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Conflict of interest statement

None declared.

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CLINICAL INVESTIGATION **Cervix**

PRACTICE PATTERNS OF RADIOTHERAPY IN CERVICAL CANCER AMONG MEMBER GROUPS OF THE GYNECOLOGIC CANCER INTERGROUP (GCIG)

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Purpose: The aim of this study was to describe radiotherapeutic practice of the treatment of cervical cancer in member groups of the Gynecologic Cancer Intergroup (GCIG).

Methods and Materials: A survey was developed and distributed to the members of the GCIG focusing on details of radiotherapy practice. Different scenarios were queried including advanced cervical cancer, postoperative patients, and para-aortic–positive lymph node cases. Items focused on indications for radiation therapy, radiation fields, dose, use of chemotherapy, brachytherapy and others. The cooperative groups from North America were compared with the other groups to evaluate potential differences in radiotherapy doses.

Results: A total of 39 surveys were returned from 13 different cooperative groups. For the treatment of advanced cervical cancer, external beam pelvic doses and total doses to point A were 47 + 3.5 Gy (mean + SD) and 79.1 + 7.9 Gy, respectively. Point A doses were not different between the North American cooperative groups compared with the others ($p = 0.103$). All groups used concomitant chemotherapy, with 30 of 36 respondents using weekly cisplatin. Of 33 respondents, 31 intervened for a low hemoglobin level. For a para-aortic field, the upper border was most commonly (15 of 24) at the T12-L1 interspace. Maintenance chemotherapy (after radiotherapy) was not performed by 68% of respondents. For vaginal brachytherapy after hysterectomy, 23 groups performed HDR brachytherapy and four groups used LDR brachytherapy. In the use of brachytherapy, there was no uniformity in dose prescription.

Conclusions: Radiotherapy practices among member groups of the GCIG are similar in terms of both doses and use of chemotherapy. © 2007 Elsevier Inc.

Cervix, Chemoradiation, Cooperative group.

INTRODUCTION

The Gynecologic Cancer Intergroup (GCIG) is a global association of cooperative groups involved in research and treatment of gynecologic neoplasms. International collaboration began in 1991 in the treatment of ovarian cancer, and regular meetings were initiated between cooperative groups in 1995 (1). By 1997 a more formal structure was adopted for cooperation among cooperative groups in gynecologic cancers, and the GCIG was created. The GCIG represents cooperative groups from Europe, Asia, Australia, and North America. There is no representation from Africa or South America. The GCIG currently represents 15 cooperative groups and receives partial administrative support from the National Cancer Institute (NCI) in the United States. The member groups of the GCIG are as follows: AGO-Austria, AGO-OVAR (Germany), ANZGOG (Australia, New Zea-

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land), EORTC (Europe), GEICO (Spain), GINECO (France), GOG (USA), JGOG (Japan), MANGO (Italy), MITO (Italy), MRC/NCRC (Great Britain), NCIC (Canada), NSGO (Scandinavia), Radiation Therapy Oncology Group (RTOG, US), and SGCTG (Scotland).

Cervical cancer is the second most common cancer diagnosed in women worldwide after breast cancer, with more than 493,000 new cases in 2002 (2). Similarly, cervical cancer is the third most common cause of death from cancer in women after breast and lung cancer. More than 273,000 women die annually of cervical cancer. Eastern and southern Africa record the highest incidence and mortality rates from cervical cancer. In the developed world the rates are markedly lower. Screening programs are responsible for the lower incidence rates in the developed countries (3).

Surgery is widely used for early cervical cancers (International Federation of Gynecology and Obstetrics [FIGO] I–IIA), whereas radiotherapy is the standard management for larger tumors or more advanced FIGO stages. Radiotherapy practice patterns of the treatment of cervical cancer have been studied in different countries over the past several decades (4–14). In the United States, practice patterns in the treatment of cervical cancer have been documented systematically through a funded mechanism (4, 10–12, 14). These studies have revealed the importance of limiting the overall treatment time, necessity of brachytherapy, institutional volume on improving umor control, and the superiority of fractionated low-dose-rate (LDR) brachytherapy over a single insertion. In Japan, Patterns of Care Studies have revealed a 20% lower dose than practiced in the United States (13). Brachytherapy practice patterns have been specifically studied in the Patterns of Care studies (5, 7, 14). In the United States between the years 1996 and 1999, 94% of patients received curative-intent brachytherapy. Of patients receiving brachytherapy in that report 77.8% received LDR and 13.3% received HDR brachytherapy (14).

In 1999 the NCI of the United States published a clinical alert indicating a survival benefit for the addition of cisplatin-based chemotherapy to radiotherapy in FIGO stages IB2–IVA (15–21). Meta-analyses have confirmed the survival advantage of chemoradiotherapy over radiotherapy alone (22). Some studies have documented the rapid incorporation of cisplatin-based chemoradiotherapy as standard treatment within a short period after the NCI 1999 clinical alert (9, 23).

In this study we describe the radiotherapeutic practice of the treatment of cervical cancer in member groups of the GCIG. We also describe the use of chemotherapy in the treatment of advanced cervical cancer.

METHODS AND MATERIALS

A survey was developed by multiple members of the GCIG and was distributed to the members of the GCIG. This survey focused on the treatment of locally advanced cervical cancer and the adjuvant, post-operative treatment (see Appendix). The use of concurrent and sequential chemotherapy was queried also.

Table 1. Radiotherapy doses posthysterectomy

Area/dose	Mean (SD)(Gy)
Pelvic	47.9 (1.8)
Vaginal cuff brachytherapy	19.1 (8.4)
Vaginal cuff dpf brachytherapy	6.4 (1.6)
Para-aortic	45.6 (2.7)
Dpf (pelvis)	1.84 (0.08)
Dpf (para-aortic)	1.81 (0.06)

Abbreviation: Dpf = dose per fraction.

Each cooperative group was asked to submit four questionnaires from separate, representative centers. Centers chosen were required to have a large volume of cancer cases within that specific cooperative group. If the cooperative group had published or written guidelines then a single questionnaire was sufficient. A total of 39 questionnaires were returned. The number of respondents per GCIG member group were AGO-Austria, three; AGO-OVAR (Germany), three; ANZGOG (Australia, New Zealand), one; EORTC (Europe), two; GOG (USA), two; JGOG (Japan), four; MANGO (Italy), four; MITO (Italy), five; MRC/NCRC (Great Britain), one; NCIC (Canada), eight; NSGO (Scandinavia), one; RTOG (US), four; and SGCTG (Scotland), one. GEICO (Spain) is a medical oncology–only group and does not perform radiation oncology. Descriptive statistics were used and the Student's t test was used to compare differences between groups. The three groups from North America (GOG, NCIC, RTOG) were compared with the other groups to evaluate potential differences in radiotherapy doses.

RESULTS

Doses

A total of 39 surveys were returned from 13 different cooperative groups. For the treatment of locally advanced cervical cancer external beam pelvic doses, total doses to point B and point A were 48.0 Gy, 57.9 Gy, and 79.2 Gy, respectively (Table 1). The doses to point A and B were crude sums of the external beam and brachytherapy doses. There was very little variation in dose per fraction with a mean (± standard deviation [SD]) of 1.85 Gy ± 0.10 Gy with a range of 1.8 to 2.15 Gy. Similarly, for the treatment of the para-aortic chain there was little difference in prescribed dose, with a mean of 46.9 Gy ± 5.0 Gy. Point A doses were compared between the North American cooperative groups (GOG, NCIC, and RTOG) compared with the other groups, and no statistical difference was noted (p = 0.103). In North America the mean point A dose was 81.8 Gy ± 6.0 Gy, compared with a mean point A dose in the other cooperative groups of 77.4 Gy ± 8.6 Gy.

