INTERNATIONAL JOURNAL OF UROLOGY
International Journal of Urology (2020)
doi: 10.1111/iju.14281

Guideline

Clinical Practice Guidelines for Bladder Cancer 2019 update by the Japanese Urological Association: Summary of the revision

Hiroaki Matsumoto,[1,†] Koji Shiraishi,[1,†] Haruhito Azuma,[2] Keiji Inoue,[3] Hirotsugu Uemura,[4] Masatoshi Eto,[5] Chikara Ohyama,[6] Osamu Ogawa,[7] Eiji Kikuchi,[8] Hiroshi Kitamura,[9] Nobuo Shinohara,[10] Satoru Takahashi,[11] Toyonori Tsuzuki,[12] Masayuki Nakagawa,[13] Yoshifumi Narumi,[14] Hiroyuki Nishiyama,[15] Tomonori Habuchi,[16] Shiro Hinotsu,[17] Yasuhisa Fujii,[18] Kiyohide Fujimoto,[19] Hiroyuki Fujimoto,[20] Takashi Mizowaki[21] and Hideyasu Matsuyama[1,‡]

[1]Department of Urology, Graduate School of Medicine, Yamaguchi University, Ube, [2]Department of Urology, Osaka Medical College, Takatsuki, [3]Department of Urology, Kochi Medical School, Kochi University, Kochi, [4]Department of Urology, Faculty of Medicine, Kindai University, Osaka, [5]Department of Urology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, [6]Department of Urology, Hirosaki University Graduate School of Medicine, Hirosaki, [7]Department of Urology, Graduate School of Medicine, Kyoto University, Kyoto, [8]Department of Urology, St. Marianna University, Kawasaki, [9]Department of Urology, Graduate School of Medicine, University of Toyama, Toyama, [10]Department of Urology, Hokkaido University Graduate School of Medicine, Sapporo, [11]Department of Urology, Nihon University Itabashi Hospital, Tokyo, [12]Department of Surgical Pathology, Aichi Medical University Hospital, Nagakute, [13]Department of Urology, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, [14]Faculty of Health Sciences, Kyoto Tachibana University, Kyoto, [15]Department of Urology, Faculty of Medicine, University of Tsukuba, Tsukuba, [16]Department of Urology, Akita University School of Medicine, Akita, [17]Department of Biostatistics and Clinical Epidemiology, Sapporo Medical University, Sapporo, [18]Department of Urology, Tokyo Medical and Dental University, Tokyo, [19]Department of Urology, Nara Medical University, Kashihara, Nara, [20]Department of Urology, National Cancer Center Hospital, Tokyo, and [21]Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Abbreviations & Acronyms
AJCC = American Joint Committee on Cancer
BCG = bacillus Calmette–Guérin
CIS = carcinoma *in situ*
CQ = clinical question
CT = computed tomography
EBM = evidenced-based medicine
GRADE = Grading of Recommendations Assessment, Development and Evaluation
LRC = laparoscopic radical cystectomy
MIBC = muscle-invasive bladder cancer
MINDS = Medical Information Network Distribution Service
MRI = magnetic resonance imaging
NBI = narrow-band imaging
NMIBC = non-muscle-invasive bladder cancer
PDD = photodynamic diagnosis
RARC = robot-assisted radical cystectomy
TUR = transurethral resection
TURBT = transurethral resection of bladder tumor
UC = urothelial carcinoma

Correspondence: Hideyasu Matsuyama M.D., Ph.D., Department of Urology, Graduate School of Medicine, Yamaguchi University, 1-1-1 Minami-Kogushi, Ube, Yamaguchi 755-8505, Japan. Email: hidde@yamaguchi-u.ac.jp

Received 17 March 2020; accepted 8 May 2020.

†Guidelines Office of Clinical Practice Guidelines for Bladder Cancer 2019.
‡Chairman of working group of Clinical Practice Guidelines for Bladder Cancer 2019.

