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Practice Guideline

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Japan Society of Gynecologic Oncology 2022 guidelines for uterine cervical neoplasm treatment

Manabu Seino,[1] **Satoru Nagase**,[1] **Hideki Tokunaga**,[2] **Wataru Yamagami**,[3] **Yoichi Kobayashi**,[4] **Tsutomu Tabata**,[5] **Masanori Kaneuchi**,[6] **Yasuyuki Hirashima**,[7] **Hitoshi Niikura**,[8] **Kiyoshi Yoshino**,[9] **Kazuhiro Takehara**,[10] **Tsukasa Baba**,[11] **Hidetaka Katabuchi**,[12] **Mikio Mikami**[13]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Yamagata University, Yamagata, Japan
[2]Department of Gynecology and Obstetrics, Tohoku University Graduate School of Medicine, Sendai, Japan
[3]Department of Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan
[4]Department of Obstetrics and Gynecology, Kyorin University, Faculty of Medicine, Tokyo, Japan
[5]Department of Obstetrics and Gynecology, Tokyo Women's Medical University, Tokyo, Japan
[6]Department of Obstetrics and Gynecology, Otaru General Hospital, Hokkaido, Japan
[7]Department of Gynecologic Oncology, Shizuoka Cancer Center, Shizuoka, Japan
[8]Department of Obstetrics and Gynecology, National Hospital Organization Sendai Medical Center, Sendai, Japan
[9]Department of Obstetrics and Gynecology, University of Occupational and Environmental Health, Kitakyushu, Japan
[10]Department of Gynecologic Oncology, National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan
[11]Department of Obstetrics and Gynecology, Iwate Medical University School of Medicine, Shiwa, Japan
[12]Department of Obstetrics and Gynecology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan
[13]Department of Obstetrics and Gynecology, Tokai University, Kanagawa, Japan

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Correspondence to
Manabu Seino
Department of Obstetrics and Gynecology, Faculty of Medicine, Yamagata University, 1 Chome-4-12 Kojirakawamachi, Yamagata 990-0021, Japan.
Email: m-seino@med.id.yamagata-u.ac.jp

ORCID iDs
Manabu Seino
https://orcid.org/0000-0002-7511-5190
Satoru Nagase
https://orcid.org/0000-0001-5212-1128
Hideki Tokunaga
https://orcid.org/0000-0002-1622-3810
Wataru Yamagami
https://orcid.org/0000-0003-3925-6057
Yoichi Kobayashi
https://orcid.org/0000-0002-8474-0625
Tsutomu Tabata
https://orcid.org/0000-0003-0243-8180
Masanori Kaneuchi
https://orcid.org/0000-0002-2479-1164

ABSTRACT

The Japan Society of Gynecologic Oncology (JSGO) Guidelines 2022 for the Treatment of Uterine Cervical Cancer are revised from the 2017 guideline. This guideline aimed to provide standard care for cervical cancer, indicate appropriate current treatment methods for cervical cancer, minimize variances in treatment methods among institutions, improve disease prognosis and treatment safety, reduce the economic and psychosomatic burden of patients by promoting the performance of appropriate treatment, and enhance mutual understanding between patients and healthcare professionals. The guidelines were prepared through the consensus of the JSGO Guideline Committee, based on a careful review of evidence gathered through the literature searches and the medical health insurance system and actual clinical practice situations in Japan. The guidelines comprise seven chapters and 5 algorithms.
The main features of the 2022 revision are as follows: 1) added discussed points at the final consensus meeting; 2) revised the treatment methods based on the International Federation of Gynecology and Obstetrics 2018 staging system; 3) examined minimally invasive surgery based on Laparoscopic Approach to Cervical Cancer trial; 4) added clinical question (CQ) for treatments of rare histological types, gastric type, and small-cell neuroendocrine carcinoma; 5) added CQ for intensity-modulated radiation therapy; 6) added CQ for cancer genomic profiling test; and 7) added CQ for cancer survivorship. Each recommendation is accompanied by a classification of recommendation categories based on the consensus reached by the Guideline Committee members. Here, we present the English version of the JSGO Guidelines 2022 for the Treatment of Uterine Cervical Cancer.

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Yasuyuki Hirashima
https://orcid.org/0000-0003-0269-9313
Hitoshi Niikura
https://orcid.org/0000-0002-2769-3922
Kiyoshi Yoshino
https://orcid.org/0000-0002-5732-5215
Kazuhiro Takehara
https://orcid.org/0000-0001-8808-3338
Tsukasa Baba
https://orcid.org/0000-0003-0066-3747
Hidetaka Katabuchi
https://orcid.org/0000-0002-2403-6134
Mikio Mikami
https://orcid.org/0000-0002-7496-3518

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INTRODUCTION

Cervical cancer is declining in developed countries due to the spread of human papillomavirus (HPV) vaccines [1]. Unfortunately, the spread of HPV vaccines has been delayed in Japan, and the number of patients has not decreased. Many cases of invasive cervical cancer are still diagnosed [2]. In Japan, 10,879 new cases of cervical cancer and 2,887 deaths occurred in 2020 across all ages [3].

The first edition of the Guidelines for Treatment of Uterine Cervical Cancer was published by the Japan Society of Gynecological Oncology (JSGO) in 2007 and was revised in the second edition in 2011 [4]. The second revision incorporated many opinions from radiation oncologists [5]. The third edition in 2017 defined cervical intraepithelial neoplasia (CIN) 3 and adenocarcinoma in situ (AIS) as precancerous lesions and added minimally invasive surgery, fertility-sparing surgery, sentinel lymph nodes navigation surgery, and hormone replacement therapy after treatment [6]. The current fourth revision has had major changes since the International Federation of Gynecology and Obstetrics (FIGO) staging system was revised from FIGO 2008 to FIGO 2018. The new version includes 7 chapters with the following contents and 5 algorithms.

