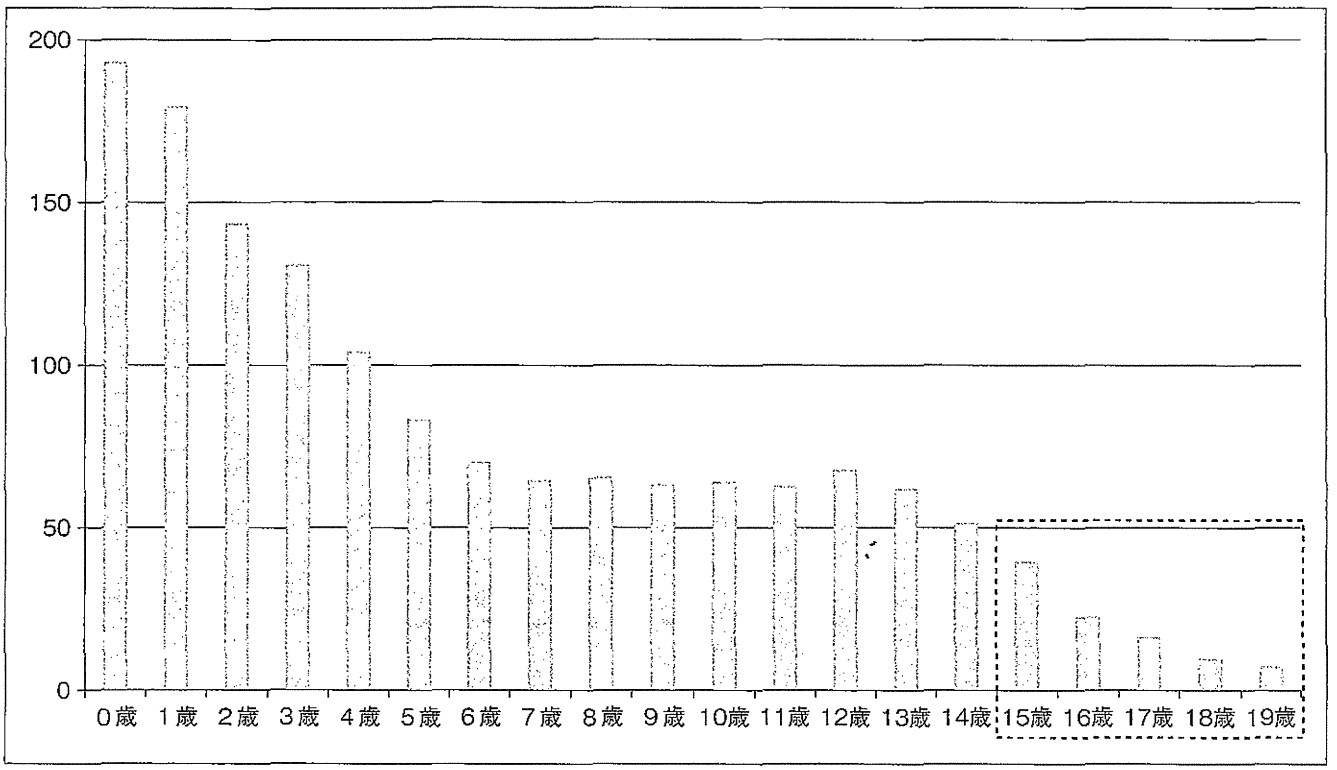
わが国における小児がんの新規発症は年間2,000～2,500人程度と考えられているが，精度の高い小児がんの登録システムが存在しないため，疾患別の正確な症例数については不明といわざるを得ない。ただしこれは，小児がんを対象とした登録が存在しない，ということを意味しているのではない。

現在，わが国で実施されている小児がん登録は，学会主導のものと，疾患研究グループ主導のものに大別することができる。前者には日本小児血液・がん学会の「20歳未満に発症する血液疾患と小児がんに関する疫学研究」(以下，学会登録)や日本小児外科学会の「小児悪性固形腫瘍登録」，さらに個別の腫瘍について当該診療科の専門学会などが実施している多くの登録がある。また，後者には造血器腫瘍，神経芽腫，横紋筋肉腫，肝腫瘍，腎腫瘍などを対象とした研究グループによる症例登録がある。ただし，これらの登録は性格が異なっている。すなわち，学会主導のものは発症数の把握，あるいはさらに個々の症例についての臨床情報を収集することを目的とするのに対し，研究グループ主導のものは中央診断を行うための匿名化(臨床研究では研究者が研究対象者の個人情報を知ることは許されない)が主目的であって，悉皆性をめざしたものではない。