Objectives: Despite just a 4-year interval from the last version (2015) of the Clinical Practice Guidelines for Bladder Cancer, several dramatic paradigm shifts have occurred in the latest clinical practice regarding both the diagnosis and treatment of bladder cancer. Herein, we updated the 2019 version of the Clinical Practice Guidelines for Bladder Cancer under the instruction of the Japanese Urological Association.

Methods: We previously reported in a revision working position paper for Clinical Practice Guidelines for Bladder Cancer 2019 edition and described the methods of revision detail.

Results: The major points of change in the 2019 version are presented and explanations are given as follows: (i) introduction of the new reference assessment system; (ii) modification of the risk classification for non-muscle-invasive bladder cancer; (iii) addition of clinical questions for the new tumor-visible techniques in non-muscle-invasive bladder cancer; (iv) inclusion of minimally invasive surgeries for muscle-invasive bladder cancer and immune checkpoint inhibitors for locally advanced/metastatic muscle-invasive bladder cancer; (v) overview chapter of the histological variant of urothelial cancer and rare cancers of the bladder; and (vi) recommendation of follow up in non-muscle-invasive bladder cancer and muscle-invasive bladder cancer.

Conclusions: Guidelines should be updated based on the current evidence and updates carried out without delay. The hope is that this guidelines will be assessed by many urologists and will be the cornerstone for the next revision.

Key words: bladder cancer, clinical practice guideline, diagnosis, evidenced-based medicine, treatment.

Introduction

The Clinical Practice Guidelines for Bladder Cancer were first published in 2009, and the first revision (2nd edition) was in 2015. This (2019) is the second revision (3rd edition). There

has been a major paradigm shift in the daily clinical practice of urology during the 4 years from the second edition to the present revision. Of note is the emergence of immune checkpoint inhibitors and the rapid dissemination of robot-assisted surgery. In this revision, clinical topics that contributed to the decision to change treatment regimens in response to such a large paradigm shift were selected and included as CQs.

Methods

This revision has been prepared and constructed by preparation committee members, members assisting the preparation committee and members of the external evaluation committee. Details of those processes have been described previously.[1] The basic stance regarding the revision was as follows.

Basic stance regarding the revision

1 The previous style of the guidelines and basic CQs were to be, for the most part, kept as is.
2 A thorough evaluation of literature references and careful selection of CQs with sufficient evidence was to be carried out in accordance with the latest preparation manual to develop guidelines proposed by the MINDS (EBM promotion project) under the Japan Council for Quality Health Care, with the aim of providing references for the preparation of future guidelines in urology departments.
3 Medical practices that are disseminated in everyday clinical practice and CQs that are not backed by evidence were to be incorporated into the general overviews.
4 Rare cancers and follow up were to be added to new chapters.
5 CQs for new diagnostic and therapeutic modalities were to be described with restraint, and due consideration given to conflicts of interest.

Overall structure and CQs

- Bladder cancer treatment algorithm (Fig. 1).

Chapter I. Epidemiology/pathology

- Only includes general overview.

Chapter II. Diagnosis

- General overview
- CQ1: Is technology to visualize the tumor (PDD, NBI) recommended for diagnosing bladder cancer?
- CQ2: Is multiparametric MRI recommended for the local staging of bladder cancer?

Chapter III. Treatment of NMIBC

- General overview
- CQ3: Is a second TUR recommended for NMIBC?
- CQ4: Is PDD or NBI recommended when treating NMIBC?
- CQ5: Is a single immediate instillation of intravesical chemotherapy recommended for low-risk NMIBC?
- CQ6: Is maintenance instillation after a single immediate instillation of intravesical chemotherapy recommended over a single immediate instillation of intravesical chemotherapy only for intermediate-risk NMIBC?
- CQ7: Is BCG maintenance, rather than BCG induction therapy only, recommended for intermediate and high-risk NMIBC?
- CQ8: Is low-dose intravesical BCG therapy recommended for intermediate and high-risk NMIBC?
- CQ9: Is a repeat induction of intravesical BCG therapy recommended for patients with residual disease or intravesical recurrence after initial BCG induction?
- CQ10: Is immediate radical cystectomy recommended for highest-risk patients?