Chapter 1: Overview of the guidelines, recommendation process, and conflict of interest.
Chapter 2: Primary treatment for cervical precancerous lesions and stage IA cervical cancer.
Chapter 3: The initial treatments for stage IB–IV cervical cancer.
Chapter 4: The adjuvant therapy.
Chapter 5: The treatment of residual lesions and recurrent cervical cancer.
Chapter 6: Follow-up after primary treatment.
Chapter 7: The treatment of cervical cancer with pregnancy.

Consensus for each recommendation was achieved by voting of the committee and external evaluation board.

CHAPTER 1. OVERVIEW OF THE GUIDELINES, RECOMMENDATION PROCESS, AND CONFLICT OF INTEREST

1. How to use the guidelines

We describe one criterion for selecting a better treatment method for uterine cervical neoplasms in Japan and show evidence for the suggested approach. This does not limit treatment to that described in the guidelines. The guidelines aim to:

1) Define appropriate treatment for uterine cervical neoplasm
2) Reduce disparities in treatment approaches among institutions
3) Improve treatment safety and patient prognosis
4) Reduce physical, psychological, and economic burdens on patients using appropriate treatment
5) Improve mutual understanding between medical staff and patients

2. Intended audience

These guidelines are meant for healthcare professionals, such as doctors, nurses, and pharmacists, who treat patients with uterine cervical neoplasm. Furthermore, these guidelines aim to assist individuals including patients and their families in comprehending uterine cervical neoplasm.

3. Diseases addressed by these guidelines

Diseases addressed by the guidelines include CIN3, AIS, primary uterine cervical cancer, and their recurrence.

4. Notes on using these guidelines

Therapy is often difficult to administer under the Japanese medical care insurance system. Thus, the guidelines follow the Committee on Clinical Practice Guidelines for Use of Anticancer Agents of the Japan Society of Clinical Oncology (JSCO).

5. Committee members

The making and evaluating of the guidelines' draft involved gynecologic oncologists, medical oncologists, radiologists, pathologists, and palliative care physicians. Furthermore, pharmacists, nurses, patients, and general (male and female) participants have cooperated from the beginning of setting clinical questions (CQs) as a third party. Those external committee members were informed of the contents and revision points of the final version of these guidelines by the chairman and vice chairman and participated in voting for consensus. The patient group Katoreanomori participated as an evaluating committee.

6. Literature retrieval

This revision requested the Japan Medical Library Association (JMLA) to prepare literature search terms for a systematic database search. The specific literature retrieval method was as follows.

1) The Formulation Committee selected an article using keywords related to the CQ, and then the JMLA prepared relevant search terms and conducted a comprehensive literature search. The keywords were changed, and more were added after review by the Formulation Committee and the JMLA if a large number of articles were found. The Formulation Committee examined the retrieved articles and finally identified approximately 20 important articles.
2) Articles in PubMed, the Japan Medical Abstract Society, and the Cochrane Library were covered in the search from January 2016 to December 2020. Articles published before 2014 that were cited in previous guideline editions and are needed for recommendations are used as references. Articles published after January 2021 were separately examined and some were used as references.
3) Literature search items are published on the web (https://jsgo.or.jp/guideline/keigan2022.html).

7. Level of evidence and grade of recommendations

1) We referred to the 2017 Minds Practice Guidelines to determine evidence levels of recommendation grades [7]. Outcomes were set for each CQ. The body of evidence was assessed considering study designs, bias risk, and indirectness of the studies selected for each outcome (**Table S1**).
2) Levels of evidence in these guidelines are determined based on the factors prescribing a body of evidence that differ from the previous "Levels of evidence," which were based on study design, such as "randomized phase III." Level of evidence might be "B

(moderate)," not "A (strong)," depending on the quality of the clinical trial although evidence arises from a randomized phase III trial.
3) The Formulation Committee evaluated recommendation grades considering not only evidence levels, balance between benefits and harms, and patient values and preferences but also the community standards and insurance coverage in Japan (**Table S2**).
4) Systematic reviews and meta-analyses have been performed for each outcome of the three CQs (CQ03, CQ08, and CQ13). A qualitative systematic review in which logic and certainty are inferred from the context was performed for the CQ unable to perform quantitative evaluation (meta-analysis).
5) Recommendations, levels of evidence, and grades of recommendation were determined in the seventh Formulation Committee. Consensus was achieved by voting.
6) The recommendation was reviewed and revised as "grades of recommendation," "levels of evidence," or recommendation itself when the consensus did not reach 75%. Then, we voted again.
7) Opinions and points of discussion for the revoted recommendations or the recommendations with consensus lower than the criteria followed the recommendations. Discussion points at voting are described in revoted CQs.
8) The external committee voted on the recommendations in CQ07–14, CQ20, CQ31–36 and those that achieved the criteria of consensus in the Formulation Committee. Thus, the consensus in these CQs show the sum of votes by both the core and external committee members.

8. Procedure for guideline creation

The Guidelines Formulation Committee and Evaluation Committee were independently established within the Committee for Treatment Guidelines for Cervical Cancer established by the Guidelines Committee of the JSGO to create these guidelines. The Chair of the Guidelines Committee was concurrently the Chair of the Committee for Treatment Guidelines for Cervical Cancer and the Chair of the Guidelines Formulation Committee. Guideline revisions took place from August 2020 to May 2022, after seven meetings of the Guidelines Formulation Committee, a consensus meeting, and a period for public comment.

9. Tips for activation of use and disclosure of information

1) Algorithms were created to boost usefulness for the audience.
2) These guidelines are published as a pamphlet and are shown on the homepages of JSGO, JSCO, and Minds to facilitate widespread use.
3) The results of systematic reviews and meta-analyses in CQ13 have been published in internationally cited journals.

10. Responsibility for treatment

The JSGO bears responsibility for the content and descriptions of these guidelines. However, the final decision to use the guidelines should be made by the individual user. Thus, the responsibility for the treatment outcomes is directly attributed to the person in charge.