疾患登録として最も把握率が高いのは学会登録であると思われるが，小児がん(特に固形腫瘍)の診療は多くの診療科にまたがっていることもあって，疫学研究的な悉皆性にはなお遠く，また学会登録の項目は診断病名のほか一部の疾患で原発部位，病期などを収集しているにすぎず，小児がんの実態についての研究には不十分である。このような欠点を少しでも補うため，前述の疾患研究グ

小児看護．38(11)：1434-1437，2015.

図1 日本小児血液・がん学会登録の年齢別年間発症例数(すべてのがん種を含む)



(日本小児血液・がん学会公表のデータより作成)

ループを統合して結成された日本小児がん研究グループ(The Japan Children's Cancer Group:JCCG)では中央診断のための匿名化を行った症例について,臨床試験参加の有無にかかわらず,その後の臨床情報を収集する前向きの観察研究を実施している。

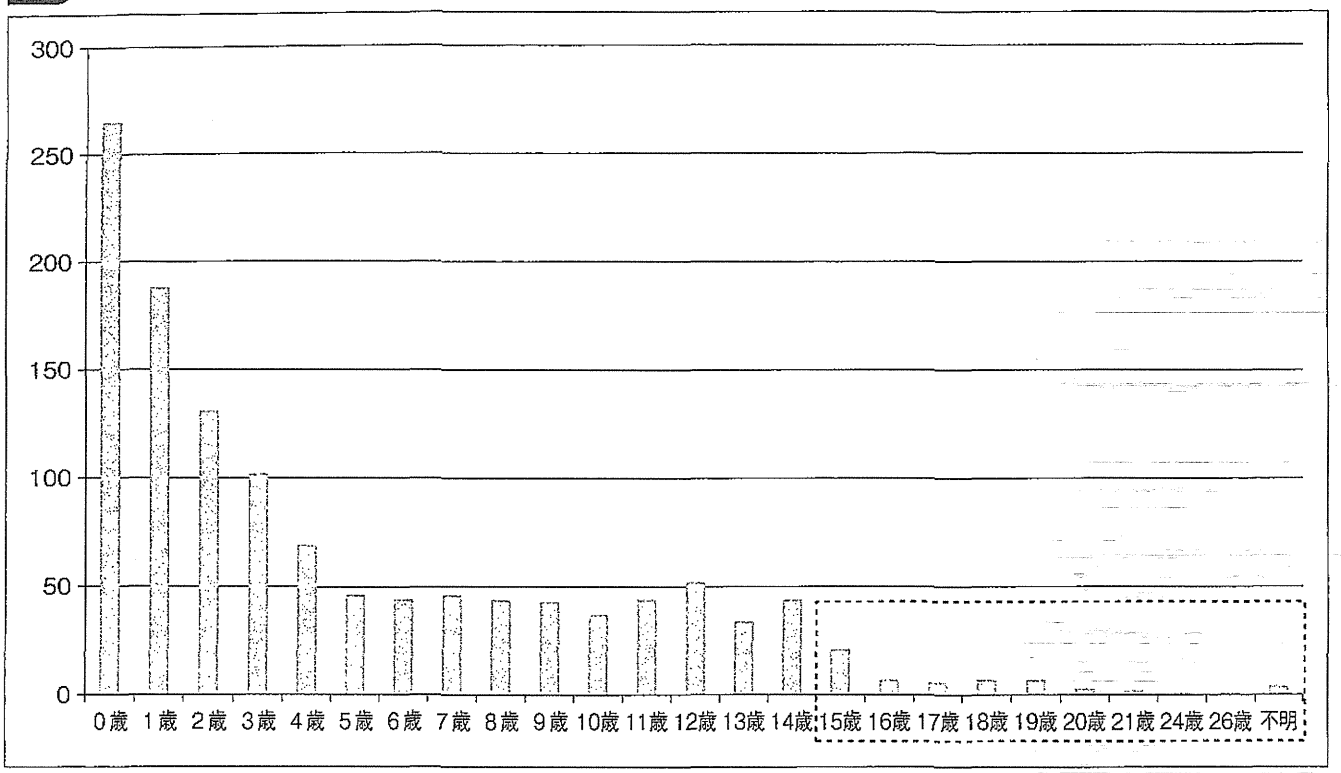
一方,2016(平成28)年1月から法制化された全国がん登録が開始される。これにはもちろん小児がんも含まれ,悉皆性という点では今後,最も信頼できるがん登録となることが予想される。しかし,小児がんは原発臓器が多種にわたることが多いため,部位に基づく分類による成人を含む集計データの有用性は必ずしも高いとはいえない。また行政によるがん登録は,がんの罹患率,進行度,生存率の変化などを算出してがんの実態の把握をめざすという点では学会登録などに類似しているが,その目的は学問的な興味よりも広報や検診などのがん対策活動の評価,医療機関への情報還元,効果的な対がん政策の立案であるため,小児がんに特異的な項目は少なく,やはり小児がんの研究にはあまり役立たない。