Chapter IV. Treatment of CIS

- CQ11: Is intravesical BCG therapy recommended for CIS in the prostatic urethra?
- CQ12: Is repeat BCG induction recommended for patients with residual CIS after initial BCG induction therapy for CIS?
- CQ13: Is radical cystectomy recommended for patients with recurrent CIS after intravesical BCG therapy?

Chapter V. Treatment of stage II and III bladder cancer

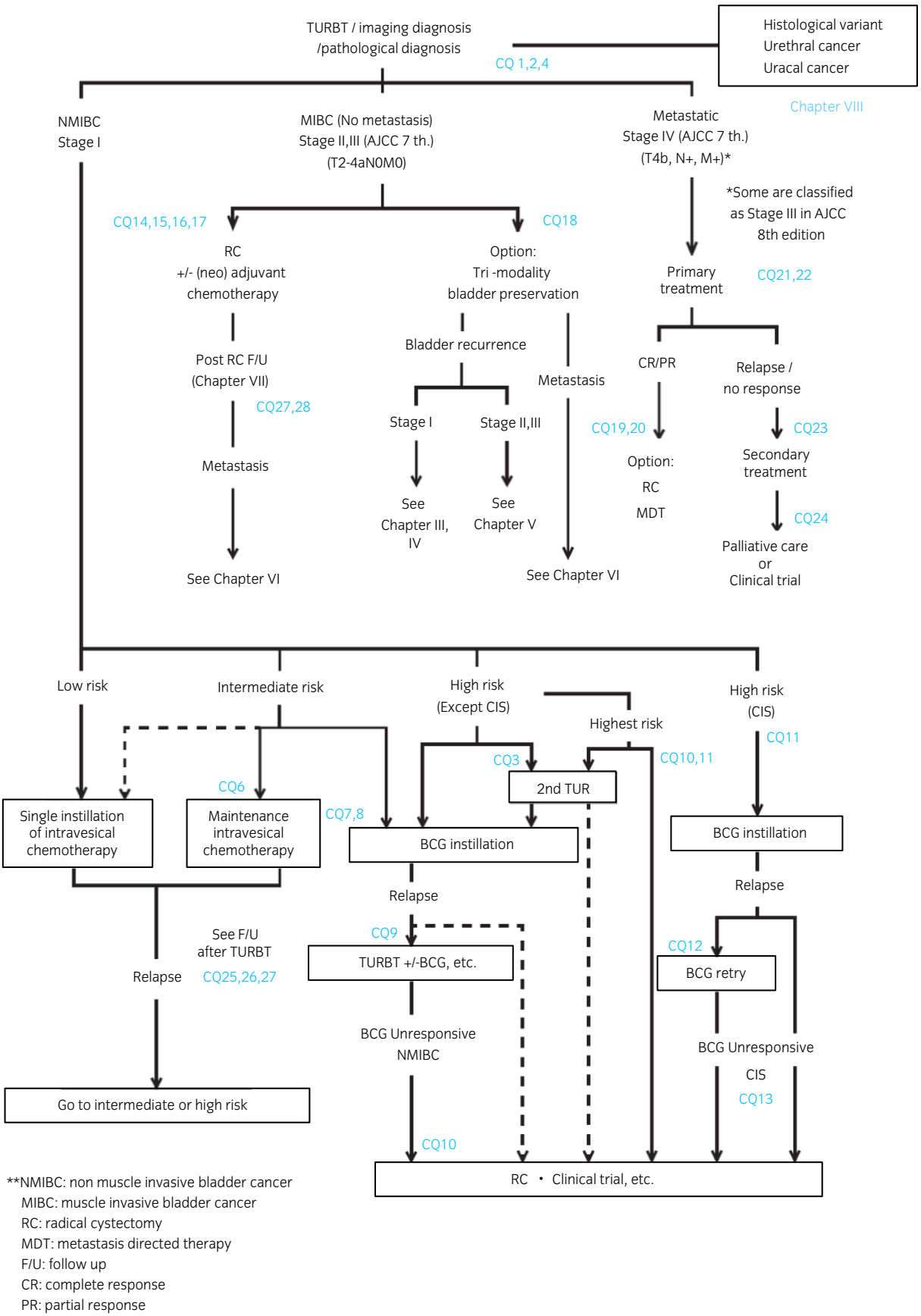
- General overview
- CQ14: Is urethrectomy recommended when carrying out radical cystectomy?
- CQ15: Is nerve-sparing surgery recommended when carrying out radical cystectomy?
- CQ16: Is gynecological organ-sparing surgery recommended when carrying out radical cystectomy in women?
- CQ17: Is laparoscopic/robot-assisted LRC recommended?
- CQ18: Is multimodality bladder-sparing treatment recommended for MIBC?