11. Monitoring and revision

1) These guidelines are continuously being revised by the Committee for Treatment Guidelines for Cervical Cancer based on medical advances and changes.
2) Evidence that is newly accumulated after the preparation of these guidelines is saved in a database.

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3) Information on clinical problems occurring with the use of these guidelines is being collected.
4) The next version, as a pamphlet, will be published in 2027.
5) Revisions are considered by the Guidelines Formulation Committee and Evaluation Committee based on new evidence and information before publishing the next pamphlet depending on necessity. Opinions from academic societies, groups, and JSGO members are also widely sought.
6) The Committee for Treatment Guidelines for Cervical Cancer will develop a revised version with JSGO approval after these processes.

12. Funding

The preparation of these guidelines was funded only by the JSGO. No assistance was provided by other organizations or companies.

13. Conflicts of interest

1) The Board of the Society Conflict of Interest Committee confirmed the absence of any conflicts of interest. A total of 24 members (12 in the Guidelines Formulation Committee and 12 in the Guidelines Evaluation Committee) in 2019 and 22 members (10 in the Guidelines Formulation Committee and 12 in the Guidelines Evaluation Committee) in 2020 had conflicts of interest due to work or social activity with a company, but none of these conflicts of interest conditions were judged to have exceeded the acceptable range.
2) The contents of these Guidelines are based on the consensus of the Guideline Committee and thus are unaffected by any interest associated with specific groups or products.

14. Summary of recommendations

Each chapter comprises CQs, recommendations, background, objectives, explanations, and references. This article summarizes the guidelines in a question-and-answer format. Recommendations from each chapter are listed under their respective chapter titles below.

15. Algorithms

The guidelines contain the following 5 algorithms:

1) Primary treatment for cervical precancerous lesions (CIN3 and AIS) and stage IA cervical cancer (**Fig. 1**).
2) Primary treatment for stages IB–II cervical cancer (**Fig. 2**).
3) Adjuvant therapy for stages IB–II cervical cancer (**Fig. 3**).
4) Primary treatment for stages III–IV cervical cancer (**Fig. 4**).
5) Therapy for relapsed cervical cancer (**Fig. 5**).