In the post-hysterectomy setting the mean pelvic dose was also 47.9 Gy ± 1.8 Gy. When a vaginal cuff boost was used the mean total dose was 19.1 Gy, delivered on average with 6.4 Gy ± 1.6 Gy fractions. For vaginal brachytherapy after hysterectomy, 23 groups performed HDR brachytherapy and four groups used LDR brachytherapy.

Table 2. Clinical parameters for locally advanced cervical cancer

Definitive RT	No. (%)
Pelvic field Size	
Large L4/5	17 (50)
Small L5/S1	4 (11.8)
NOS	5 (14.7)
CT planned	8 (23.5)
Type of simulation	
CT	33 (94.3)
Fluoroscopic	1 (2.9)
MR fusion	1 (2.9)
Implant device	
Tandem and ovoid	25 (86.2)
Tandem and ring	1 (3.4)
Either	3 (10.3)
Normal tissue points recorded	
Bladder and Rectum	20 (66.7)
Rectum	2 (6.7)
Bladder, Rectum and VSD	8 (26.7)
Intervene for low Hb	
Yes	31 (93.9)
no	1 (3)
Maybe	1 (3)
Type of chemo (concomitant)	
CDDP	30 (81.1)
5FU/CDDP	2 (5.4)
5FU/Nedaplatin	1 (2.7)
CDDP/Taxol	4 (10.8)
Indication for PA RT	
+ lymph nodes	14
+ para-aortic nodes	20
+ common iliac nodes	18
+ ext iliac nodes	1
Not performed	1
Upper border of PA field	
T10/11	4 (12.9)
T11/12	5 (16.1)
T12/L1	15 (48.4)
CT planned	7 (22.6)

Abbreviations: CDDP = cisplatin; CT = computed tomography; Hb = hemoglobin; MR = magnetic resonance; NOS = not otherwise specified; RT = radiotherapy; VSD = vaginal surface dose; PA = para aortic. Plus sign (+) denotes positive. In the CT-planned cases the upper border was not explicitly stated. When more than one response is indicated, a percentage is not given.

Locally advanced cervical cancer

For locally advanced cervical cancer the upper border of the pelvic field was set at L4/5, L5/S1, and not specifically stated for 17, 4, and 13 respondents, respectively (Table 2). Of the 35 respondents, 33 used computed tomographic simulation. A tandem and ovoid device was used exclusively in 25 of 29 respondents. For brachytherapy treatment planning, bladder and rectal points were recorded in 28 of 30 respondents. For locally advanced cervical cancer, all groups used concomitant chemotherapy, with 30 of 37 respondents using weekly cisplatin (CDDP). The dose of CDDP was 40 mg/m^2 in 27 respondents, 30 mg/m^2 in 1 respondent, 8 mg daily in one respondent, and 20 mg/m^2 times 5 days every 21 days in one respondent. Of 33 respondents, 31 intervened for a low hemoglobin level. For a para-aortic field, the upper border was most commonly at the T12 to L1 interspace (15 of 24 respondents).

Adjuvant treatment after a radical hysterectomy

In the adjuvant treatment after a radical hysterectomy multiple factors were used as indications to deliver radiotherapy or brachytherapy (Table 3). A large pelvic field (upper border at the junction of L4–L5) was most commonly prescribed (18 of 39 respondents, 46%). Concomitant chemotherapy was routinely used 28 of 36 respondents. Maintenance chemotherapy (after radiotherapy) was not performed in 68% of respondents. For vaginal brachytherapy after hysterectomy, 23 groups performed HDR brachytherapy and four groups used LDR brachytherapy. For brachytherapy the prescription point was at the vaginal surface, 0.5 cm, and 1 cm in eight, 18, and one respondent, respectively. In terms of length of the vagina treated, 13 groups prescribed treatment to a fraction of the vagina and 9 prescribed treatment to a definitive length in centimeters. A vaginal cylinder was used in 25 of 30 respondents, and 5 respondents used either a cylinder or ovoids.

DISCUSSION

Overall, this international collaborative study sponsored by the GCIG reveals very similar practice patterns in member groups of the GCIG. No serious impediments to international collaboration were identified. External beam and intracavitary doses were similar (Table 1). The SD in external beam doses for the definitive cases and postoperative treatment were 3.5 and 1.8 Gy, respectively. The SD in the daily dose per fraction was only 0.10 Gy. A previous report indicated a 20% lower dose prescribed in Japan compared with the US (13). Differences in doses practiced in North America compared with elsewhere were not documented in this study. This series also demonstrated that 97% (34 of 35 respondents) used either computed tomographic or magnetic resonance simulation. Field sizes were also similar among respondents (Tables 2 and 3).

In the use of brachytherapy after hysterectomy, HDR was most commonly used. Of the respondents, 23 used HDR and four used LDR. In the postoperative setting, there was no uniformity in the fraction of the vagina treated or in the doses and schedules used. The method of prescription varied, with nine centers prescribing to a specific length and 13 centers prescribing a dose to a specific fraction of the vagina with 1 of 3 being reported most frequently. For the definitive radiotherapy cases, the tandem and ovoid device was used exclusively in 86% of centers, either a tandem and ovoid or tandem and ring in 10% of cases, and a tandem and ring in only 3% of cases. Bladder and rectal dose points were recorded for 28 of 30 respondents.

For the definitive radiotherapy cases, there was high concordance in the use of chemotherapy, with all respondents using concurrent chemotherapy and with 30 of 33 respondents

Table 3. Clinical parameters for posthysterectomy cervix cancer

Adjuvant RT	No. (%)
RT Indications	
+ lymph nodes	32
+ margins	28
Deep stromal invasion	22
> 4 cm	14
Parametrial involvement	9
LVSI	22
Close margins	9
≥T2	7
≥IB2	5
Unfavorable histology	1
Pelvic field size	
LargeL4/5	18 (46.2)
Small L5/S1	9 (23.1)
NOS	9 (23.1)
CT planned	3 (7.7)
Concomitant chemotherapy	
Yes	28 (77.8)
No	1 (2.8)
Varies	7 (19.4)
Type of chemotherapy(concomitant)	
CDDP	28 (80.0)
5FU/CDDP	3 (8.6)
5FU/Nedaplatin	1 (2.9)
CDDP/Taxol	3 (8.6)
Dose of CDDP	
40 mg/m2 q wk	25 (89.3)
45 mg/m2 q wk	1 (3.6)
30 mg/m2 q wk	1 (3.6)
8 mg/m2 qd	1 (3.6)
Adjuvant chemotherapy after RT	
Yes	2 (5.9)
No	23 (67.6)
Varies	9 (26.5)
Indication for PA RT	
+ lymph nodes	12
+ para-aortic nodes	17
+ common iliac nodes	14
+ ext iliac nodes	1
No LN dissection	1
Not performed	3
Upper border of PA field	
T10/11	3 (9.7)
T11/12	7 (22.6)
T12/L1	18 (58.1)
CT planned	3 (9.7)
Vaginal cuff RT Indications	
Positive margins	26
Vaginal involvement	2
Close margins	7
≥TIB	3
LVSI	1
Deep stromal invasion	1
T2	1
Proportion of vagina treated	
1/3	6 (24)
	4 (16)
2/3	1 (4)
Whole	2 (8)
2 cm	1 (4)
4 cm	6 (24)
5 cm	2 (8)
	Varies 2 (8)
	Ovoids only 1 (4)
Normal tissue points recorded	
Bladder and rectum	23 (44.2)
Rectum	2 (3.8)
Prescription point	
cm	18 (34.6)
Vaginal surface	8 (15.4)
1 cm	1 (1.9)

Abbreviations: CDDP = cisplatin; LN = lymph node; LVSI = lymph vascular space invasion; NOS = not otherwise specified; PA = para aortic. RT = radiotherapy. Plus sign (+) denotes positive. When more than one answer is recorded then a percentage is not given.

using single-agent CDDP. Previous studies have indicated rapid incorporation of chemoradiotherapy as standard practice (9, 23). In patients treated with a radical hysterectomy, concomitant chemotherapy was routinely used in 28 of 36 respondents. Maintenance chemotherapy (after radiotherapy) was not performed by 23 of 34 respondents (68%).