Chapter VI. Treatment of stage IV bladder cancer

- General overview
- CQ19: Is radical cystectomy recommended for patients with locally progressing disease or pelvic nodal metastases?
- CQ20: Is metastasectomy recommended for bladder cancers with metastases?
- CQ21: Is gemcitabine plus cisplatin therapy recommended as first-line treatment for patients with unresectable or metastatic disease?
- CQ22: Is gemcitabine plus carboplatin therapy recommended for patients with unresectable or metastatic disease and renal dysfunction?
- CQ23: Is the use of immune checkpoint inhibitors recommended for locally advanced or metastatic bladder cancer that has recurred or progressed after first-line chemotherapy?
- CQ24: Is palliative external-beam radiation recommended for locally advanced or metastatic bladder cancer?

Chapter VII. Follow up for bladder cancer

- General overview



**NMIBC: non muscle invasive bladder cancer
MIBC: muscle invasive bladder cancer
RC: radical cystectomy
MDT: metastasis directed therapy
F/U: follow up
CR: complete response
PR: partial response

Fig. 1 Bladder cancer treatment algorithm in Clinical Practice Guidelines for Bladder Cancer 2019.

- CQ25: Is follow up in line with the risk classification recommended for patients with NMIBC?
- CQ26: Is the use of urinary molecular markers and tumor visualization techniques recommended in the follow up of patients with NMIBC?
- CQ27: Is upper urinary tract evaluation recommended in NMIBC, as well as in the follow up after radical cystectomy?
- CQ28: Is follow up in accordance with histopathological findings and risks for recurrence after radical cystectomy recommended?

Chapter VIII. Rare cancers

- General overview of UC variants and rare subtypes
- General overview of urethral cancer
- General overview of urachal cancer

Main changes and corresponding explanations

The main changes in the 2019 edition were as follows:

1 The descriptions for changes with the evaluation method of evidence and methods for assessment of recommendations
2 Inclusion of changes to the risk classification and new techniques to diagnose NMIBC
3 Inclusion of minimally invasive surgery for MIBC and immune checkpoint inhibitors
4 Inclusion of histological variants or subtypes and the addition of new text regarding rare cancers
5 Addition of a new chapter regarding follow up