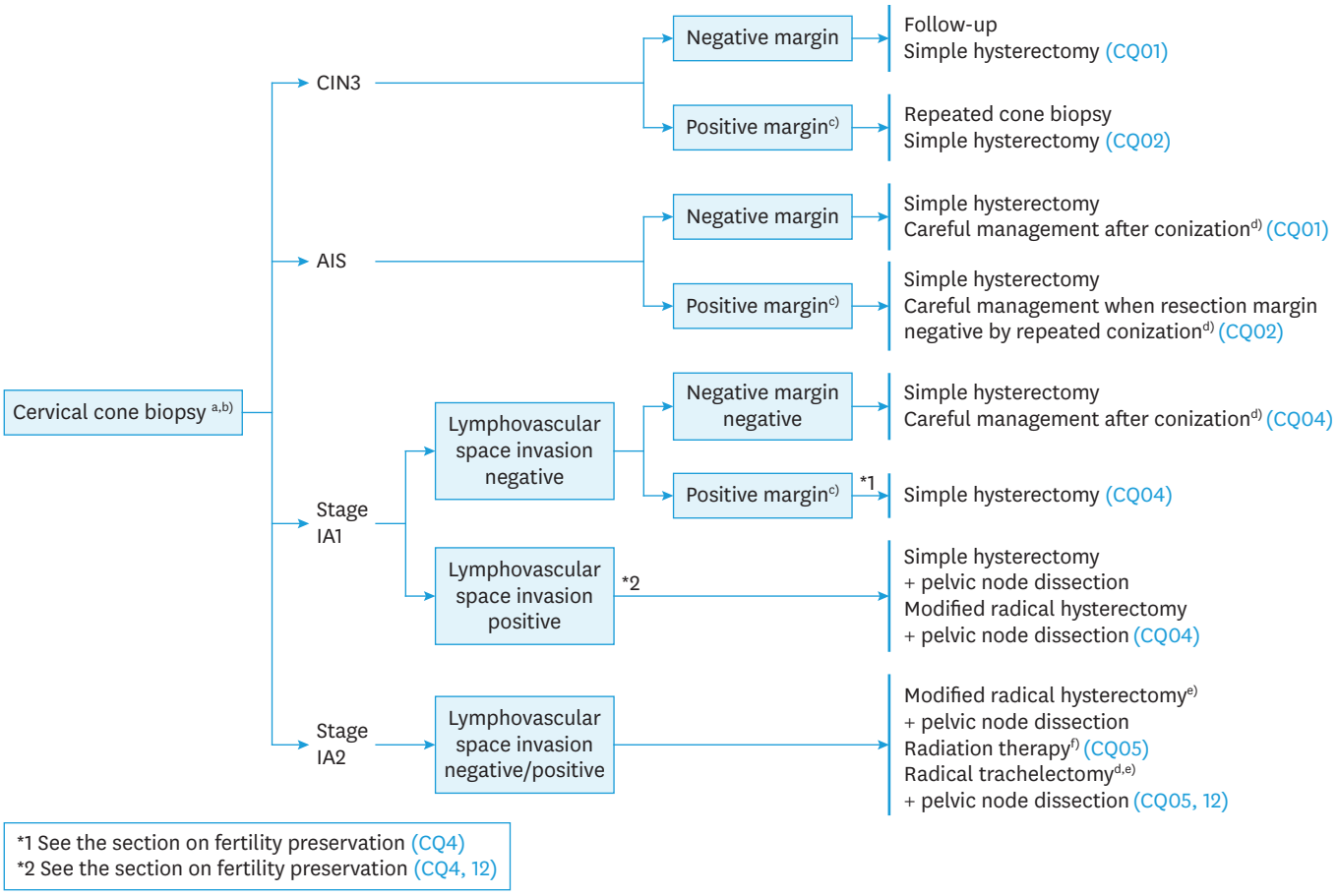

Fig. 1. Flow chart 1: primary treatment for cervical precancerous lesions (CIN3 and adenocarcinoma in situ) and IA cervical cancer. The flow of the treatment is based on a cone biopsy diagnosis.
AIS, adenocarcinoma in situ; CIN, cervical intraepithelial neoplasia; CQ, clinical question.
[a)]The cone biopsy should aim for a diagnosis or a diagnosis and treatment. The patient should be treated as if they have positive margins if cervical curettage is positive. [b)]The flow chart is based on a diagnosis with the resected specimen of the cone biopsy. However, if cone biopsy is difficult because of cervical atrophy, such as in older patients, the omission of cone biopsy may be suggested. However, preoperatively, it is necessary to carefully review the cytology, colposcopy, and biopsy tissue findings; this allows for a hysterectomy suitable for the estimated lesion. [c)]A lesion should be diagnosed as more than CIN3 (squamous lesions) or AIS (glandular lesions) in the case of a positive stump. [d)]This is suggested when the patient strongly wishes to preserve her fertility. Careful inspection is required to preserve fertility. [e)]Operative procedures should be individualized according to the histopathological findings of the cone biopsy specimens, namely the extent of invasion and the presence or absence of lymphovascular space invasion. [f)]Radiation therapy is also an option when surgical treatment is difficult because patients are elderly or with medical complications.

CHAPTER 2. PRIMARY TREATMENT FOR CERVICAL PRECANCEROUS LESIONS AND STAGE IA CERVICAL CANCER

CQ01: Are additional treatments that are recommended for CIN3/AIS diagnosed by cone biopsy?

Recommendations

1. No additional treatment is recommended for CIN3 with negative margin.
   Grade 1 (↑↑); level of evidence: A; consensus: 100%.
2. Simple hysterectomy is recommended for AIS with negative margin.

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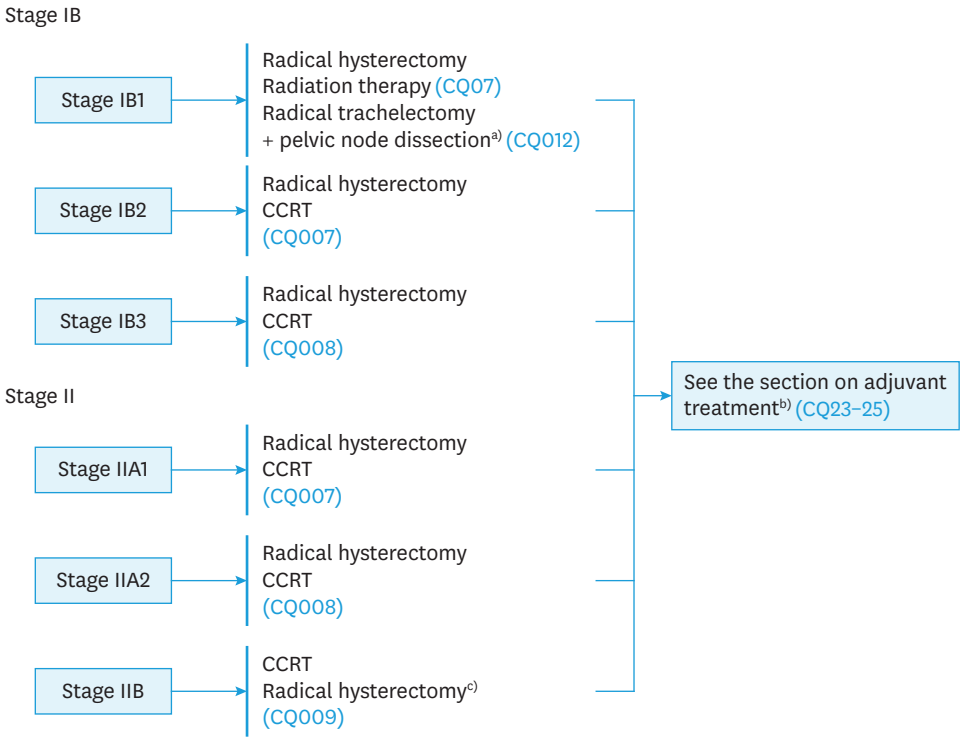

Fig. 2. Flow chart 2: primary treatment for stage IB–II cervical cancer.
CCRT, concurrent chemoradiotherapy; CQ, clinical question.
[a]This is suggested when the patient strongly wishes to preserve her fertility. Residual lesions are reported with negative margin, and careful inspection is required to preserve the uterus. Fertility and perinatal prognosis should also be considered. [b]See the section on CQ26 when the primary treatment is radiation therapy or CCRT. [c]Background and histological type should be considered, and the operator should be carefully selected.

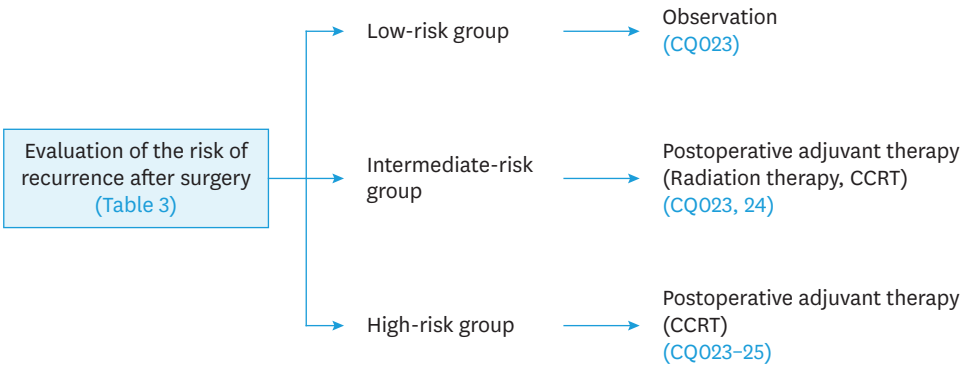

Fig. 3. Flow chart 3: postoperative therapy for stage IB–II cervical cancer. Many discussions and reports exist on risk assessment for postoperative recurrence. Postoperative therapy must be considered according to the individual case.
CCRT, concurrent chemoradiotherapy; CQ, clinical question.

Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

3. Fertility-sparing is suggested for patients with AIS who strongly hope for a baby. However, the margins must be negative, with no residual lesion, and the patients require close management. Fertility-sparing is suggested for patients with AIS with a negative resection margin and who strongly desire fertility preservation; however, careful management is required.
Strength of recommendation: 2 (↑); level of evidence: C; consensus: 94%.

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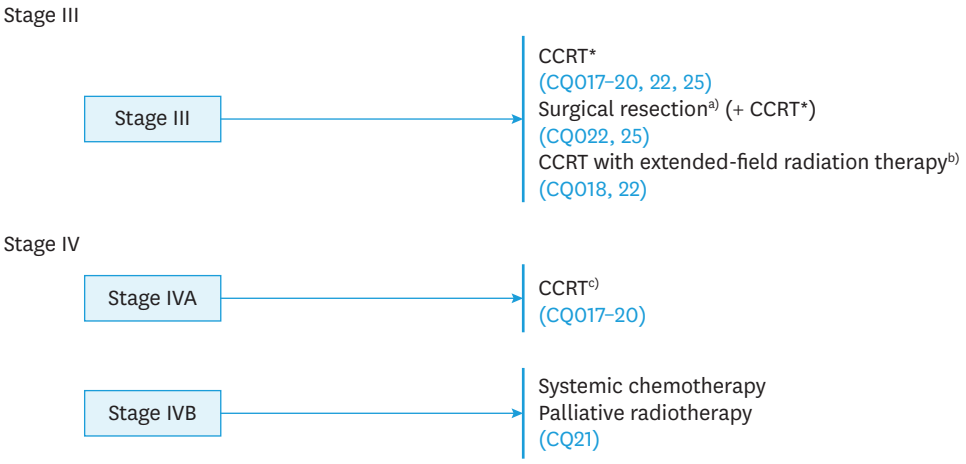

Fig. 4. Flow chart 4: primary treatment for stage III–IV cervical cancer.
CCRT, concurrent chemoradiotherapy; CQ, clinical question.
[a]For stage IIIC1 (T1, 2). [b]For stage IIIC2. [c]Radiation therapy to regional lymph nodes is decided according to stage III.
*Prophylactic irradiation to the para-aortic region is not recommended if only positive pelvic lymph nodes are present.

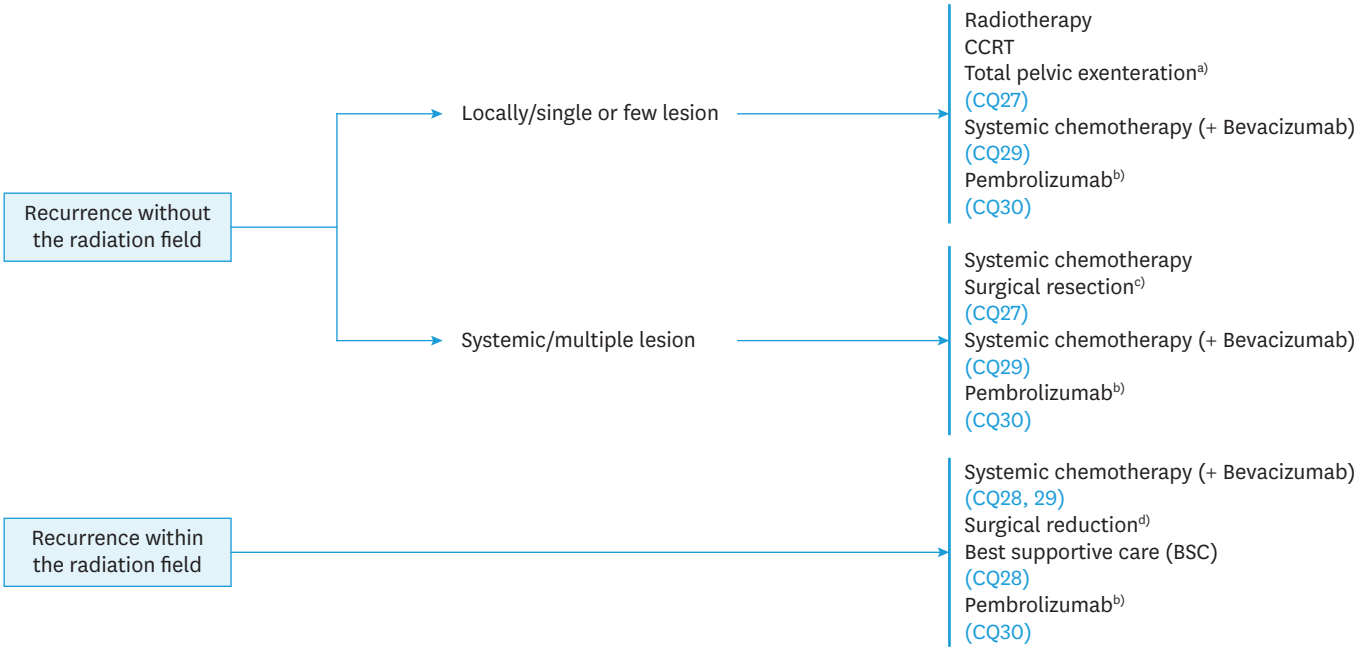

Fig. 5. Flow chart 5: therapy for relapsed cervical cancer.
CCRT, concurrent chemoradiotherapy; CQ, clinical question.
[a]Total pelvic exenteration is indicated in a case that forms vesicovaginal fistula and rectovaginal fistula in the vagina stump center recurrence case, etc. However, careful consideration of indications is required because total pelvic exenteration is associated with a higher incidence of postoperative morbidity. [b]It is necessary to pay attention to the indication. [c]Surgical resection is indicated, for example, if a single or few brain metastases are resectable, and the intracranial lesion is controlled with good performance status. [d]Surgical resection involves local pelvic recurrence, vaginal stump, and central cervical recurrence; however, the same caution as in [a] is required.