This study was not documentation of radiotherapy delivered. This was a survey of best practice by select member groups of the GCIG. Also, this study is not a population average of radiotherapy practice. Some groups had higher numerically representation. It may or may not be representative of typical practice patterns within the country of the GCIG member. However, it does likely reflect best practice patterns, as institutions participating have express interest in clinical research in gynecologic cancers. In addition, in attempts to cover many aspects of cervical cancer treatment including concomitant and maintenance chemotherapy, we did not specifically enquire about LDR of HDR doses in the definitive cases. Thus, the doses reported here should not be used as justification of the appropriate LDR or HDR dose. The data do indicate that there are little differences in doses used by different groups in different countries. It is also the first global survey that we are aware of in radiotherapy for cervical cancer. In addition, the survey was a broad overview of radiotherapy practice for the international community. It did not include many details of prescriptive brachytherapy practice as have been documented previously (14).

Radiotherapy practices among member groups of the GCIG are similar in terms of fields and doses. For definitive radiotherapy cases, the predominant brachytherapy device is a tandem and ovoid; and after hysterectomy, a vaginal cylinder. At this time there is no uniformity in vaginal brachytherapy prescription after hysterectomy. All respondents used concomitant chemotherapy in definitive radiotherapy cases, and 83% used weekly cisplatin. Radiotherapy practices should not be a limitation to international participation in cervical cancer clinical trials.

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APPENDIX

Gynecologic Cancer Intergroup radiation oncology standard clinical practices survey

(Please single-click on each field to answer)

Cervical cancer

Post–radical hysterectomy adjuvant pelvic radiotherapy (RT)
- Indications: []
- Dose/fractions: []
- Field (provide borders): []
- Concomitant chemotherapy: []
  - Drug (s) (List if more than one; e.g. TIP, Carbo taxol, cis taxol): []
  - Dose: []
  - Schedule: []
  - Additional chemotherapy after radiation therapy: []

Post–radical hysterectomy adjuvant para-aortic RT
- Indications: []
- Dose/fractions: []
- Field (provide borders): []

Post–radical hysterectomy vaginal cuff RT
- Indications: []
- Total dose (brachytherapy): []
- Dose per fraction: []
- Number of insertions: []
- LDR: []
- HDR: []
- Device: []

Prescription point: []
Vaginal length: []
Normal tissue points recorded: []
Primary radiation for locally advanced disease
External pelvic dose/fractions: []
Field (provide borders): []
Method of planning/simulation: []
Computed tomographic simulation: []
Intensity-modulated radiotherapy: []
Conventional simulation: []
Do you routinely shield? []
Total pelvic dose: []
Total dose to point A: []
Total dose to point B: []
Device: []
Normal tissue points recorded: []
Hemoglobin/hematocrit goal: []
At start of RT: []
During RT: []
Do you intervene during RT and what is your target level? []
Concomitant chemotherapy: []
Drugs: []
Dose: []
Schedule: []
Indications for para-aortic RT: []
Dose/fractions: []
Field (provide borders): []

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CLINICAL INVESTIGATION **Cervix**

PATTERNS OF RADIOTHERAPY PRACTICE FOR PATIENTS WITH CERVICAL CANCER (1999–2001): PATTERNS OF CARE STUDY IN JAPAN

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Purpose: To describe the patterns of definitive radiotherapy practice for patients with uterine cervical cancer from 1999 to 2001 in Japan.

Methods and Materials: The Japanese Patterns of Care Study (JPCS) working group conducted a third extramural audit survey of 68 institutions and collected specific information on 324 cervical cancer patients treated with definitive radiotherapy.

Results: Almost all patients (96%) were treated with whole pelvic radiotherapy using opposing anteroposterior fields (87%). A midline block was used in 70% of the patients. Intracavitary brachytherapy (ICBT) was applied in 82% of cases. Most patients (89%) were treated with high-dose rate (HDR) ICBT. Calculation of doses to organs at risk (ICRU 38) was performed for rectum in 25% of cases and for bladder in 18% of cases. Only 3% of patients were given intravenous conscious sedation during ICBT applicator insertions. The median total biologically effective dose at point A (EBRT+ICBT) was 74 Gy_{10} in cases treated with HDR-ICBT. There was no significant difference in total biologically effective dose between stages. The median overall treatment time was 47 days. Concurrent chemoradiation was applied in 17% of patients.

Conclusions: This study describes the general patterns of radiotherapy practice for uterine cervical cancer in Japan. Although methods of external radiotherapy seemed to be appropriate, there was room for improvement in ICBT practice, such as pretreatment. A substantial difference in total radiotherapy dose between Japan and the United States was observed. © 2008 Elsevier Inc.

Patterns of care study, Cervix, Radiotherapy.

INTRODUCTION

Several randomized controlled trials (RCTs) conducted in the 1990s have demonstrated that concurrent chemoradiotherapy (CCRT) reduced the mortality risk in uterine cervical cancer patients by 30%–50% compared with radiotherapy alone (1–3). Another RCT demonstrated no difference in the survival rates between definitive radiotherapy and surgery for early-stage cancer patients with Stages IB and IIA (4). Consequently, radiation therapy has become the more appropriate option in the treatment of cervical cancer. In the United States, the American Brachytherapy Society (ABS) issued the radiotherapy guidelines for uterine cervical cancer (5, 6), and in Japan, the General Rules for Clinical and Pathological Study of Uterine Cervical Cancer provide treatment guidelines, including the standard treatment schedule of radiotherapy (7). Currently, organizations such as the Gynecologic Cancer Intergroup (GCIG) are trying to set up international clinical trials of radiotherapy for uterine cervical cancer (8). Although international standardization of radiotherapy is an important issue, some between-country differences in the clinical practice of radiotherapy can be expected.

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The Patterns of Care Study (PCS) initially surveyed radiotherapy practice in the United States. The subjects of the survey were selected by the two-staged cluster sampling method (medical institutions and patients) from institutions providing radiotherapy throughout the United States. The national averages for radiotherapy practice can be demonstrated using this method (9). In the United States, PCSs have been conducted for more than 30 years, and the structure, process, and outcome of radiotherapy, as well as various problems in clinical practice, have been identified for uterine cervical cancer (10–13). In Japan, the Japanese Patterns of Care Study (JPCS) began in 1996 and used the same methods (14). We previously reported the PCS results for radiotherapy practice in uterine cervical cancer patients treated in 1992–1994 and 1995–1997 (15, 16). We report here the corresponding results for 1999–2001. We compared the data from this study with those of the preceding JPCS (1995–1997) and the U.S. PCS. The changes over the years in radiotherapy practice were examined for cervical cancer in Japan, and the differences between Japan and the United States were also examined.