Results and discussion

Evidence, methods for assessment of recommendations and changes in descriptions

In the field of bladder cancer, the development of diagnostic techniques, new drugs and the widespread use of minimally invasive treatments have been exemplary. Since the previous edition in 2015, a paradigm shift has occurred in clinical practice, and these changes were included in the current 2019 revision.[2] Currently, the recommendations on guideline development push for the use of more transparent and rational methods, such as grading the quality of evidence and the recommendation levels according to the GRADE approaches developed by the GRADE Working Group in 2000, with the goal of overcoming the shortcomings of grading systems in the field of healthcare. Even recently, this GRADE approach has been revised (http://www.gradeworkinggroup.org/; last access date 30 September 2019) accordingly, and many international organizations now view it as a standard for guideline development. In Japan, the preparation manual for the development of clinical practice guidelines was drafted according to GRADE approaches as part of the EBM promotion project, led by MINDS under the Japan Council for Quality Health Care. The guideline for each clinical field since 2017 has become standardized in accordance with the MINDS 2014 preparation manual for clinical practice guidelines[3] and the MINDS 2017 preparation manual for clinical practice guidelines.[4]

Accordingly, the 2019 edition was also drafted in accordance with the MINDS 2014 preparation manual for clinical practice guidelines[3] and the MINDS 2017 preparation manual for clinical practice guidelines.[4] Conventional evidence and methods for evaluating recommendations were reviewed and changes in notation methods were also made. As an example, the actual CQ1 and the corresponding answer is shown in Table 1.

Treatment algorithms were also reviewed, specifically defining the high-risk group as having either pT1 or high-grade UC or concomitant CIS, creating the highest risk group (Fig. 1).

Additionally, as the AJCC Staging Manual's staging system for bladder cancer was updated from the 7th to the 8th edition[5] during this revision, the changes were included in the general overviews, particularly because they might affect the treatment strategy for stage III disease in the future.

Inclusion of changes to the risk classification and new techniques for diagnosing NMIBC

In the treatment of bladder cancer, therapy is roughly divided based on the presence/absence of muscle invasion, CIS and metastases. In the diagnosis of bladder cancer in patients where TURBT is feasible, complete resection of the tumor is attempted, and the tissue resected up to the muscle layer is sent for pathological evaluation.

Patients with NMIBC are divided into low, intermediate, high and highest risk, and prevention of recurrence and progression after TURBT is carried out. Compared with the 2015 risk classification, the intermediate-risk group was reorganized, and the concept of BCG unresponsive disease was introduced into the high-risk group.[6] Additionally, in accordance with overseas guidelines, a highest risk group was added (Tables 2,3).

Tumor visualization techniques

Evidence, such as diagnoses, reductions in residual tumors with TURBT and recurrence-inhibiting effects, clearly led to the recommendations for use of tumor visualization techniques, PDD and NBI. In Japan, oral 5-aminolevulinic acid used as an intraoperative imaging-assisted diagnostic modality (PDD-assisted TURBT, hereinafter PDD-TUR) for NMIBC is covered by public health insurance. A meta-analysis of a number of articles showed improved tumor diagnostic

Table 1 CQ1 and its answer

CQ1	Is technology to visualize the tumor (PDD, NBI) recommended for diagnosing bladder cancer?
Answer	Use of tumor visualization techniques in the diagnosis of bladder cancer is recommended because of improved cancer detection sensitivity (PDD: strength of recommendation 1, certainty of evidence A; NBI: strength of recommendation 1, certainty of evidence B)

Table 2 Risk classification of non-MIBC (cited from Reference [1])

Low-risk group	The group meets all factors: single tumor, initial diagnosis, <3 cm, Ta, low grade, without concurrent CIS
Intermediate-risk group	The group meets other than low and high risk†
High-risk group	The group contains any of the following factors: T1, high grade, CIS (including concurrent CIS)
Highest-risk group	The group is further defined as a highest-risk group that includes the following factors: 1 T1 high grade with any of the following factors • Concomitant bladder CIS or prostatic urethral CIS • Frequent or recurrent or ≥3 cm • Variant histology or LVI 2 BCG-unresponsive NMIBC/CIS

†Those that satisfy all factors; namely, relapses, multiple occurrences, Ta, low grade, ≥3 cm, are classified as high risk in EAU guidelines.