AYA世代のがん

日本小児・思春期・若年成人がん関連学会協議会会則では,思春期・若年成人とは15歳以上30歳未満とされている。この年齢層において,悪性新生物は年齢階級別死因順位の第3位,疾病による死亡原因では首位を占めており,AYA世代のがんの実態把握と治療成績向上の重要性は明らかである。

一般に小児がんの好発年齢は2峰性,すなわち乳幼児期の第1のピークに加えて,小児期後期からAYA世代に第2のピークがみられるとされている[1]。米国の報告でも,がんの罹患率は小児期では0～4歳が最も高く,5～14歳で低くなるが,15～19歳ではふたたび増加して5～14歳の約2倍,20～24歳は約3倍,25～29歳は

図2 日本小児がん研究グループ(JCCG)小児固形腫瘍観察研究登録の年齢別累積発症例数(対象は固形腫瘍のみ)

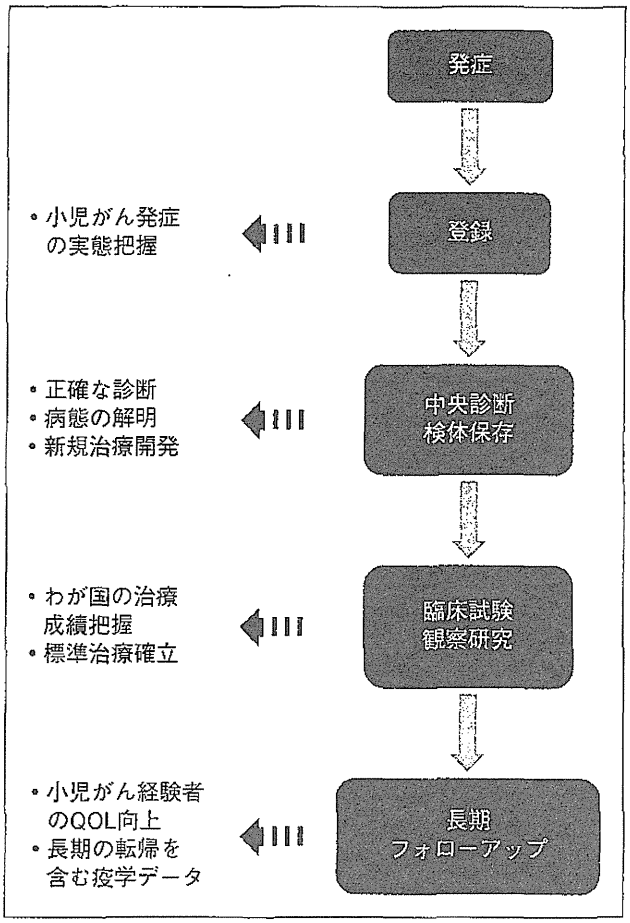


5倍以上となっている[2]。一般に15～19歳では急性白血病，悪性リンパ腫，胚細胞腫瘍，中枢神経系腫瘍，甲状腺がん，悪性黒色腫，骨軟部肉腫などが多い一方で，神経芽腫，腎芽腫，肝芽腫，網膜芽腫などの幼若児に多い胎児性の腫瘍はほとんどみられなくなる。さらに20歳を超えると，乳がんや消化管のがん，子宮頸部がんなどの成人にみられるがんが増加してくるとされている[3]。

