

Original Article



Quality indicators for cervical cancer care in Japan

Tomone Watanabe ,¹ Mikio Mikami ,² Hidetaka Katabuchi ,³ Shingo Kato,⁴ Masanori Kaneuchi,⁵ Masahiro Takahashi,⁶ Hidekatsu Nakai ,⁷ Satoru Nagase ,⁸ Hitoshi Niikura,⁹ Masaki Mandai,¹⁰ Yasuyuki Hirashima,¹¹ Hiroyuki Yanai,¹² Wataru Yamagami ,¹³ Satoru Kamitani ,¹ Takahiro Higashi

¹Division of Health Services Research, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan

²Department of Obstetrics and Gynecology, Tokai University, Kanagawa, Japan

³Department of Obstetrics and Gynecology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

⁴Department of Radiation Oncology, Saitama Medical University International Medical Center, Saitama, Japan

⁵Department of Obstetrics and Gynecology, Otaru General Hospital, Hokkaido, Japan

⁶Department of Medical Oncology, Tohoku University Hospital, Miyagi, Japan

⁷Department of Obstetrics and Gynecology, Kindai University Faculty of Medicine, Osaka, Japan

⁸Department of Obstetrics and Gynecology, Yamagata University Faculty of Medicine, Yamagata, Japan

⁹Department of Obstetrics and Gynecology, Tohoku University, Miyagi, Japan

¹⁰Department of Gynecology and Obstetrics, Kyoto University Graduate School of Medicine, Kyoto, Japan

¹¹Division of Gynecology, Shizuoka Cancer Center Hospital, Shizuoka, Japan

¹²Department of Pathology, Okayama University Hospital, Okayama, Japan

¹³Department of Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan

OPEN ACCESS

Received: Oct 6, 2017

Revised: Jul 9, 2018

Accepted: Jul 9, 2018

Correspondence to

Tomone Watanabe

Division of Health Services Research, Center for Cancer Control and Information Services, National Cancer Center, 5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045 Japan.

E-mail: tomonwat@ncc.go.jp

Copyright © 2018. Asian Society of Gynecologic Oncology, Korean Society of Gynecologic Oncology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Tomone Watanabe
<https://orcid.org/0000-0002-8337-5005>

Mikio Mikami
<https://orcid.org/0000-0002-7496-3518>

Hidetaka Katabuchi
<https://orcid.org/0000-0002-2403-6134>

Hidekatsu Nakai
<https://orcid.org/0000-0002-9994-2131>

Satoru Nagase
<https://orcid.org/0000-0001-7894-0914>

Wataru Yamagami
<https://orcid.org/0000-0003-3925-6057>

Satoru Kamitani
<https://orcid.org/0000-0001-7188-2141>

Takahiro Higashi
<https://orcid.org/0000-0002-9933-2106>

ABSTRACT

Objective: We aimed to propose a set of quality indicators (QIs) based on the clinical guidelines for cervical cancer treatment published by The Japan Society of Gynecologic Oncology, and to assess adherence to standard-of-care as an index of the quality of care for cervical cancer in Japan.

Methods: A panel of clinical experts devised the QIs using a modified Delphi method. Adherence to each QI was evaluated using data from a hospital-based cancer registry of patients diagnosed in 2013, and linked with insurance claims data, between October 1, 2012, and December 31, 2014. All patients who received first-line treatment at the participating facility were included. The QI scores were communicated to participating hospitals, and additional data about the reasons for non-adherence were collected.

Results: In total, 297 hospitals participated, and the care provided to 15,163 cervical cancer patients was examined using 10 measurable QIs. The adherence rate ranged from 50.0% for 'cystoscopy or proctoscopy for stage IVA' to 98.8% for 'chemotherapy using platinum for stage IVB'. Despite the variation in care, hospitals reported clinically valid reasons for more than half of the non-adherent cases. Clinically valid reasons accounted for 75%, 90.9%, 73.4%, 44.5%, and 88.1% of presented non-adherent cases respectively.

Conclusion: Our study revealed variations in pattern of care as well as an adherence to standards-of-care across Japan. Further assessment of the causes of variation and non-adherence can help identify areas where improvements are needed in patient care.

Keywords: Quality Indicators; Uterine Cervical Neoplasms; Standard of Care; Guideline Adherence; Practice Guideline

Presentation

The abstract has been presented in the ASCO Quality Care Symposium on 4 March 2017 in Orlando, FL, U.S.A.