METHODS AND MATERIALS

Between July 2002 and June 2004, the JPCS conducted a third national survey of patients with uterine cervical cancer treated with radiotherapy. Eligibility criteria for the survey were as follows: (*1*) carcinoma, (2) treated between January 1999 and December 2001, (*3*) no distant metastases, (*4*) no prior or concurrent malignancy, (*5*) no gross para-aortic lymph node metastases, and (*6*) no previous pelvic radiotherapy. Sixty-eight of 640 institutions were selected for the survey using a stratified two-staged cluster sampling method. Before the random sampling, all institutions were classified into four groups. Institutions were classified by type and number of patient treated with radiotherapy. The criteria for stratification have been detailed elsewhere (14). In brief, the JPCS stratified Japanese institutions as follows: A1, academic institutions treating ≥430 patients annually; A2, <430 patients; B1, nonacademic institutions treating ≥130 patients annually; B2, <130 patients. Academic institutions included cancer center hospitals and university hospitals. Nonacademic institutions consisted of other facilities, such as national, prefectural, municipal, and private hospitals.

The JPCS surveyors performed on-site chart review at each participating facility using an originally developed database format for uterine cervical cancer. Data collection included patient characteristics (e.g., patient's history, age, performance status, laboratory data, pathology, and stage), details of pretreatment workup, therapeutic information (e.g., radiotherapy, chemotherapy, and surgery), and treatment outcome. The JPCS collected clinical data on 631 patients with uterine cervical cancer who were treated with radiotherapy from 68 institutions. In this study, 324 patients treated by radiotherapy without planned surgery were analyzed. These included 115 patients from A1 institutions, 70 patients from A2 institutions, 104 patients from B1 institutions, and 35 patients from B2 institutions.

Statistical significance was tested using the chi-square test. Unknown and missing data were combined in the tables because these were the same in most cases: no valid data were found in the given resources (17). Ratios were calculated using unknown or missing data, but continuous variables did not include these data (17), as seen in a U.S. PCS report (18).

RESULTS

Table 1 shows the characteristics of the 324 patients in our survey. In total, 276 patients (85%) were hospitalized for treatment. Of these, 190 patients (59%) were hospitalized during both external beam radiotherapy (EBRT) and brachytherapy, 78 (24%) were hospitalized only during EBRT, and 8 (2%) only during brachytherapy.

External beam radiotherapy

External beam radiotherapy (EBRT) was performed in 320 patients (99%). Twenty-two patients (7%) received EBRT at another facility. In 142 cases (44%), multileaf collimators (MLC) were used to shape the portals. For 308 patients (96%), the planning target volume (PTV) included the whole pelvic region. The upper border of the pelvic field was at the L4 to L5 interspace in 238 of the 308 patients (77%). Only 10 patients (3%) received extended field radiotherapy including the para-aortic region. Treatment parameters of pelvic EBRT are shown in Table 2. The most frequently used beam energy was 10-14 MV X-rays. Pelvic EBRT was most often given using an opposing anteroposterior (AP-PA) technique. The median isocenter depth of the AP-PA portals was 9 cm (range, 6.5–12.9 cm). A midline block was used in 70% of the patients. A single-daily fraction dose of 1.8 or 2.0 Gy was used for most patients.

Brachytherapy

No patient surveyed received interstitial brachytherapy. Table 3 shows the details of intracavitary brachytherapy (ICBT). ICBT was applied in more than 80% of cases. The ICBT application rate by Fédération Internationale de

Table 1. Patient and tumor characteristics of 324 patients with uterine cervical cancer treated with radiotherapy.

Characteristics	No. of patients	(%)
Total no.	324	
Age (yrs)		
Range	26-100	
Median	71	
KPS		
<=70	64	20
80	103	32
90	114	35
100	21	6
Unknown/missing	22	7
Histology		
Squamous cell carcinoma	300	93
Adenocarcinoma	14	4
Adenosquamous cell carcinoma	4	1
Other	2	1
Unknown/missing	4	1
FIGO stage		
I	43	13
II	102	31
III	122	38
IVA	35	11
Unknown/missing	22	7

Table 2. Treatment parameters of pelvic external beam radiotherapy

Parameters	*n*	%
Beam energy		
Co-60	2	1
3–5 MV	30	10
6–9 MV	45	15
10–14 MV	220	71
15 MV	9	3
other	0	0
Unknown/missing	2	—
Technique		
AP-PA	269	87
Four-field box	21	7
Other	17	6
Unknown/missing	1	—
Midline block		
Yes	215	70
No	72	23
Unknown/missing	21	7
Daily fraction size (Gy)		
<1.8	25	8
1.8	135	44
1.8–2	2	1
2	137	45
>2	6	2
Missing	3	—

Gynécologie Obstétrique (FIGO) stages was 88% for Stage I, 88% for Stage II, 89% for Stage III, and 51% for Stage IVA. Its application was significantly less frequent in stage IVA patients (p <0.0001). Sixty-four patients (25%) received ICBT at another facility. Approximately 90% of the patients were treated with high-dose rate (HDR) ICBT. The most frequent radionuclide for ICBT source was cobalt-60 (Co-60), followed by iridium-192 (Ir-192). A rigid-type applicator was used for about 60% of the patients. In vivo rectal dosimetry was performed in approximately one quarter of the patients, whereas bladder dosimetry was rarely performed. ICRU 38 reference doses at the rectum and bladder were calculated in one quarter or less of the patients. Supportive medication before or during the applicator insertion was almost never given; when it was administered, it seemed to be inadequate. The dose calculation was performed for every HDR-ICBT fraction for more than three quarters of the patients. In most patients, all HDR-ICBT procedures (applicator insertion, radiograph generation and treatment) were performed in the same room.

Radiation dose and overall treatment time

Table 4 shows radiotherapy dose as a function of the FIGO stage. Total EBRT dose to the central pelvis (point A dose) significantly increased with increasing FIGO stage. Although a significant difference was also observed in total dose to the lateral pelvis (point B dose), median dose was almost the same at all stages. Median ICBT fraction size at point A was 524 cGy for HDR and 1740 cGy for LDR. The most frequent HDR-ICBT dose per fraction at point A was 500–599 Gy (79/215, 37%), followed by 600–699 cGy (48/215, 22%),

Table 3. Details of intracavitary brachytherapy

Parameters	*n*	%
ICBT given		
Yes	265	82
No	58	18
Unknown/missing	1	0
Dose rate		
HDR	215	89
LDR	27	11
HDR+LDR	0	0
Other	0	0
Unknown/missing	23	-
Source		
Co-60	112	46
Ir-192	102	42
Cs-137	21	9
Ra-226	7	3
Unknown/missing	23	-
Method of ICBT		
Tandem + vaginal applicator	202	83
Tandem only	26	11
Vaginal applicator	16	6
Unknown/missing	21	-
Applicator		
Rigid	166	63
Nonrigid	66	25
Unknown/missing	33	12
In vivo dosimetry: bladder		
Yes	8	3
No	207	78
Unknown/missing	50	19
In vivo dosimetry: rectum		
Yes	71	27
No	145	55
Unknown/missing	49	18
ICRU38: bladder		
Yes	48	18
No	146	55
Unknown/missing	71	27
ICRU38: rectum		
Yes	65	25
No	128	48
Unknown/missing	72	27
Preparation		
None	90	54
NSAIDs; orally/rectally	68	41
IV continous sedation	5	3
other	3	2
Unknown/missing	99	-
All procedures in same room*		
Yes	167	78
No	11	5
Unknown/missing	37	17
Each fraction planned*		
Yes	159	74
No	49	23
Unknown/missing	7	3

Abbreviations: HDR = high dose rate; ICBT = intracavitary brachytherapy; ICRU = International Commission on Radiation Units and Measurements; LDR = low dose rate, NSAIDs = nonsteroidal anti-inframmatory drugs.

* 215 patients treated with HDR-ICBT.