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CQ02: Are additional treatments recommended for positive cervical resection margins for CIN3/AIS?

Recommendations

1. Repeated cone biopsy or simple hysterectomy is recommended for CIN3 with positive margin and residual CIN3 lesion.
   Strength of recommendation: 1 (↑↑); level of evidence: A; consensus: 100%.
2. Simple hysterectomy is recommended for patients with positive resection margins for AIS.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
3. Repeated cone biopsy is suggested for patients with AIS with a positive resection margin and who strongly desire fertility preservation. However, strict management is required.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

CQ03: Is repeated cone biopsy recommended for recurrent CIN3 following conservative treatment?

Recommendations

1. Repeated cone biopsy is recommended for patients with recurrent CIN3 who strongly desire fertility preservation.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
2. Simple hysterectomy is suggested for patients with recurrent CIN3 who do not desire fertility preservation when there is no evidence of any invasive disease.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

Discussion points at voting: First, the consensus of recommendation 1 was <75% (63%): "1. Repeated cone biopsy is recommended, level of evidence is B, and strength of recommendation is 1 (↑↑)." A total hysterectomy is often performed when the patient does not wish to preserve fertility in practice, and there is insufficient evidence for re-cone biopsy. Therefore, "who strongly desire fertility preservation" was added to the previous recommendation 1. The revote resulted in 100% consensus.

CQ04: What treatments are recommended for stage IA1 disease?

Recommendations

1. Simple hysterectomy is recommended for patients without lymphovascular space invasion.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
2. In case with lymphovascular space invasion, pelvic lymph node dissection is suggested in addition to simple hysterectomy or modified radical hysterectomy.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
3. Fertility-sparing is suggested for patients who strongly hope for a baby. However, those patients must have no lymphovascular space invasion, negative margin, and no residual lesions with the endocervical curettage specimens.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

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CQ05: Is modified radical hysterectomy with pelvic lymph node dissection recommended for stage IA2 disease?

Recommendation

1. Modified radical hysterectomy with pelvic lymph node dissection is suggested.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 90%.

Discussion points at voting: An opinion was raised on the poor rationale about a modified radical hysterectomy for IA2 disease. A radical hysterectomy for IA2 may become the excessive treatment in the guideline preparation in the process so far although radical hysterectomy was often performed for IA2 in Japan. Conversely, no sufficient evidence proved simple hysterectomy is enough for stage IA2. Therefore, a modified radical hysterectomy is suggested in IA2. An opinion was raised that separating the recommended sentences in the presence or absence of lymphovascular space invasion is better since the previous version of the guidelines suggested omission of pelvic lymphadenectomy in the absence of lymphovascular space invasion, and the consensus did not reach 75% in the first vote (73%). Subsequent discussions suggested that the present FIGO staging system involves previous IB1, uncertainty about the pathologic diagnosis of lymphovascular space invasion and IA2, and there is insufficient evidence that the omission of lymphadenectomy does not affect prognostic. As annotated, the lymphadenectomy is suggested in the absence of vascular invasion, and the above recommendation sentence achieved the consensus of 90% by revoting. Further, the omission of lymphadenectomy for stage IA2 was agreed to be based on sentinel lymph node assessment.

CQ06: Is adjuvant radiation therapy recommended for stage IB and/or advanced disease after a simple hysterectomy?

Recommendation

1. Radiotherapy or concurrent chemoradiotherapy is suggested.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 94%.

CHAPTER 3. THE INITIAL TREATMENTS FOR STAGE IB–IV CERVICAL CANCER

CQ07: Between surgery or radiotherapy, which treatment is recommended for clinical stages IB1–2 and IIA1?

Recommendation

1. The survival rate is not different between radical hysterectomy and concurrent chemoradiotherapy (CCRT); thus, either treatment is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

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CQ08: Between surgery or radiotherapy, which treatment is recommended for clinical stages IB3 and IIA2?

Recommendation

1. The survival rate is not different between radical hysterectomy and CCRT; thus, either treatment is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

CQ09: Between surgery or radiotherapy, which treatment is recommended for clinical stage IIB?

Recommendations

1. CCRT is recommended for stage IIB disease.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 94%.
2. Surgery for stage IIB disease should be performed by a well-trained gynecological oncologist with a certificate.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

CQ10: Is neoadjuvant chemotherapy recommended for clinical stage IB–II diseases?

Recommendation

1. Neoadjuvant chemotherapy is not suggested for clinical stages IB–II before primary surgical resection.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 88%.

Discussion points at voting: The consensus in the first vote was 36%. Although there was a consensus that chemotherapy should not be recommended prior to surgery, there was an opinion that preoperative chemotherapy may be selected depending on clinicopathological factors such as tumor size and histological type, as well as social factors that require waiting time until surgery due to infection or restrictions on the surgical frame. Finally, since the evidence for recommending preoperative chemotherapy was weak, a re-voting was conducted with the above recommendation on the condition that the points should be described in this "Discussion points at voting" section, with a consensus rate of 88%.

CQ11: Is laparoscopic surgery, or robotic-assisted surgery recommended for clinical stages IB–IIA?

Recommendations

1. Minimally invasive surgery with prevention methods of cancer spread is suggested if the tumor diameter is ≤2 cm after sufficiently explaining the treatment results in Japan and other countries, as well as the experience and treatment results of the institution.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 83%.
2. Minimally invasive surgery is not suggested for a tumor size of >4 cm.
   Strength of recommendation: 2 (↓); level of evidence: B; consensus: 89%.