Funding

This work was funded by a grant from the National Cancer Center, Japan.

Conflict of Interest

Dr. Hirashima received grant from ONO PHARMACEUTICAL CO., LTD, TAIHO PHARMACEUTICAL CO., LTD, AbbVie, AstraZeneca, TAKEDA PHARMACEUTICAL COMPANY LIMITED, EIZAI CO., LTD during the 36 months prior to publication. Other authors declare that there is no potential conflict of interest relevant to this article.

Author Contributions

Conceptualization: W.T., M.M., K.H., K.S., K.M., T.M., N.H., N.S., N.H., M.M., H.Y., Y.H., Y.W., K.S., H.T.; Data curation: W.T., K.S., H.T.; Formal analysis: W.T., K.S., H.T.; Funding acquisition: H.T.; Investigation: W.T., K.S.; Methodology: H.T.; Project administration: W.T., K.S., H.T.; Resources: M.M., H.T.; Software: W.T., K.S., H.T.; Supervision: M.M., H.T.; Validation: M.M., H.T.; Visualization: W.T., M.M., H.T.; Writing - original draft: W.T.; Writing - review & editing: W.T., M.M., K.H., K.S., K.M., T.M., N.H., N.S., N.H., M.M., H.Y., Y.H., Y.W., K.S., H.T.

INTRODUCTION

Cervical cancer is one of the most common gynecological cancers globally. Each year, more than 500,000 women are diagnosed with cervical cancer [1]. Although its incidence has been decreasing worldwide, cervical cancer is still common, especially in the developing regions. In contrast to most developed countries [2], the incidence of this cancer is on the rise in Japan, especially among the younger generation, casting a deep shadow over the Japanese cancer demography. According to statistics, the number of patients in their 20s has more than doubled annually over the last two decades [3]; a similar trend has also been observed for women in their 30s and 40s. With current 5-year survival rates of 92.6% for stage I, 75.2% for stage II, 59.3% for stage III, and 22.2% for stage IV [4], cervical cancer continues to exhibit high mortality and morbidity among gynecologic malignant tumors in Japan [5]. In addition, urologic complications such as bladder dysfunction, which are associated with treatments, can significantly lower patients' quality of life [6,7].

Despite the growing number of patients, the quality of care for cervical cancer has remained unexamined. Quality of care (efficiency and effectiveness of care), is widely believed to help minimize disease aggravation, thus improving survival as well as quality of life [8]. Since the Japanese Diet passed the Cancer Control Act in 2007, ensuring, monitoring, and evaluating quality of patient care has gained attention at the national level [9]. Propelled by the national mandate for cancer control, The Japan Society of Gynecologic Oncology published its first treatment guideline for cervical cancer in 2007, which was revised in 2011, in order to promote standardized high-quality care in Japan [10,11]. To ensure that all patients receive high-quality care, it is thus imperative to evaluate the adherence of treatment centers to the recommendations outlined in these clinical guidelines.

Therefore, we aimed to propose a set of quality indicators (QIs) based on the clinical guidelines for cervical cancer treatment and to assess adherence to standard-of-care as an index of the quality of care for cervical cancer in Japan.

MATERIALS AND METHODS

1. Development of QIs

We developed a set of process-of-care QIs for cervical cancer care. QIs describe the care processes that a specific group of patients should receive as the standard-of-care treatment. The QIs serve to translate guideline recommendations into measurable indices with clear specifications of target patients and care processes. The QIs were devised by a panel of nationally renowned clinical experts in cervical cancer, using the Research AND Development (RAND)/University of California, Los Angeles (UCLA) modified Delphi method [12]. Each expert initially proposed QI candidates based on relevant literature and clinical practice guidelines. Then, the QI candidates were individually and anonymously rated for QI validity and significance of the measurement by each expert, on a scale of 1–9 (1=extremely invalid/not significant; 9=extremely valid/significant). The expert panel discussed each potential QI candidate after the initial rating, and introduced any modifications that were agreed upon, by consensus. Each QI candidate was then rated again. The QIs were considered valid if the median ratings for both QI validity and the significance of measurement were 7 or higher (i.e., more than half of the panel members rated a QI ≥ 7 , and 2 or fewer members rated a QI ≤ 3). The QI candidates that were considered worth measuring (i.e., median rating for significance-in-measurement was 7 or higher), but not valid

as QIs (i.e., median rating for validity being lower than 6), were considered pattern-of-care items (PCIs). Measurability was assessed using the available data.