Table 3 Definition of terms related to BCG failure (cited from Reference [1])

Terminology	Definition
BCG failure	Generic term of recurrence cases after BCG intravesical instillation therapy†
BCG refractory	At 3 months after adequate BCG intravesical instillation therapy, recurrence or tumor remains high-grade, tumors that do not disappear at 6 months (including maintenance therapy and including relapse of T1 high-grade cancer within 3 months of the last dose of BCG after BCG induction therapy)
BCG relapsing	After sufficient BCG intravesical instillation therapy, the high-grade tumor recurs after disappearance at 6 months from the last BCG dose: the time to recurrence is divided into subgroups, early: ≤12 months; intermediate: 12–24 months; late: >24 months
BCG unresponsive	Generic term for BCG refractory and BCG-early-relapsing (relapse within 12 months from the last dose of BCG)
BCG intolerant	Repeated recurrence due to serious adverse events and inability to administer sufficient instillation therapy
Adequate BCG intravesical instillation therapy	If any of the following applies 1 BCG induction therapy (six administrations at least five times) and one or more maintenance treatments (three administrations at least twice) 2 When BCG induction therapy (scheduled six times and administered more than five times) and BCG reinduction therapy (scheduled six times and administered more than twice)

†Recurrent events after BCG intravesical instillation might include only those that include either T1, high grade or CIS.

performance (particularly in flat lesions) and decreased tumor recurrence with PDD-TUR compared with TUR under white light,[7] wherein the recommendation level is 1 and the certainty of the evidence is A (CQ1, 4). Conversely, for NBI, there were reports of randomized controlled trials that showed an improvement in tumor diagnostic performance (particularly in flat lesions) compared with white light; however, a reduction in recurrence when TUR was combined with NBI was not observed.[8] The recommendation level for the treatment efficacy is 2 and the certainty of the evidence is B (CQ4). The utility of the DNA fluorescence *in situ* hybridization test, UroVysion (in detecting aneuploidy in chromosomes 3, 7 and 17 of cells in the urine and deletion of the 9p21 locus), and its contribution in detecting early recurrence by complementing the sensitivity and specificity of conventional urine cytology in the follow up of CIS is described in the general overview. However, the approval for UroVysion in Japan stipulates that the test can only be carried out twice in the 2-year postoperative follow-up period for CIS patients.

Evaluation of muscle invasion in bladder cancer using MRI

Traditionally, T stage diagnoses have been carried out mainly using CT and MRI. CT is used mainly for the diagnosis of lymph node and distant metastases because of its wide imaging range; however, the muscle layer and tumor cannot be clearly distinguished, and it is difficult to identify intramuscular invasion. Nevertheless, to assess the risks of muscle invasion in bladder cancer in recent years, the standardization of interpretation and reporting was considered based on size, localization, tumor number and morphology of bladder cancer using multiparametric MRI, and the Vesical Imaging–Reporting and Data System was advocated.[9] With this revision, the introduction of the Vesical Imaging–Reporting and Data System assessment method is expected to inform treatment decisions, particularly for NMIBC, and it is recommended in CQ2 (recommendation level 1, certainty of evidence A).

Intravesical instillation therapy

Low-risk patients receive single immediate intravesical instillation of anthracyclines or mitomycin C to prevent recurrence. Administration of maintenance intravesical chemotherapy in addition to single immediate intravesical instillation of chemotherapy has been recommended for patients with intermediate-risk disease, but no conclusions about the regimen have been reached. In addition, intravesical BCG therapy is administered to intermediate- and high-risk patients (in Japan, only Immunobladder can be used). The addition of maintenance therapy after six to eight courses of intravesical induction therapy is recommended. In CQ8, low-dose BCG therapy for intermediate and high-risk NMIBC is described as recommendation level 2 and certainty of evidence C. However, in revision of 2019, we need to be aware that low-dose BCG therapy could be used as an alternative, particularly for comorbid patients or intermediate-risk patients, not as a routine regimen of BCG therapy. CQ9 also addresses the issue of repeating induction therapy for patients with residual disease or intravesical recurrence after BCG therapy, and recommends considering radical cystectomy for