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CQ12: Is radical trachelectomy recommended for patient who strongly desire fertility preservation?

Recommendation

1. Radical trachelectomy is suggested for clinical stages IA2–IB1 as one of the fertility preservation methods.
   Strength of recommendation: 2 (↑); level of evidence: B; consensus: 94%.

CQ13: Is omission of pelvic lymph node dissection recommended when negative for sentinel node by the sentinel lymph node navigation surgery?

Recommendation

1. The omission of systematic lymphadenectomy is suggested when negative for the sentinel node with a well-trained team for sentinel lymph node biopsy collaborated pathologist.
   Strength of recommendation: 2 (↑); level of evidence: B; consensus: 100%.

CQ14: Is ovarian preservation recommended for patients who undergo radical hysterectomy?

Recommendations

1. Ovarian preservation is recommended for adolescents and young adults with squamous cell carcinoma in clinical stage IB2 or less.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
2. Ovarian preservation is suggested after considering age, histological type, stage and other clinical backgrounds in cases other than the recommendation 1.
   Strength of recommendation: 2(↑); level of evidence: C; consensus: 100%.

Discussion points at voting: The consensus for recommendation 2 was 36% when the first voting in the level of evidence B. No evidence supporting ovarian preservation was cited as an opinion, and the revoting as the level of evidence C resulted in a consensus of 100%.

CQ15: Is pelvic and/or para-aortic lymph node biopsy recommended before primary treatment?

Recommendation

1. Pelvic and/or para-aortic lymph node biopsy is suggested before the primary treatment when lymph node metastasis is suspected but cannot be confirmed by diagnostic imaging.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

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CQ16: What treatment is recommended for clinical stages I–II with rare variants?

Recommendations

1. Mainly surgical resection, and/or other treatment options, are suggested for gastric-type mutinous carcinoma.
   Strength of recommendation: 2 (↑); level of evidence: D; consensus: 100%.
2. Bothe of local therapy, i.e., surgical resection or radiotherapy, and systemic chemotherapy are suggested for small-cell neuroendocrine carcinoma.
   Strength of recommendation: 1 (↑↑); level of evidence: C; consensus: 90%.

Discussion points at voting: The consensus for recommendation 2 was 73% when the first voting was in the strength of recommendation 2 (↑). The strength of recommendation changed to 1 (↑↑) and revoted because many review articles reported the efficacy of systemic chemotherapy, resulting in a 90% consensus.

CQ17: Is surgery recommended for clinical stages IIIA, IIIB, IIIC (T3), and IVA?

Recommendation

1. Surgical resection is not suggested for clinical stages IIIA, IIIB, IIIC (T3), and IVA.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 100%.

CQ18: Is CCRT recommended for clinical stages IIIA, IIIB, IIIC (T3), and IVA?

Recommendation

1. CCRT is recommended rather than radiotherapy.
   Strength of recommendation: 1 (↑↑); level of evidence: A; consensus: 100%.

CQ19: What CCRT regimens are recommended for local advanced cervical cancer?

Recommendation

1. Cisplatin alone is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: A; consensus: 100%.

CQ20: Is neoadjuvant or adjuvant chemotherapy recommended for stages III and IVA?

Recommendations

1. Neoadjuvant chemotherapy is not suggested preoperatively or prior to CCRT.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 100%.
2. Adjuvant chemotherapy is not suggested after CCRT.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 94%.

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CQ21: What treatment is recommended for stage IVB disease?

Recommendations

1. Systemic chemotherapy is suggested for patients having activity and adequate organ functions.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
2. Bevacizumab is recommended to add to systemic chemotherapy.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
3. Radiation therapy is suggested for an oligometastatic lesion, if possible, in addition to controlling the primary tumor and regional lymph nodes.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
4. Palliative radiotherapy is recommended for lesions that cause severe symptoms.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

CQ22: What treatment is recommended for stage IIIC (T1 and T2) patients with lymph node metastasis confirmed by imaging or biopsy before the main treatment?

Recommendations

1. CCRT or surgery is suggested for patients with pelvic lymph nodes metastasis.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
2. CCRT with extended-field radiation therapy is suggested for patients with para-aortic lymph nodes metastasis.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 91%.

CHAPTER 4. ADJUVANT THERAPY

CQ23: What adjuvant therapy is recommended for postoperative patients?

Recommendations

1. CCRT is recommended for high-risk groups (**Table S3**).
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 90%.
2. Radiation therapy or CCRT is suggested for the intermediate-risk group considering the number and grade of the risk factors (**Table S3**).
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 90%.

CQ24: Is intensity-modulated radiation therapy (IMRT) recommended for adjuvant whole pelvic radiotherapy?

Recommendation

1. IMRT is suggested for adjuvant whole pelvic radiotherapy with appropriate clinical and medical physical quality assurance.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

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CQ25: Is prophylactic para-aortic irradiation recommended for stage IIIC1 disease?

Recommendations

1. Prophylactic para-aortic irradiation is not suggested for stage IIIC1r.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 100%.
2. Prophylactic para-aortic irradiation is not suggested for stage IIIC1p.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 100%.

CHAPTER 5. THE TREATMENT OF RESIDUAL LESIONS AND RECURRENT CERVICAL CANCER

CQ26: Is additional hysterectomy recommended for whom primary radiation therapy was performed?

Recommendation

1. Additional hysterectomy is not suggested after primary radiotherapy.
   Strength of recommendation: 2 (↓); level of evidence: C; consensus: 100%.

CQ27: Is radiotherapy recommended for recurrence confined to the pelvis if radiotherapy has not been previously performed?

Recommendations

1. Radiotherapy or CCRT is suggested when localized or single to few lesions due to control the lesions.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 91%.
2. Palliative irradiation is recommended for systemic or multiple recurrent lesions.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 91%.