2. Data

We used a database that linked the national database of the Hospital-Based Cancer Registry (HBCR) [13] and health insurance claims data from the Diagnosis Procedure Combination (DPC) survey. The HBCR is a compulsory cancer incidence reporting system for all designated cancer care hospitals, and is also voluntarily operated in several non-designated hospitals that play similar roles in their respective communities. The HBCR data contains clinical information such as clinical and pathological stages, tumor-node-metastasis (TNM) classifications, tumor location, and histopathological findings based on the International Classification of Diseases Oncology 3rd edition (ICD-O-3). All patients with cervical cancer (ICD-O morphology: C53.0–53.9) were included in the analyses. The DPC survey data contains information on all health services provided. While the DPC itself is a grouping system used to determine the global amount of per-day health insurance reimbursement to hospitals, the DPC survey data have the equivalent data for fee-for-service claims which code individual tests, images, procedures, and prescription drugs, along with the dates and unit costs of the services from both inpatient and outpatient settings.

Designated cancer care hospitals across Japan were invited to participate in the study. We collected claims data from October 2012 to December 2014, and linked them to the HBCR data. The time period for DPC data collection was selected to allow inclusion of all treatments performed for cancers diagnosed during 2013. The details of the data collection process are described elsewhere [14].

During implementation, several QI specifications which required data not included in the current version of HBCR were adjusted. For example, several QIs use sub-classifications of TNM, such as T1a and T2b, which is information that is mandated to be coded for all cases from the year 2016 onwards. Because the subclassifications of TNM will soon be available, the QIs that required this information were accepted in the development phase. For this reason, calculability of each QI was evaluated prior to analysis. The HBCR has adopted the Union for International Cancer Control (UICC) cancer staging system. However, as the International Federation of Gynecology and Obstetrics (FIGO) staging system is widely used in Japan, the T classification was resolved to correspond with the FIGO staging, while the cases presenting with metastasis were included in FIGO stage IV.

3. Data analysis

Adherence to each QI and its 95% confidence interval (CI) were calculated. The analysis included all patients who received first-line treatment at the participating facility. Three QIs pertained to treatment for cervical intraepithelial neoplasia 3 (CIN3), 3 for stage III or IVA disease, and one QI for stage IVB cancer. One QI addressed the examination of the extent of cancer and another QI pertained to brachytherapy regardless of the stage.

All analyses were performed on Stata version 13.2 (StataCorp LP, College Station, TX, USA). This study protocol was approved by the Institutional Review Board of the National Cancer Center, Japan (approval No. 2013-081).

4. Reasons for non-adherence to QIs

The analysis results were communicated to participating hospitals, which were requested to report back on the reasons for non-implementation of the care guidelines outlined as per the

QIs. The reasons cited were recorded and the frequency with which each reason was cited was examined. The reasons cited for less than 10 patients were not reported. Clinically valid reasons were categorized as ‘sufficient reasons’ and those that were not clinically valid as ‘insufficient reasons’.

Non-adherent cases were examined also from a different point of view. After the result of QI calculation was aggregated, limited use of radiation-based therapy has been particularly discussed amongst the expert panel. Therefore, we looked into the types of alternative treatments that were performed in patients who would otherwise have been treated with radiation-based therapy such as concurrent chemotherapy and radiation therapy (CCRT).

RESULTS

1. QI development

The panel of experts proposed 43 QI candidates in total. Among them, only 10 QIs were considered measurable, due to the lack of sub-stage information in the HBCR. Four candidates were designated as PCIs. For example, when the QI targeted patients with high-recurrence risks — such as in ‘post-surgery CCRT for pN1/pT2b patients without preoperative chemotherapy’ — we only included pN1 stage patients. Although QIs generally describe the care that should be provided, 3 QIs describe care not recommended for the target patient population — suggesting lower score (i.e., QI1 and QI10).

2. QI adherence scores

In total, 297 hospitals participated, and the care received by 15,163 cervical cancer patients was examined using 10 measurable QIs. Patient characteristics are presented in **Table 1**.