Table 4. Radiotherapy dose according to Fédération Internationale de Gynécologie Obstétrique stage

Dose (Gy)	Missing (n)	Stage I	Stage II	Stage III	Stage IVA	Total
EBRT						
Total point A dose						p<0.001
0–20	1	6 (18%)	5 (5%)	0	2 (6%)	13 (5%)
20–30	6	8 (24%)	19 (19%)	10 (8%)	3 (9%)	40 (14%)
30–40	3	10 (30%)	38 (38%)	65 (54%)	8 (24%)	121 (42%)
40–50	7	4 (12%)	19 (19%)	32 (27%)	7 (21%)	62 (22%)
50–60	2	5 (15%)	18 (18%)	12 (10%)	11 (34%)	46 (16%)
>60	0	0	0	1 (1%)	2 (6%)	3 (1%)
Missing	3	10	3	2	2	39
Median		30	30.6	34.9	41.1	32.4
Total point B dose						p=0.0003
0–20	0	2 (5%)	0	0	2 (6%)	4 (2%)
20–30	2	2 (5%)	1 (1%)	3 (3%)	2 (6%)	8 (3%)
30–40	1	3 (8%)	2 (2%)	5 (4%)	3 (9%)	13 (4%)
40–50	11	15 (38%)	35 (35%)	38 (31%)	7 (21%)	95 (32%)
50–60	5	17 (44%)	60 (60%)	72 (59%)	16 (49%)	165 (56%)
>60	0	0	2 (2%)	3 (3%)	3 (9%)	8 (3%)
Missing	3	4	4	1	2	31
Median		46.0	50.0	50.0	50.0	50.0
HDR-ICBT						
Total point A dose						p=0.025
0–10	0	0	2 (3%)	2 (2%)	1 (7%)	5 (2%)
10–20	3	5 (17%)	14 (18%)	34 (40%)	5 (36%)	58 (28%)
20–30	3	18 (62%)	49 (64%)	40 (47%)	6 (43%)	113 (54%)
30–40	0	2 (7%)	5 (6%)	1 (1%)	0	8 (4%)
>40	0	1 (3%)	0	0	0	1
Missing	4	3 (11%)	7 (9%)	8 (10%)	2 (14%)	24 (11%)
Median		23.1	22.0	20.0	20.0	20.3

Abbreviations: EBRT= external beam radiotherapy; HDR-ICBT= high dose rate intracavitary brachytherapy.

0–499 cGy (43/215, 20%), and 700–799 cGy (15/215, 7%). A single dose to point A over 8 Gy was applied only in two patients. The median number of HDR-ICBT insertions was 4 (range, 1–8). The median total dose of ICBT at point A was 20.3 Gy for HDR and 40.1 Gy for LDR. In cases of HDR-ICBT, total dose to point A decreased significantly with increasing stages. Median total dose of HDR-ICBT at point A was 23.1 Gy for Stage I, 22.0 Gy for Stage II, 20.0 Gy for Stage III, and 19.9 Gy for Stage IVA ($p = 0.025$). For calculation of total dose of EBRT and HDR-ICBT, biologically effective doses (BED) for tumor effect were calculated on the basis of $\alpha/\beta = 10$. The median total BED at point A was 74 Gy_{10} in cases treated with HDR-ICBT. There was no significant difference in total BED among the stages. Median total point A BED was 72 Gy_{10} for Stage I, 75 Gy_{10} for Stage II, 72 Gy_{10} for Stage III, and 77 Gy_{10} for Stage IVA ($p = 0.47$).

The median overall treatment time (OTT) was 47 days. OTT exceeded 8 weeks in 88 patients (28%).

Chemotherapy

Chemotherapy was applied in 104 patients (32%). Fifty-six patients (17%) were treated with concurrent chemoradiation (CCRT). Use of CCRT significantly varied according to FIGO stage ($p = 0.0039$). Chemotherapy was administered to 3 patients (7%) in Stage I, 12 patients (12%) in Stage II, 34 patients (28%) in Stage III, and 5 patients (14%) in Stage IVA. Neoadjuvant chemotherapy (NAC) before radiation therapy was given in 52 patients (16%).

DISCUSSION

This study describes the general patterns of radiotherapy practice for uterine cervical cancer from 1999 to 2001 in Japan. We examined the changes within Japan over the years and the differences in practice between Japan and the United States (Table 5).

External beam radiotherapy

For the radiation field (planning target volume [PTV]), almost all patients were treated with whole pelvic radiotherapy. Only a small number of patients received radiotherapy with an extended field including the para-aortic region. These results did not change over the years when comparisons were made with the previous JPCS (16). The U.S. PCS reported that only 11% of patients received extended field radiotherapy (12). Despite the positive results of the Radiation Therapy Oncology Group trial 79-20 (19), the standard PTV for EBRT in clinical practice in both Japan and the United States remained the whole pelvic region without para-aortic irradiation.

Table 5. Comparison of patterns of radiotherapy in cervical cancer patients between Japan and the United States

Parameters	Japan PCS 1995–1997*	Japan PCS 1999–2001	US PCS
Exrternal beam			
PTV			
Extended field	1%	3%	11%†
Beam energy			
Co60–9 MV	30%	26%	17%†
10–14 MV	57%	71%	19%†
15 MV≤	8%	3%	62%†
Technique			
Anteroposterior	95%	87%	19%†
Four-field box	2%	7%	80%†
Midline block			
Yes	69%	70%	6%†
Intracavitary brachytherapy			
Performed			
Yes	77%	82%	93%‡
Dose-rate			
LDR	8%	11%	78%‡
HDR	85%	89%	13%‡
Total dose to central tumor§ (median BED)	—	74 Gy_{10}	103 Gy_{10}‡
Overall treatment time (median)	49 days	47 days	57 days‡

Abbreviations: BED = biologically effective dose; LDR = low dose rate; HDR = high dose rate; PTV = planning target volume.
* Recalculated % including missing values.
§ point A dose (EBRT+HDR-ICBT).
† 1992–1994.
‡ 1996–1999.

As for beam energy, use of 9 MV or less decreased, and use of 10–14 MV increased (16). In the United States, the percentage of patients receiving 15 MV was largest (9, 12). The four-field technique was applied slightly more frequently in the present JPCS than the preceding JPCS (16). However, most patients were treated with the opposing AP-PA technique. In contrast, the four-field technique was applied in 80% of the patients in the United States (12). In the present survey, median isocenter depth of the AP-PA portals was 9 cm, indicating that the body thickness of females in Japan is small. Although there are no data, the body thickness is presumed to be larger in American patients compared with Japanese patients. Therefore, after taking body thickness into account, we thought that the beam energy and method of external beam radiotherapy used in Japan is appropriate. Even in Japanese patients whose body thickness is smaller than that of American patients, multiple field radiotherapy (*e.g.*, four-field) should be selected when a low-energy beam is used.

In this survey, a midline block was used in most patients, and no change in this practice was observed over the years (16). In contrast, the midline block was rarely used in the United States (12). The widespread use of the midline block was considered the result of following schedules specified in Japanese guidelines (7). One reason for less frequent use of the midline block in the United States may be the use of the four-field technique. Mell *et al.* (20) reported use of intensity-modulated radiation therapy (IMRT) in 27% of patients with gynecologic cancer in the United States. Because the use of IMRT could increase in Japan as well, it will be necessary to reexamine the advantages of using the midline block.

Intracavitary brachytherapy

The application rate of ICBT slightly increased compared with the previous PCS (16). However, the application rate was less in Japan than in the United States (12, 13). Intracavitary brachytherapy should be applied more routinely for patients treated by definitive radiotherapy in Japan. One fourth of the patients had received ICBT at another medical institution. In contrast, the percentage of such patients was reported as 8.5% in the United States (21).