BCG-unresponsive disease (recommendation level 2, certainty of evidence B).[6] BCG-unresponsive disease is defined as "persistent or recurrent high-grade disease despite adequate intravesical BCG therapy and is a disease for which repeat induction of BCG intravesical therapy is considered ineffective." In particular, these are patients who progress within 3 months after completion of BCG therapy or those with residual disease at 6 months or recurrence within 12 months of experiencing a response. The concept of BCG unresponsive disease is also addressed in the United States Food and Drug Administration's guidance for developing new drugs, and patients falling into this category have very poor outcomes.

In contrast, repeat induction is recommended as an option (recommendation level 2, certainty of evidence C) for patients who respond to BCG therapy and relapse after 1 year (BCG-intermediate/late-relapsing disease).

Inclusion of minimally invasive surgery for MIBC and immune checkpoint inhibitors

Surgical treatment

Radical cystectomy as a curative treatment modality is still the standard therapy for patients with MIBC. In recent years, LRC and RARC have become covered by public health insurance, and are rapidly gaining popularity in Japan as well. In CQ17, the question was set to whether LRC/RARC is recommended. The recommendation was to consider LRC/RARC (recommendation level 2, certainty of evidence B) based on the results of the RAZOR study, wherein RARC was compared with conventional open surgery (open radical cystectomy) and a 2-year non-recurrence rate of 72% was observed for both, showing the non-inferiority of RARC to open radical cystectomy.[10]

Urethrectomy after radical cystectomy has not been addressed in the European Association of Urology or Western guidelines. However, "Is urethrectomy recommended when conducting radical cystectomy?" was included as CQ14 to allow for the consideration of urethrectomy when the creation of a neobladder is not being considered (recommendation level 2, certainty of evidence C) and to explain to the patient the risks if the creation of a neobladder is being considered (recommendation level 1, certainty of evidence C). With regard to the significance of ovarian and uterine preservation at the time of radical cystectomy for women and whether salpingectomy can be carried out, "the recommendation is to consider gynecological organ-sparing surgery if the tumor is T2 or less and there is no tumor in the bladder neck or urethra" (CQ16, recommendation level 2, certainty of evidence C).

Pharmacotherapy for metastatic/locally advanced bladder cancer

Although gemcitabine plus cisplatin therapy is strongly recommended as the first-line treatment for patients with metastatic or unresectable MIBC, there were no established regimens for second-line systemic treatment, and outcomes were unsatisfactory for many years. However, in a randomized controlled trial (KEYNOTE-045) of pembrolizumab versus other chemotherapy drugs in locally advanced or metastatic bladder cancer that recurred or progressed after first-line chemotherapy, the median overall survival was 10.3 months and 7.4 months in the patient groups receiving pembrolizumab and other chemotherapy, respectively. The primary end-point showed superiority in the pembrolizumab-treated group.[11] In CQ23, there was a strong push stating that "pembrolizumab is recommended for bladder cancer that has recurred or progressed after first-line platinum combination chemotherapy or has recurred or metastasized prior to or within 12 months after completion of neoadjuvant or adjuvant platinum combination chemotherapy (recommendation level 1, certainty of evidence A)." However, the efficacy of immune checkpoint inhibitors is limited to their overall response rate (21.1% in intention-to-treat population and 20.0% in Japanese patients[12]), and the absence of effective third-line treatments is an ongoing issue.

Additionally, in select patients, multimodality bladder-sparing treatment that is a combination of TUR plus chemotherapy plus radiotherapy can be considered. In CQ18, the recommendation for multimodality bladder-sparing therapy was "to consider this as a treatment option for select patients" (recommendation level 2, certainty of evidence C). Although patients for whom radical cystectomy is not indicated because of underlying diseases, such as the elderly, those with hepatic/respiratory/cardiac insufficiency or instances wherein the patient does not wish to undergo the procedure, there is a need to decide the treatment after obtaining sufficient informed consent.