The adherence data are shown in **Tables 2** and **3**. The adherence rate ranged from 50.0% for ‘cystoscope or proctoscope for stage IVA’ (QI8) to 99.1% for ‘chemotherapy using platinum for stage IVB’ (QI7). The adherence rate varied across facilities. Apart from the 4 PCIs, the greatest inter-facility variation was seen for ‘radical hysterectomy for stage II adenocarcinoma’ (QI3) and for ‘cystoscope or proctoscope for stage IVA’ (QI8), with adherence rates of 67.7% (standard deviation [SD]=41.6) and 50.0% (SD=45.6), respectively. The smallest variation was seen for ‘chemotherapy using platinum for stage IVB’ (QI7) and for ‘post-treatment maintenance therapy using oral chemotherapy’ (QI10), with adherence rates of 98.7% (SD=2.3) and 1.2% (SD=4.9), respectively.

3. Reasons for non-adherence to QI

Forty-seven hospitals submitted data pertaining to non-adherence to QIs. The frequency and the reasons for non-adherence to QIs are shown in **Table 4**. Overall, more than half of patients had clinically valid reasons for not receiving the specified care. Comorbidities accounted for more than 60% of the reasons listed for non-adherence to the guideline recommending the use of CCRT as the first-line treatment among stage III and IVA patients (QI4). Kidney failure (14%) and poor general condition due to age (38%) were the major comorbidities reported. Four patients (26%) were reported to have been treated with nedaplatin, though cisplatin was recommended for CCRT among stage III and IVA patients (QI5). Kidney failure was the only comorbidity reported in these patients. Among the reasons listed as ‘unknown’ in QI8, 70% of patients were reported to have been evaluated by computed tomography (CT) and magnetic resonance imaging (MRI) to determine the degree

Table 1. Patient demography analysed using the HBCR and the DPC (n=15,163)

Variables	Values
Age, mean (SD)	45.1 (15.0)
<20	13 (0.1)
20–29	1,528 (10.1)
30–39	5,041 (33.2)
40–49	4,113 (27.1)
50–59	1,614 (10.6)
≥60	2,854 (18.8)
Histology type*	
Squamous cell carcinoma	13,314 (87.8)
Squamous cell carcinoma in situ	9,092
Adenocarcinoma	1,371 (9.0)
Adenocarcinoma in situ	296
Other	478 (3.1)
FIGO stage	
I	2,288 (15.1)
II	1,314 (8.7)
III	552 (3.6)
IV	780 (5.1)
Unknown [†]	806 (5.3)
Tis [‡]	9,423 (62.1)
First-line treatment	
Surgery	10,129 (66.8)
Radiotherapy	743 (4.9)
Chemotherapy	167 (1.1)
Surgery+chemotherapy	672 (4.4)
Radiotherapy+chemotherapy [§]	1,261 (8.3)
Other	2,191 (14.4)

Values are presented as mean (SD) or number (%).

CCRT, concurrent chemotherapy and radiation therapy; CIN3, cervical intraepithelial neoplasia 3; DPC, Diagnosis Procedure Combination; FIGO, International Federation of Gynecology and Obstetrics; HBCR, Hospital-Based Cancer Registry; ICD-O-3, International Classification of Diseases Oncology 3rd edition; SD, standard deviation.

*The number of patients in each category was extracted using ICD-O-3 codes; [†]In HBCR, the category includes patients who were resected before definitive diagnoses; [‡]Although “Tis” is not included in the FIGO system, patients with CIN3 and adenocarcinoma in situ were extracted from this stage using ICD-O-3 codes. Further description of stage was refrained due to the complicated nature of code extraction; [§]Those who have received both radiation therapy and chemotherapy regardless of time gaps between treatments (includes CCRT).

of tumor invasion. The category ‘other’ for QI9 included ‘insertion difficulty’ and ‘large tumor size’.

Since the results elucidated that the use of CCRT remained conservative across the QIs and PCIs, we looked into the alternative first-line treatment provided to these patients. They were: chemotherapy only (5.7%), radio therapy only (32.9%), surgery (1.1%), and others (5.1%). In patients aged below 70 years, the first-line treatment was CCRT in 74.7% of patients, chemotherapy in 8.3%, radiation therapy in 12.8%, surgery in 1.5%, and other in 2.8% of patients.