学会登録(図1)，あるいはJCCGの小児固形腫瘍観察研究(図2)はいずれも15歳以上も登録対象としている。しかしながら，登録症例数は乳幼児で最も多い点は米国の報告と同様であるが，15歳以上ではきわめて少なくなっている。ホジキンリンパ腫や悪性黒色腫など，米国に比してわが国で明らかに頻度が低いことが知られている腫瘍もあるとはいえ，高校生以上は成人の診療科を受診するという診療の実態を考慮すれば，やはり発症例の把握が不十分である可能性は高いと思われる。その一方で，15～19歳の年齢層ではがん全体として米国の半分以下の罹患率であることを示唆する報告もみられる[4]。わが国のAYA世代のがん発症は，実際に米国と異なっているのであろうか？ 前項では小児がんを対象とした，高い悉皆性をもって詳細な臨床情報を収集できる疾患登録は存在しないと述べたが，AYA世代に関するこのような疑問の答えを得るためにも，小児・AYA世代のがん登録システムの確立が急務である。

AYA世代のがんに関するもう一つの重要なポイントは治療戦略である。AYA世代の急性リンパ性白血病(acute lymphoblastic leukemia；ALL)を小児および成人の治療方式で治療した結果，小児の治療方式のほうが有意に成績が良好であったとの報告が欧米で出され，わが国においても同様の治療戦略がとられるようになりつつある[5]。わが国の小児がんの生存率は現在80%に近づいている。ALLに限らず小児に特徴的ながん種については，小児系診療科が中心となって診療や臨床試験を行うことが適切ではないかと考えられる[3]。

図3 小児がん登録を入口とする小児がんの治療成績向上戦略



小児がん登録の意義

小児がんは疾患を克服した後の時間が長いため，長期的合併症への対策を含めたフォローアップが必要という成人にはみられない特徴がある。このような長期的合併症は原疾患だけでなく，放射線照射，化学療法などのがんに対する治療とも関連するため，個々の患者が受けた治療内容を把握することが重要になる。また，特にAYA世代については，心理社会的な支援も重要な課題である。

小児がんは稀少であるがゆえに全例を把握することは不可能ではない。したがって，今後はAYA世代も含む小児がんの登録体制を整備し，これを入口として中央診断によって正確な診断を担保し，臨床試験あるいは観察研究に登録したうえで(これによってデータセンターで治療内容の把握もできる)，長期フォローアップにつなげていくという流れを確立する必要がある(図3)。このようながん登録を入口とする小児がんの治療成績向上戦略によって，中央診断後の余剰検体を利用した研究による病態の解明や新規治療法の開発，臨床試験による標準治療の確立，さらには小児がん経験者のQOL向上などにも効率よく取り組むことができる。すなわち，小児・AYA世代のがん登録は成人とは違った意味でのがん対策の起点になり得ると考えられ，このようなシステムの構築が急がれるところである。

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SPECIAL ARTICLE

Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus April 2012 edited by the Japan Esophageal Society

Hiroyuki Kuwano · Yasumasa Nishimura · Tsuneo Oyama · Hiroyuki Kato · Yuko Kitagawa · Motoyasu Kusano · Hideo Shimada · Hiroya Takiuchi · Yasushi Toh · Yuichiro Doki · Yoshio Naomoto · Hisahiro Matsubara · Tatsuya Miyazaki · Manabu Muto · Akio Yanagisawa

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Keywords Clinical guidelines · Esophagus · Neoplasm

Introduction

Purpose

These guidelines are intended for doctors who are engaged in the diagnosis and treatment of esophageal carcinoma, for the following purposes: (1) to present the standard practice for the diagnosis and treatment of esophageal carcinoma with a high regard for the principles of evidence-based medicine (EBM); (2) to improve the safety and results of treatment, thereby reducing the difference in treatment results among different institutions; (3) to reduce unnecessary costs and efforts; (4) help enable people to undergo treatment without anxiety.

These guidelines provide only guidance on the indications for treatment and do not restrict or prohibit the use of any treatment deviating from those described herein.

Responsibilities

The Japan Esophageal Society assumes responsibility for the content described in these guidelines.