HDR was used in approximately 90% of the patients, which was almost the same rate as that of the previous JPCS (16). In the United States, this rate was lower than that of Japan: 24% according to the ABS survey (1995) (22) and 16% according to the U.S. PCS survey (1996–1999) (21). We consider that the difference in the dose rate is one of the major differences between Japan and the United States. In the present study, the ICBT sources Co-60 and Ir-192 were used in roughly the same number of cases. The use of Ir-192 increased compared with the previous JPCS (16). In the early 2000s, the Japanese Society for Therapeutic Radiology and Oncology recommended the discontinuation of Co-60 as a remote afterloading brachytherapy source in Japan. The increase in the use of Ir-192 could be the result of compliance with this recommendation. Further increase in the use of Ir-192 and decrease in the use of Co-60 are expected in the next survey.

The ABS made a number of recommendations regarding HDR-ICBT techniques (5). The present study showed that analysis of the dose to organs at risk was performed in only a small percentage of patients. The doses were more often determined by using a dosimeter than the ICRU 38 reference point calculation. Sakata *et al.* indicated that the measured rectal dose significantly correlated with the incidence of rectal complications (23). In the United States, the practice of using a dosimeter for dosimetry has been called into question. The ABS recommended the use of the ICRU 38 reference point calculation (5). Many studies showed that late rectal complications can be predicted by the calculated doses at the ICRU 38 reference points (24, 25). According to the ABS survey, rectal/bladder doses are evaluated in 80% or more of patients at U.S institutions where HDR is performed (22).

The ABS also recommends conscious sedation for HDR-ICBT applicator insertions (5). However, it was surprising to discover that many patients in both the present and previous JPCS (16) received no pretreatment for HDR-ICBT applicator insertion. Intracavitary brachytherapy plays an important role in the radiotherapy of uterine cervical cancer. Accurate insertion can hardly be achieved if patients

Table 6. Standard radiotherapy schedule for uterine cervical cancer in Japan

FIGO stage	Central pelvic dose of EBRT (Gy)	Point A dose of HDR-ICBT (Gy/fc.)	Total BED at point A (Gy_{10})
I	0	29/5	46
II small	0	29/5	46
II large	20	23/4	60
III (small-medium)	20–30	23/4	60–72
III (large)	30–40	15/3–20/4	71–78
IVA	30–50	15/3–20/4	71–83

Abbreviations: BED = biologically effective dose; EBRT = external beam radiotherapy; FIGO = Fédération Internationale de Gynécologie Obstétrique; HDR-ICBT: high dose rate intracavitary brachytherapy.

experience discomfort. Therefore, we consider that pretreatment, such as conscious sedation, should be used for HDR-ICBT applicator insertion.

The single, total dose of HDR-ICBT was lower in the present study than the previous JPCS (16). The reason is unknown, but it might be related to an increase in the use of concurrent chemoradiotherapy (CCRT), which will is discussed subsequently.

Radiation dose

Table 6 shows the radiotherapy schedules indicated in the aforementioned general rules (7) and their biologically effective doses (BED) by stages. It also shows that the dose for the cervical tumor—namely, the total dose of EBRT and HDR-ICBT (point A dose)—increases with stage progression. In this present study, BED ranged from 72 to 77 Gy_{10} among the stages, indicating that differences among the stages were small. The schedules advocate the use of the midline block starting at 0–20 Gy of EBRT for Stages I and II. However, only 20% of patients followed the rule in this present study. Many other patients received EBRT exceeding these doses without the midline block. As a result, the total dose (EBRT+HDR-ICBT) to the central pelvis in early FIGO stages was higher than estimated. In contrast, treatment of patients in Stage III and IVA followed the schedules indicated in the general rules.

It was reconfirmed that the dose to uterine cervical tumors was lower in Japan than in the United States (25–27). The biologically effective dose (BED) of the schedules recommended by the ABS is approximately 100 Gy_{10} (5). In the United States PCS, the mean value of the linear quadratic equivalent dose was 85.5 Gy for patients treated using HDR-ICBT in 1996–1999 (21). When converted to BED, this value was 103 Gy_{10}. The difference in dose between Japan and the United States may be attributed to the difference in the standard schedules recommended in each country. The issue of dose range will need to be resolved before an international collaborative study can be initiated (8). The validity of each dose needs to be evaluated by outcome analysis.

Overall treatment time

Overall treatment time (OTT) is considered an important factor that affects the outcome of radiotherapy for uterine cervical cancer (28, 29). The ABS proposed that the OTT should be limited to within 8 weeks (5). The median OTT was shorter in this study (47 days) than in the previous JPCS (16). However, the OTT exceeded 8 weeks in almost 30% of patients. More effort to avoid treatment interruption to limit OTT within 8 weeks should be made. In the United States, the median OTT was reported to be 57 days (21). This difference between Japan and the United States may be due to differences in treatment schedules. In Japan, a midline block is inserted and ICBT starts in the middle of the EBRT treatment period.

Chemotherapy

In the present study, 32% of the patients received chemotherapy, indicating an increase from the previous JPCS (16). In particular, the rate of CCRT increased from 5% to 17% (16). The increase could be due to adoption of practices shown effective by RCTs published in 1999 (1–3). In the U.S. PCS (1996–1999), the percentage of patients who received chemotherapy was reported to be 19% in 1996, 28% in 1997, and 26% in 1998. However, it dramatically increased to 63% in 1999 (13). Further increase in the use of CCRT is expected in both Japan and the United States, and the monitoring of such changes should be continued.

Whereas several RCTs revealed negative therapeutic value of neoadjuvant chemotherapy (NAC) before radiotherapy in the mid-1990s, 16% of the patients were still treated with this strategy during this surveyed period. Surprisingly, the application rate was almost the same as that reported in the 1995–1997 JPCS survey (14%) (16). The usage of this strategy should be further monitored closely as well as CCRT.

Conclusions

We describe the status of definitive radiotherapy for uterine cervical cancer in Japan from 1999 to 2001. As in the previous survey (1995–1997), the EBRT conditions, such as the beam energy and technique of EBRT, were different between Japan and the United States. However, conditions of EBRT in Japan were becoming more standardized. For ICBT, aspects of the technique, such as dosimetry of organs at risk and supportive medication (*i.e.*, conscious sedation), can be improved. The total BED (EBRT + HDR-ICBT) delivered to the primary lesion in Japan was approximately 70% of that in the United States. The median OTT in Japan was approximately 80% of that in the United States. Compared with the previous JPCS, our study found that the use of CCRT has increased. This increase is considered to be due to the adoption of practices shown effective by RCT results published in 1999.

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Patterns of Pretreatment Diagnostic Assessment and Staging for Patients with Cervical Cancer (1999–2001): Patterns of Care Study in Japan*

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Objective: To evaluate the patterns of pretreatment diagnostic assessment in uterine cervical cancer patients treated with definitive radiotherapy in Japan.
Methods: The Japanese Patterns of Care Study working group conducted a second extramural audit survey of 68 institutions and collected specific information on 631 patients with cervical cancer. All patients were treated with radiotherapy in 1999–2001. Of these, 324 patients treated without surgery were the subjects of this study.
Results: International Federation of Gynecology and Obstetrics-prescribed diagnostic procedures were performed at moderate rates in our study cohort. The performance rates of chest X-ray, intravenous urography, cystoscopy, and proctoscopy were 74, 54, 53, and 33%, respectively. Cross sectional imaging studies were frequently performed. Pelvic CT, abdominal CT, and pelvic MRI were performed in 88, 80, and 76%, respectively. Lymphangiography (1%) and surgical evaluation (1%) were rarely done. Only one patient underwent PET scans in this survey period.
Conclusions: This study demonstrated the patterns of pretreatment diagnostic assessment in cervical cancer patients treated with definitive radiotherapy in Japan.