DISCUSSION

We developed 43 QI candidates, among which 10 QIs were measured using the nationwide hospital-based cancer registry and insurance claims data. Practice patterns were also measured using 4 PCIs to provide reference data to discuss the current status and the development of future standards. Variations in providing standard care were observed among participating facilities. In general, adherence rate for QIs describing care that is not

Quality indicators: cervical cancer care in Japan
Table 2. Adherence rates for various QIs

QIs	Target patients (denominator)	Specified care (numerator)	No.	Adherence rate (95% CI)
Q11*	Conization for CIN3 CIN3 patients who are under age 43 years	Patients who had total hysterectomy without conization	242/6,256	3.9% (3.4–4.4)
Q12	Total hysterectomy for adenocarcinoma in situ Patients who had adenocarcinoma in situ over age 44 years	Patients who had total hysterectomy as the last treatment	81/93	87.1% (78.5–93.2)
Q13	Radical hysterectomy for stage II adenocarcinoma Stage II adenocarcinoma patients	Patients who had radical hysterectomy	115/170	67.6% (60.1–74.6)
Q14	CCRT as the first-line treatment for stage III or IVA Stage III or IVA patients	Patients who had CCRT as the first-line treatment	397/720	55.1% (51.4–58.8)
Q15	CCRT using cisplatin for stage III or IVA Stage III or IVA patients who had CCRT	Patients who had cisplatin-based regimen for CCRT	333/417	79.9% (75.7–83.6)
Q16*	Chemotherapy for stage III or IVA Stage III or IVA patients who had curative radiation therapy or CCRT as main treatment	Patients who had chemotherapy before the main treatment	8/663	1.2% (0.5–2.4)
Q17	Chemotherapy using platinum for stage IVB Stage IVB patients who had chemotherapy	Patients who had platinum-based chemotherapy	422/426	99.1% (97.6–99.7)
Q18	Cystoscope or proctoscope for stage IVA Stage IVA patients	Patients who had cystoscope or proctoscope before the treatment	87/174	50.0% (42.3–57.7)
Q19	Curative radiation therapy using brachytherapy Patients who had curative radiation therapy without surgery	Patients who had brachytherapy	1,211/1,536	78.8% (76.7–80.9)
Q110*	Post-treatment maintenance therapy using oral chemotherapy Stage I or II patients who had surgery, radiation or CCRT for the first time.	Patients who used oral chemotherapy	28/2,313	1.2% (0.8–1.7)

CI, confidence interval; CIN3, cervical intraepithelial neoplasia 3; CCRT, concurrent chemotherapy and radiation therapy; QI, quality indicator.

*Treatment modality defined as not recommended.

Table 3. Adherence rates for PCIs

PCIs	Target patients (denominator)	Specified care (numerator)	No.	Adherence rate (95% CI)
PCI1	Total hysterectomy for CIN3 CIN3 patients who are over age 50 years	Patients who had total hysterectomy	562/1,188	47.3% (44.4–50.2)
PCI2	Post-operative CCRT for pN1 pN1 patients who had surgery without preoperative chemotherapy JSGO guideline recommendation for the denominator population: CCRT	Patients who had post-operative CCRT	163/368	44.3% (39.1–49.5)
PCI3	Post-operative therapy for pN1 pN1 patients who had surgery without preoperative chemotherapy JSGO guideline recommendation for the denominator population: CCRT	Patients who had adjuvant chemotherapy without CCRT as post-operative therapy	162/349	46.4% (41.1–51.8)
PCI4	Post-operative therapy for pN0 or pT1 pN0 or pT1 patients who had surgery without preoperative chemotherapy JSGO guideline recommendation for the denominator population: radiation therapy (CCRT)	Patients who had adjuvant chemotherapy without CCRT as post-operative therapy	248/469	52.9% (48.2–57.5)

CI, confidence interval; CIN3, cervical intraepithelial neoplasia 3; CCRT, concurrent chemotherapy and radiation therapy; JSGO, Japan Society of Gynaecologic Oncology; PCI, pattern-of-care item.