However, responsibility for the treatment results should be borne by the doctor providing the treatment and shall not rest with the Japan Esophageal Society.

Basic principles adopted for the preparation of these guidelines

These guidelines only present indications for the treatment procedures and do not address the technical problems of each treatment modality. The principles of presenting adequate treatment procedures include the following:

This article originally appeared in Japanese as *Shokudo gan shindan · chiryo gaidorain* (Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus), published by Kanehara, Tokyo, April.

This article does not contain any studies with human or animal subjects performed by any author(s). This paper consists of summary and text of Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus April 2012 edited without references and clinical questions and answers and grade of recommendation.

H. Kuwano (✉) · T. Miyazaki
Department of General Surgical Science, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan
e-mail: hkuwano@gunma-u.ac.jp

Y. Nishimura
Department of Radiation Oncology, Kinki University Faculty of Medicine, Osaka-Sayama, Osaka, Japan

T. Oyama
Department of Gastroenterology, Saku Central Hospital, Nagano, Japan

H. Kato
First Department of Surgery, Dokkyo Medical University, Tochigi, Japan

Y. Kitagawa
Department of Surgery, School of Medicine, Keio University, Tokyo, Japan

M. Kusano
Department of Endoscopy and Endoscopic Surgery, Gunma University Hospital, Maebashi, Gunma, Japan

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SPECIAL ARTICLE

Comprehensive Registry of Esophageal Cancer in Japan, 2007

Yuji Tachimori · Soji Ozawa · Hodaka Numasaki · Mitsuhiro Fujishiro · Hisahiro Matsubara · Tsuneo Oyama · Masayuki Shinoda · Yasushi Toh · Harushi Udagawa · Takashi Uno · The Registration Committee for Esophageal Cancer of the Japan Esophageal Society

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Preface 2007

We deeply appreciate the great contributions of many physicians in the registry of esophageal cancer cases. The Comprehensive Registry of Esophageal Cancer in Japan, 2007, was published here, despite some delay. The registry complies with the Act for the Protection of Personal Information. The encryption with a HASH function is used for ''anonymity in an unlinkable fashion''.

These data were first made available on December 25, 2014, as the Comprehensive Registry of Esophageal Cancer in Japan, 2008. Not all the pages are reprinted here; however, the original table and figure numbers have been maintained.

The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

Y. Tachimori (✉)
Esophageal Surgery Division, National Cancer Center Hospital, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
e-mail: ytachimo@ncc.go.jp

S. Ozawa
Department of Gastroenterological Surgery, Tokai University School of Medicine, Isehara, Japan

H. Numasaki
Department of Medical Physics and Engineering, Osaka University Graduate School of Medicine, Osaka, Japan

M. Fujishiro
Department of Endoscopy and Endoscopic Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan

H. Matsubara
Department of Frontier Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

We briefly summarized the Comprehensive Registry of Esophageal Cancer in Japan, 2007. Japanese Classification of Esophageal Cancer 10th and UICC TNM Classification 6th were used for cancer staging according to the subjected year. A total of 5216 cases were registered from 257 institutions in Japan. Tumor locations were cervical: 4.4 %, upper thoracic: 12.7 %, middle thoracic: 49.5 %, lower thoracic: 25.1 % and EG junction: 5.9 %. Superficial carcinomas (Tis, T1a, and T1b) were 35.7 %. As for the histologic type of biopsy specimens, squamous cell carcinoma and adenocarcinoma accounted for 90.1 % and 3.9 %, respectively. Regarding clinical results, the 5-year survival rates of patients treated using endoscopic mucosal resection, concurrent chemoradiotherapy, radiotherapy alone, chemotherapy alone, or esophagectomy were 88.1, 25.1, 16.0, 9.4, and 52.8 %, respectively. Esophagectomy was performed in 2834 cases. Concerning the approach used for esophagectomy, 19.8 % of the cases were treated thoraco-

T. Oyama
Department of Gastroenterology, Saku General Hospital, Nagano, Japan

M. Shinoda
Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Aichi, Japan

Y. Toh
Department of Gastroenterological Surgery, National Kyushu Cancer Center, Fukuoka, Japan

H. Udagawa
Department of Gastroenterological Surgery, Toranomon Hospital, Tokyo, Japan

T. Uno
Department of Radiology, Graduate School of Medicine, Chiba University, Chiba, Japan