CQ28: What treatments are recommended for recurrence within the previous radiation field?

Recommendations

1. Palliative chemotherapy is suggested due to control the symptom.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
2. Pelvic exenteration or hysterectomy is suggested for central recurrence in the vaginal stump or uterine cervix.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
3. Best supportive care is suggested instead of invasive anticancer therapy.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

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CQ29: Is combination chemotherapy recommended for recurrent disease?

Recommendations

1. Paclitaxel and cisplatin combination therapy is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
2. Conventional paclitaxel and carboplatin combination therapy is recommended for patients administered platinum agents previously or for renal dysfunction.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.
3. Bevacizumab combination therapy is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

Discussion points at voting: The consensus for recommendation 2 was 55% when the first voting in the strength of recommendation of 2 (↑), level of evidence B. Paclitaxel and cisplatin combination therapy rather than paclitaxel and carboplatin combination therapy was agreed to be recommended if paclitaxel and cisplatin combination therapy was available, but there was an opinion that the strength of recommendation 1 was appropriate in the setting described in recommendation 2. Revoting with the above recommendation resulted in a consensus of 100%.

CQ30: Is treatment based on a cancer genome profiling test using a next-generation sequencer recommended for patients with cancer who are expected to complete standard treatment?

Recommendations

1. Cancer genomic profiling test at appropriate timings is suggested as well as treatments based on genomic variants.
   Strength of recommendation: 2 (↑); level of evidence: D; consensus: 90%.
2. Pembrolizumab is suggested with MSI-H and/or TMB-H tumor.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

CHAPTER 6. FOLLOW-UP AFTER PRIMARY TREATMENT

CQ31: Are periodic examinations recommended to detect recurrence after cervical cancer treatment?

Recommendations

1. We recommend periodic surveillance every 3–6 months for 2 years after the end of treatment and every 6–12 months for 5 years thereafter depending on the risk of recurrence.
   Strength of recommendation: 1 (↑↑); level of evidence: C; consensus: 100%.
2. A medical history taking and physical examination should be performed at each visit.
   Strength of recommendation: 1 (↑↑); level of evidence: C; consensus: 100%.
3. Imaging, tumor markers, and cervical/vaginal cytology screening are suggested as needed.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

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CQ32: What points should be kept in mind regarding lifestyle guidance after cervical cancer treatment?

Recommendations

1. Care for complications associated with treatment is recommended.
   Strength of recommendation: 1 (↑↑); level of evidence: C; consensus: 100%.
2. Lifestyle improvements and cancer screenings other than cervical cancer are suggested.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

CQ33: Is hormone replacement therapy recommended after treatment?

Recommendation

1. Hormone replacement therapy is recommended with advantages and disadvantages explanations before proceeding.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

CQ34: What points should be kept in mind when guiding reproductive activity after trachelectomy?

Recommendations

1. Contraception for at least 6 months postoperatively to ensure no recurrence.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.
2. Assisted reproductive technology is suggested considering infertility factors (age, cervical factor, ovarian function, fallopian tube factor, etc.).
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

CHAPTER 7. THE TREATMENT OF CERVICAL CANCER WITH PREGNANCY

CQ35: Is cone-biopsy during pregnancy recommended for patients with CIN3, AIS, or stage IA cancer diagnosed by biopsy during pregnancy?

Recommendations

1. Cone-biopsy during pregnancy is not recommended if CIN3 diagnosed by biopsy is consistent with the cytology and colposcopy findings.
   Strength of recommendation: 1 (↓↓); level of evidence: B; consensus: 100%.
2. Diagnostic cone-biopsy during pregnancy is recommended for AIS diagnosed by biopsy.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 94%.
3. Diagnostic conization during pregnancy is recommended for suspected stage IA.
   Strength of recommendation: 1 (↑↑); level of evidence: B; consensus: 100%.

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CQ36: Is waiting before definitive therapy for patients with stage IB1 or higher disease?

Recommendations

1. Definitive treatment is recommended after the delivery of the fetus if diagnosed at a gestational age where extrauterine survival of the fetus is possible.
   Strength of recommendation: 1 (↑↑); level of evidence: C; consensus: 100%.
2. Waiting before definitive treatment is suggested depending on the patient if diagnosed at the gestational age where extrauterine survival of the fetus is not possible, considering the gestational age, stage and the wishes of the patient and family.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 94%.
3. Terminating the pregnancy as soon as possible and administering definitive treatment are suggested for patients with stage II disease or more advanced disease.
   Strength of recommendation: 2 (↑); level of evidence: C; consensus: 100%.

SUPPLEMENTARY MATERIALS

Table S1

Certainty ratings for outcomes to determine grades of recommendation

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Table S2

Strength of recommendation

Click here to view

Table S3

Classification of risk of postoperative cervical cancer recurrence

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REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7-34.
PUBMED | CROSSREF
2. Simms KT, Hanley SJ, Smith MA, Keane A, Canfell K. Impact of HPV vaccine hesitancy on cervical cancer in Japan: a modelling study. Lancet Public Health 2020;5:e223-34.
PUBMED | CROSSREF
3. Cancer Information Service. National Cancer Center [Internet]. Tsukiji, Tokyo: Cancer Information Service, National Cancer Center; 2022 [cited 2023 Apr 10]. Available from: https://ganjoho.jp/reg_stat/statistics/stat/cancer/17_cervix_uteri.html.
4. 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

5. 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
6. Ebina Y, Mikami M, Nagase S, Tabata T, Kaneuchi M, Tashiro H, et al. Japan Society of Gynecologic Oncology guidelines 2017 for the treatment of uterine cervical cancer. Int J Clin Oncol 2019;24:1-19.
PUBMED | CROSSREF
7. Kojimahara N, Nakayama T, Morizane T, Yamaguchi N, Yoshida M. Minds manual for guideline development 2017. Tokyo: Japan Council for Quality Health Care; 2017.