Table 4. Reasons for non-adherence to specified care* (47 hospitals)

QI	QI descriptor	No. of patients	QI score (%)	Sufficient reasons (%)					Insufficient reasons (%)	
				Comorbidities	Referral	Patient preference	Errors in data	Other	Unknown	
Q13	Radical hysterectomy for stage II adenocarcinoma	12	67.7	41.2	-	8.3	8.3	16.7	25.0	
Q14	CCRT as the first-line treatment for stage III or IVA	66	55.1	63.6	6.1	12.1	3	6.1	9.1	
Q15	CCRT using cisplatin for stage III or IVA	15	79.9	66.7	-	6.7	-	-	26.6	
Q18	Cystoscope or proctoscope for stage IVA	14	50.0	7.1	14.3	7.1	7.1	7.1	57.1	
Q19	Curative radiation therapy using brachytherapy	59	78.8	30.5	18.6	6.8	1.7	30.5	11.9	

CCRT, concurrent chemotherapy and radiation therapy; QI, quality indicator.

*Reasons cited for less than 10 patients were excluded from the list.

recommended was generally high. However, other QIs had markedly variable adherence rates, implying non-uniform practice patterns among facilities. Additional data collection relating to reasons for non-adherence helped in elucidation of the causes of the variations.

Trimble et al. studied the change in patterns of care through a period in which a series of new evidences was published and distributed by the National Cancer Institute as part of a clinical announcement for cervical cancer patients in the United States [15]. As per this study, surgery for stage I, radiation therapy — either with or without chemotherapy — for stage II to IVA, and chemotherapy for stage IVB disease, appeared to be the dominant treatment regimens in clinical practice. Overall, our results correlated well with the trend of clinical practice revealed through this study, and suggest that efforts to adhere to optimal care guidelines are the norm. However, the use of CCRT as per our study remained disturbingly low, in contrast to the sharp increase of this treatment modality in the United States as reported by the aforementioned study [16-18].

Comparative analysis of similar studies conducted globally highlights one of the unique traits of Japanese practice patterns — conservative use of radiation therapy, especially CCRT. Currently, in the United States, radiation therapy (including CCRT) is gaining popularity, with a concomitant decrease in surgical resection for gynecological cancers [19]. The guideline published by the National Comprehensive Cancer Network recommends CCRT as an effective treatment modality comparable to any surgical method, in stage IB and IIA patients [20]. Moreover, for those with stage IIB disease and above, CCRT is now regarded as a primary choice of treatment after several randomized clinical trials (RCTs) revealed an improved survival rate [17,21,22]. Although CCRT is the recommended treatment option, almost 50% of stage IIB patients still receive surgery in Japan [23]. Moreover, our study shows that the adherence rate for QIs and PCIs pertaining to the use of CCRT, such as ‘CCRT as the first-line treatment for stage III or IVA’ (QI4) or ‘post-operative CCRT for pN1’ (PCI2), remained relatively low.

The trend was also evident in the choice of adjuvant therapy. Although CCRT is now the standard for adjuvant therapy for high recurrence risk patients [23], as adherence data for ‘post-operative therapy for pN1’ (PCI3) shows, chemotherapy was selected in a substantial number of cases as post-operative therapy across the board in Japan. As a study by Ikeda et al. [24] showed, disagreements regarding the optimal adjuvant therapy remain unresolved. To resolve this issue, a nation-wide retrospective study comparing the effect of adjuvant chemotherapy with that of radiation-based therapy was conducted. The results revealed similar overall recurrence as well as mortality for high-risk patients [25]. To further confirm the findings, a new prospective trial conducted by the Japanese Gynecologic Oncology Group is currently ongoing.

The lack of widespread use of radiation therapy is partially explained by the history of gynecological medicine in Japan. With the delayed availability of radiation therapy, surgical resection had long been chosen as a primary source of treatment [5]. Surgical expertise is believed to be the reason for the limited use of radiation therapy and CCRT [11,23]. In addition, side effects such as postsurgical ileus and severe lymphedema have prevented this procedure from gaining popularity. Finally, with regard to curative radiation therapy, a study has shown that the median age in RCTs conducted in the United States from which the conclusion was drawn was 40, while median age of those receiving such care in Japan is 70 [26]. The presented age gap could prevent direct application of the RCT findings to the

Japanese population, making further studies necessary for solidifying the optimal choice of treatment for this population.

Although the trend was most clearly elucidated for the QI referring to radiation therapy, reasons for non-adherence implicated comorbidities as the major reason for choosing alternatives for most of the QIs. Although the comorbidities were varied, a substantial number of patients were treated with alternative treatment due to age-related issues such as impairment of the liver and/or the kidney. Overall, except for QI8, which showed heavy use of CT and MRI as diagnostic tools, ‘insufficient reasons’ for non-adherence were observed in as low as 10% to 20% of the cases. We conclude from our results that though there is room for improvement, efforts were made by the participating hospitals to provide care in accordance with the guidelines.