Key words: cervix neoplasm – radiotherapy – patterns of care – FIGO

INTRODUCTION

The pretreatment assessment of cancer extension is extremely important for prognosis estimation and treatment planning. Additionally, a well-defined initial assessment enables the comparison of cancer treatment results among institutions or different treatment methods. The International Federation of Gynecology and Obstetrics (FIGO) provides a global staging system for gynecologic cancers (1). Most clinicians use this staging system in the treatment of uterine cervical cancer. The system describes the rules for stage classification in detail, and the permitted diagnostic procedures are clearly stated. However, some of the procedures included, such as intravenous urography, and skeletal X-rays, could be considered outdated. Although tumor diameter and pelvic nodal status are not accounted for in the FIGO staging system, they are estimated to be the important prognostic factors for cervical cancer (2). In several studies, tumor diameter as assessed by MRI was a significant prognostic indicator for patients with cervical cancer (3–5). Evaluation of pelvic or para-aortic lymph node status with optional imaging studies, such as CT, MRI, and lymphangiography, may also be useful for predicting prognosis (6).

Several studies describe the patterns of pretreatment work-up of cervical cancer in the USA (7–9); however, there are few studies from Japan. The objective of this study

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was to review the patterns of pretreatment diagnostic assessment of cervical cancer in Japan.

MATERIALS AND METHODS

Between July 2002 and June 2004, the Japanese Patterns of Care Study group (JPCS) conducted a national survey of patients with cervical cancer treated with radiotherapy. Sixty-eight out of 640 institutions were selected for the survey with a stratified 2-staged cluster sampling method (10). Prior to random sampling, all institutions were classified into one of four groups. The criteria for stratification have been detailed elsewhere (10). In brief, the JPCS stratified Japanese institutions as follows: A1, academic institutions treating ≥430 patients annually; A2, <430 patients; B1, non-academic institutions treating ≥130 patients annually; B2, <130 patients. Academic institutions included cancer center hospitals and university hospitals. Non-academic institutions consisted of other facilities, such as national, prefectural, municipal, and private hospitals.

The JPCS surveyors performed on-site chart reviews at each participating facility using an originally developed format for cervical cancer. Data collection included patient characteristics (e.g. patient history, age, performance status, laboratory data, pathology, and stage), details of pretreatment work-up, therapeutic information (e.g. radiotherapy, chemotherapy, and surgery), and treatment outcome. Patient eligibility criteria of the survey were as follows: (i) carcinoma, (ii) treatment between January 1999 and December 2001, (iii) no distant metastases, (iv) no prior or concurrent malignancy, (v) no gross para-aortic lymph node metastases, and (vi) no previous pelvic radiotherapy. The JPCS collected clinical data on 631 patients with uterine cervical cancer who were treated with radiotherapy from 68 institutions. In this study, 324 patients treated by radiotherapy without planned surgery (definitive radiotherapy) were analysed. These included 115 patients from A1 institutions, 70 patients from A2 institutions, 104 patients from B1 institutions, and 35 patients from B2 institutions.

Statistical significance was tested using the chi-square test. Cases with 'unknown' and 'missing' values were combined in the tables because their meanings were the same in most cases: no valid data were found in the given resources (11).

RESULTS

Table 1 describes the patient characteristics in the JPCS 1999–2001 survey of cervical cancer patients treated with definitive radiotherapy. Table 2 shows the performance rates of the diagnostic procedures. Of the diagnostic procedures prescribed by FIGO, three quarters of the patients underwent a chest X-ray. Other examinations, such as intravenous urography, cystoscopy, and proctoscopy, were performed in approximately 30–50% of the patients. Table 3 shows the performance of the examinations according to stage. A substantial number of early stage (I, II) patients underwent these diagnostic tests prescribed by the FIGO system. Majority of the patients underwent both pelvic and abdominal CT. Pelvic MRI was also frequently performed. CT and MRI were performed mostly irrespective of stage. Lymphangiography (LAG) and surgical staging were rarely performed. Only one patient underwent PET examination in the survey period.

Tumor diameter was recorded in 75% (242/324). The tumor diameter evaluation rates by FIGO stage were 67% (29/43) for stage I, 83% (85/102) for stage II, 77% (94/122) for stage III, and 80% (28/35) for stage IVA ($P = 0.01$). MRI was the most common modality for evaluating tumor size (47%) followed by CT (16%). Only a small percentage of patients had a tumor size evaluation consisting of only a pelvic examination (6%). Tumor size increased significantly with increasing stage. Median tumor size was 26 mm (range: 0–45 mm) for stage I, 40 mm (range: 15–90 mm) for stage II, 46 mm (range: 15–100 mm) for stage III, and 55 mm (range: 30–100 mm) for stage IVA ($P < 0.0001$). Pelvic nodal status was recorded in 82% (266/324) of the patients surveyed. The pelvic nodal assessment rate by stage was 88% (38/43) for stage I, 86% (88/102) for stage II, 83%

Table 1. Patient and tumor characteristics of 324 patients with uterine cervical cancer treated with radiotherapy

Characteristics	No. of patients	(%)
Total no.	324	
Age (years)		
Range	26–100	
Median	71	
KPS		
≤ 70	64	20
80	103	32
90	114	35
100	21	6
Unknown/missing	22	7
Histology		
Squamou cell carcinoma	300	93
Adenocarcinoma	14	4
Adenosquamous cell carcinoma	4	1
Other	2	1
Unknown/missing	4	1
FIGO stage		
I	43	13
II	102	31
III	122	38
IVA	35	11
Unknown/missing	22	7

KPS, Karnofsky performance status; FIGO, International Federation of Gynecology and Obstetrics.

Table 2. Pretreatment diagnostic procedures performed

Procedure	No. of patients	(%)
Chest X-ray		
Yes	241	74
No	7	2
Unknown/missing	76	24
Intravenous urography		
Yes	176	54
No	68	21
Unknown/missing	80	25
Cystoscopy		
Yes	171	53
No	60	19
Unknown/missing	93	28
Proctoscopy		
Yes	108	33
No	114	35
Unknown/missing	102	32
Pelvic CT		
Yes	286	88
No	8	3
Unknown/missing	30	9
Abdominal CT		
Yes	258	80
No	14	4
Unknown/missing	52	16
Pelvic MRI		
Yes	246	76
No	39	12
Unknown/missing	39	12
Lymphangiography		
Yes	3	1
No	241	74
Unknown/missing	80	25
PET		
Yes	1	-
No	254	79
Unknown/missing	69	21
Surgical staging		
Yes	3	1
No	257	79
Unknown/missing	64	20

PET, positron emission tomography.

(101/122) for stage III, and 94% (33/35) for stage IVA ($P = 0.12$). CT was most frequently used for the assessment of nodal status (72%). PET and surgical examination were never utilized for this purpose. Positive nodal status significantly correlated with FIGO stage: 2% for stage I, 6% for stage II, 16% for stage III, and 49% for stage IVA ($P = 0.0001$).

DISCUSSION

This study demonstrated the patterns of pretreatment diagnostic assessment for cervical cancer patients who underwent definitive radiation therapy between 1999 and 2001 in Japan. Several of the cases reviewed in this survey had unknown or missing data; and this was a theoretical weaknesses of our audit. Inclusion of cases with incomplete information in the ratio calculations, however, reduced the potential for overestimation of performance rates of the tests.