Our study has several limitations. The primary limitation is the inability to capture details of care provided at hospitals other than those at which the relevant cases were registered, though such cases are infrequent, as revealed by our survey of reasons for non-adherence. In addition, lack of sub-stage information in the HBCR prevented QIs and PCIs requiring sub-stage information from defining target patients effectively. This was unavoidable, since the mandate to record disease sub-stage data was implemented only in the year 2016. Likewise, the scarce information available on operative procedure in claims data, especially the extent of lymph node dissection, limited the range of measurable QIs. Augmenting data sources by linkage, and refining the procedure codes, could expand the application of QIs to broader aspects of care in the future.

Finally, although we recognize the importance of validity test, the validity of the QIs in terms of the process-outcome link is yet to be proven. Although many standards of care are derived from well-designed RCTs, effectiveness of those standards may not apply in real world settings in which many patients have comorbidities or even multiple primary cancers. Bristow et al. in a study conducted in the United States, revealed a positive correlation between QI adherence and survival rate in ovarian cancer [27], and a similar study performed in a Japanese population in the field of cervical cancer would be valuable. Future studies are needed to confirm the association of QIs with survival, and broaden its potential as a measure of quality care.

REFERENCES

1. International Agency for Research on Cancer. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012 [Internet]. Lyon: International Agency for Research on Cancer; 2012 [cited 2017 Jun 30]. Available from: <http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp>.
2. National Institutes of Health Consensus Development Conference statement on cervical cancer. April 1–3, 1996. *Gynecol Oncol* 1997;66:351-61.
[PUBMED](#) | [CROSSREF](#)
3. Hori M, Matsuda T, Shibata A, Katanoda K, Sobue T, Nishimoto H, et al. Cancer incidence and incidence rates in Japan in 2009: a study of 32 population-based cancer registries for the Monitoring of Cancer Incidence in Japan (MCIJ) project. *Jpn J Clin Oncol* 2015;45:884-91.
[PUBMED](#) | [CROSSREF](#)
4. National Cancer Center. National database of hospital-based cancer registries: 5 year survival report 2008 [Internet]. Tokyo: National Cancer Center; 2017 Aug [cited 2018 Jul 2]. Available from: https://ganjoho.jp/data/reg_stat/statistics/brochure/hosp_c_reg_surv_2008.pdf.