FIGO permitted procedures were performed more frequently than expected in the patients surveyed. The use of FIGO permitted examinations (e.g. intravenous urography, cystoscopy, and proctoscopy) is gradually decreasing in the USA (7–9). In a 2000–02 US study on the pretreatment evaluation of patients with stage IIB or less disease, the rates for performing intravenous urography, cystoscopy, and proctoscopy were 1, 16, and 17%, respectively (9). In contrast, the present study demonstrated that these exams were performed frequently even for early stage cases in Japan. Schmitz et al. (12) proposed that since the likelihood of upstaging using these examinations was very low in clinical stage IB patients, these exams could be omitted in those with stage IB disease. Now, the National Comprehensive Cancer Network (NCCN) guideline states that cystoscopy and proctoscopy are optional exams for the pretreatment assessment of cervical cancer patients with a disease stage of IB2 or higher (http://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf).

This study demonstrated that CT and MRI were routinely utilized during the surveyed period in Japan. Tumor size and pelvic nodal status are considered to be extremely important prognostic factors for cervical cancer (2). Several studies showed the accuracy of MRI for measuring tumor diameter for uterine cervical cancer (13,14). In the 1990s, several researchers reported that tumor diameter, as assessed by MRI, significantly affected the outcome of cervical cancer patients treated with definitive radiotherapy (3–5). The radiological evaluation of lymph node metastases is also valuable in cervical cancer patients, with both CT and MRI having high predictive values (6). MR imaging had an accuracy of 93%, with 62.2% sensitivity and 97.9% specificity when a minimum axial diameter of 1.0 cm was adopted as a size criterion for detection of pelvic nodal metastases (15). The results of our study reflect the penetration of these findings into the clinical practice in Japan. Unfortunately, we were unable to precisely measure the performance rates of the assessments of tumor diameter and lymph node status due to a flaw in the survey format. Namely, we were unable to distinguish whether the assessments were performed by

Table 3. Pretreatment diagnostic procedures performed according to the FIGO stage

Procedure	Stage				Missing/unknown
	I	II	III	IVA	
Intravenous urography	17/43 (40%)	53/102 (52%)	74/122 (61%)	26/35 (70%)	6/22
Cystoscopy	18/43 (42%)	58/102 (57%)	64/122 (52%)	25/35 (71%)	6/22
Proctoscopy	12/43 (28%)	32/102 (31%)	43/122 (35%)	17/35 (49%)	4/22
Pelvic CT	40/43 (93%)	89/102 (87%)	112/122 (92%)	34/35 (97%)	11/22
Abdominal CT	35/43 (81%)	83/102 (81%)	103/122 (84%)	29/35 (83%)	8/22
Pelvic MRI	31/43 (72%)	84/102 (82%)	88/122 (72%)	27/35 (77%)	16/22

the treating physicians or were performed anew by the visiting surveyors at the time of the analysis. Despite this limitation, we were able to roughly approximate the tumor diameter and the lymph node status in each stage. In the next JPCS presently being conducted, the format has been revised to clarify the aforementioned points. Our data will aid in comparing outcome between Japan and other countries. Abdominal CT has diagnostic value in detecting extrapelvic metastases (i.e. liver and para-aortic node) and the presence of hydronephrosis or a non-functioning kidney. Despite the potential usefulness of CT and MRI, these cross-sectional imaging studies are listed as optional examinations in the FIGO system (1). FIGO also acknowledges the usefulness of these exams. However, FIGO does not accept them for staging purposes, primarily because these instruments are not generally available in developing countries. The FIGO system clearly states that findings from these exams should not be the basis for staging (1). Improper application of these exams could lead to staging migration (2). However, we believe that these cross-sectional imaging studies should be applied universally not to determine FIGO stage but to assess important prognostic factors, namely tumor diameter and nodal status.

Several randomized clinical trials (RCTs) performed in the USA demonstrated the therapeutic value of concurrent chemoradiotherapy (http://www.cancer.gov/newscenter/cervicalcancer). Most of these trials required extensive evaluation of para-aortic lymph nodes by surgical exploration or LAG. This limits the translatability of the recommendations from these trials to the Japanese clinical practice. LAG and surgical staging were rarely performed for patients in our survey. Although Eifel reported that lymph nodal status was assessed by LAG in 13.6%, and surgical evaluation in 12.2% in the US PCS (1996–99), other studies revealed that, the performance of LAG has been decreasing recently (7–9). A similar problem exists in the evaluation of tumor diameter. In the US RCTs, tumor diameter was determined by physical examination. However, tumor size assessment by physical examination is highly subjective. Thus an objective method such as CT or MRI is preferable particularly when patients are being stratified in a clinical trial. This would facilitate the translation of evidence to clinical practice.

PET was rarely performed during the study period in Japan despite being shown to be useful in the late 1990s (16). Its application is expected to increase in the future, because the Japanese health insurance plan has covered it since 2004.

In summary, the JPCS describes the general patterns of pretreatment diagnostic assessment in cervical cancer patients treated with definitive radiotherapy during 1999–2001 in Japan. Patterns of pretreatment work-up should be continuously monitored in order to avoid staging migration, to properly treat individual patients, and to fairly compare treatment methods.

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Conflict of interest statement

None declared.

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Results of the 1999–2001 Japanese Patterns of Care Study for Patients Receiving Definitive Radiation Therapy without Surgery for Esophageal Cancer

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Background: The third Japanese Patterns of Care Study (JPCS) was conducted for esophageal cancer patients receiving radiotherapy (RT). The aim of this study is to analyse the data of the non-surgery group.
Methods: Of the 621 patients receiving RT from 1999 to 2001, 385 non-surgical patients were analysed.
Results: Median age was 71 years and 85% were male. Karnofsky performance status (KPS) was $\geq$80 in 71% and better in T1 cases than in T2–4 cases. Ninety-nine per cent had squamous cell carcinoma and 56% had the main lesion in the middle thoracic esophagus. Twenty-one per cent had T1 disease, 12% T2, 38% T3 and 29% T4. Endoscopic ultrasound was used in 29% and mainly in T1 cases. Endoscopic mucosal resection was performed in 40% of mucosal cancer. Utilization of chemotherapy had remarkably increased compared with the 1995–1997 JPCS (61% versus 35%), however was significantly less in T1 cases than in T2–4 cases. The most frequently used agents for concurrent use were 5-fluorouracil and cisplatin. The median total dose of external beam RT (ERT) was 60 Gy and did not differ between T1 and T2–4 cases and also in comparison with the 1995–1997 JPCS. Brachytherapy was used in 10% and mainly in T1 cases.
Conclusions: Utilization of chemotherapy had remarkably increased. However the common treatment for T1 cases was RT alone. The standard dose of ERT was 60 Gy in spite of the increase in chemotherapy administration. Moreover, this survey showed significant differences in many parameters of treatment process between T1 and T2–4 cases.

Key words: Patterns of Care Study – esophageal cancer – radiotherapy – depth of tumor invasion

INTRODUCTION

To improve the quality of radiotherapy (RT), the Patterns of Care Study (PCS) was introduced to Japan from the USA, courtesy of the American College of Radiology in 1996. So far, three Japanese PCS (JPCS) surveys for esophageal cancer patients receiving RT have been performed. The first survey was conducted from 1996 to 1998 collecting data of patients treated from 1992 to 1994. In this 1992–1994 JPCS, the feasibility of JPCS was confirmed and the author concluded that institutional stratification including equipment and personnel had significantly affected the patterns of care for esophageal cancer (1). The second survey was carried out from 1998 to 2001, collecting data of patients treated from 1995 to 1997. The report of this survey emphasized that there had been several problems that needed resolving immediately, such as the use of inappropriate lower photon beam energy and the excess dose applied to the spinal cord (2,3). Moreover, the utilization rate of chemo-radiotherapy (CRT) in this survey was about 40%, and CRT was not

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