5. Yamagami W, Nagase S, Takahashi F, Ino K, Hachisuga T, Aoki D, et al. Clinical statistics of gynecologic cancers in Japan. *J Gynecol Oncol* 2017;28:e32.
[PUBMED](#) | [CROSSREF](#)
6. Fujikawa K, Miyamoto T, Ihara Y, Matsui Y, Takeuchi H. High incidence of severe urologic complications following radiotherapy for cervical cancer in Japanese women. *Gynecol Oncol* 2001;80:21-3.
[PUBMED](#) | [CROSSREF](#)
7. Mabuchi S, Okazawa M, Isohashi F, Matsuo K, Ohta Y, Suzuki O, et al. Radical hysterectomy with adjuvant radiotherapy versus definitive radiotherapy alone for FIGO stage IIB cervical cancer. *Gynecol Oncol* 2011;123:241-7.
[PUBMED](#) | [CROSSREF](#)
8. Institute of Medicine Committee on Quality of Health Care in America. *Crossing the quality chasm: a new health system for the 21st century*. Washington, D.C.: National Academies Press (US); 2001.
9. Ministry of Health, Labour and Welfare. Overview of the “Cancer Control Act” [Internet]. Tokyo: Ministry of Health, Labour and Welfare; 2012 [cited 2017 Jun 20]. Available from: <http://www.mhlw.go.jp/english/wp/wp-hw3/dl/2-077.pdf>; http://www.mhlw.go.jp/bunya/kenkou/dl/gan_keikaku02.pdf.
10. Nagase S, Inoue Y, Umesaki N, Aoki D, Ueda M, Sakamoto H, et al. Evidence-based guidelines for treatment of cervical cancer in Japan: Japan Society of Gynecologic Oncology (JSGO) 2007 edition. *Int J Clin Oncol* 2010;15:117-24.
[PUBMED](#) | [CROSSREF](#)
11. Ebina Y, Yaegashi N, Katabuchi H, Nagase S, Udagawa Y, Hachisuga T, et al. Japan Society of Gynecologic Oncology guidelines 2011 for the treatment of uterine cervical cancer. *Int J Clin Oncol* 2015;20:240-8.
[PUBMED](#) | [CROSSREF](#)
12. Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lázaro P, et al. The RAND/UCLA appropriateness method user's manual [Internet]. Santa Monica, CA: RAND; 2001 [cited 2017 Jun 20]. Available from: https://www.rand.org/pubs/monograph_reports/MR1269.html.
13. Higashi T, Nakamura F, Shibata A, Emori Y, Nishimoto H. The national database of hospital-based cancer registries: a nationwide infrastructure to support evidence-based cancer care and cancer control policy in Japan. *Jpn J Clin Oncol* 2014;44:2-8.
[PUBMED](#) | [CROSSREF](#)
14. Iwamoto M, Nakamura F, Higashi T. Monitoring and evaluating the quality of cancer care in Japan using administrative claims data. *Cancer Sci* 2016;107:68-75.
[PUBMED](#) | [CROSSREF](#)
15. Trimble EL, Harlan LC, Gius D, Stevens J, Schwartz SM. Patterns of care for women with cervical cancer in the United States. *Cancer* 2008;113:743-9.
[PUBMED](#) | [CROSSREF](#)
16. Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL 3rd, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med* 1999;340:1154-61.
[PUBMED](#) | [CROSSREF](#)
17. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* 1999;340:1137-43.
[PUBMED](#) | [CROSSREF](#)
18. Ryu SY, Lee WM, Kim K, Park SI, Kim BJ, Kim MH, et al. Randomized clinical trial of weekly vs. triweekly cisplatin-based chemotherapy concurrent with radiotherapy in the treatment of locally advanced cervical cancer. *Int J Radiat Oncol Biol Phys* 2011;81:e577-81.
[PUBMED](#) | [CROSSREF](#)
19. Carlson JA, Rusthoven C, DeWitt PE, Davidson SA, Schefter TE, Fisher CM. Are we appropriately selecting therapy for patients with cervical cancer? Longitudinal patterns-of-care analysis for stage IB–IIB cervical cancer. *Int J Radiat Oncol Biol Phys* 2014;90:786-93.
[PUBMED](#) | [CROSSREF](#)
20. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (cervical cancer) [Internet]. Fort Washington, PA: National Comprehensive Cancer Network; [cited 2017 Jun 30]. Available from: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
21. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler WC Jr, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB–IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. *J Clin Oncol* 1999;17:1339-48.
[PUBMED](#) | [CROSSREF](#)

22. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999;340:1144-53.
[PUBMED](#) | [CROSSREF](#)
23. Japan Society of Obstetrics and Gynecology. The annual report of cervical cancer patients 2008 [Internet]. Tokyo: Japan Society of Obstetrics and Gynecology; 2008 [cited 2017 Jun 30]. Available from: http://plaza.umin.ac.jp/~jsog-go/kanja_2008.pdf.
24. Ikeda Y, Furusawa A, Kitagawa R, Tokinaga A, Ito F, Ukita M, et al. Practice patterns of adjuvant therapy for intermediate/high recurrence risk cervical cancer patients in Japan. *J Gynecol Oncol* 2016;27:e29.
[PUBMED](#) | [CROSSREF](#)
25. Matsuo K, Shimada M, Aoki Y, Sakamoto M, Takeshima N, Fujiwara H, et al. Comparison of adjuvant therapy for node-positive clinical stage IB–IIB cervical cancer: Systemic chemotherapy versus pelvic irradiation. *Int J Cancer* 2017;141:1042-51.
[PUBMED](#) | [CROSSREF](#)
26. Toita T, Kodaira T, Shinoda A, Uno T, Akino Y, Mitsumori M, et al. Patterns of radiotherapy practice for patients with cervical cancer (1999–2001): patterns of care study in Japan. *Int J Radiat Oncol Biol Phys* 2008;70:788-94.
[PUBMED](#) | [CROSSREF](#)
27. Bristow RE, Chang J, Ziogas A, Anton-Culver H. Adherence to treatment guidelines for ovarian cancer as a measure of quality care. *Obstet Gynecol* 2013;121:1226-34.
[PUBMED](#) | [CROSSREF](#)