Inclusion of histological variants or subtypes and the addition of new text regarding rare cancers

Although most bladder cancers are histopathologically dominated by UCs, it has become clear that histological variants or subtypes (e.g. squamous and glandular differentiation, sarcomatoid type and neuroendocrine tumors) are associated

Table 4 Histopathological classification of UC variants and rare subtypes (cited from Reference [1])

UC variant histology
UC with squamous differentiation
UC with glandular differentiation
Micropapillary
Lymphoid/plasmacytoid
Nested and microcystic
Sarcomatoid variant
Lymphoepithelioma-like
Giant cell
Clear cell
Lipoid rich
Rare subtype (non-UC)
Squamous cell carcinoma
Adenocarcinoma
Neuroendocrine (small cell) carcinoma
Hematopoietic tumors (malignant lymphoma, leukemia)
Soft tissue tumors (leiomyosarcoma, angiosarcoma, etc.)

Table 5 Follow-up strategy for NMIBC†

Low risk	Cystoscopy after 3 months. After that, cystoscopy every 6 months for 2 years. Then every year with cystoscope up to 5 years. After that, by clinical decision
Intermediate risk	Cystoscopy + cytology 3 months later. After that, cystoscopy + cytology every 6 months for 3 years. Thereafter, cystoscopy and cytology every year until 5 years. After that, by clinical decision
High risk	Cystoscopy + cytology every 3 months for 2 years. Cystoscopy + cytology every 6 months for 3–5 years. Cystoscopy + cytology every year until the 10th year. After that, by clinical decision. Urinary molecular markers are considered as appropriate. CT + CT urography every year up to 3 years, thereafter every 2 years for a total of 10 years observation
Upper urinary tract observation	Screening with CT urography at the initial consultation. Thereafter, the low/medium risk is CT urography as appropriate based on clinical judgment. For high risk, observe the CT urography every year for up to 3 years and thereafter every 2 years for a total of ~10 years

†The follow up in this table is a typical follow-up protocol, and it is desirable to make appropriate corrections based on clinical judgment, such as the patient's condition, medical condition, pathological findings and whether or not intravesical instillation therapy has been carried out.

with poor prognoses and evidence is gradually accumulating. Responses to radiation, anticancer drugs and immune checkpoint inhibitors have also been reported to be different from a UC with uniform histology, and have become a clinically relevant factor; thus, new types have been added (Table 4). However, pure squamous cell carcinoma, adenocarcinoma and small cell carcinoma reportedly should be pathologically distinguished from the histological variant. An overview of rare cancers, such as urethral and urachal cancers, was also added. However, evidence to assess CQs for either disease is still lacking; thus, the corresponding sections only include an overview. In general, more aggressive treatment is often used for histological variants compared to pure UC. For example, the actual stage is likely to be more advanced in patients who appear to have NMIBC, and intensive treatment, including immediate radical cystectomy, might be utilized. Neoadjuvant chemotherapy followed by localized treatment (radical cystectomy or radiation therapy) is recommended when small cell carcinoma components are included, as the efficacy of neoadjuvant chemotherapy is observed regardless of stage.

Addition of new chapter regarding follow up

Follow up is one of the points that is already included in global guidelines, but has not been included in the clinical practice guidelines to date. Efficient follow up that ensures metastatic recurrences are not missed and that are in accordance with evidence-based posttreatment follow-up guidelines is critical, and is summarized in terms of NMIBC and MIBC disease (Tables 5,6). Because superficial recurrences are common within 2–3 years after surgery in low- and intermediate-risk NMIBC patients, careful follow up 2–3 years after surgery is recommended, with additional careful imaging of the upper urinary tract carried out for high-risk patients to take into account the risk of progression. Future follow up might be altered with the release of novel therapeutic agents, including immune checkpoint inhibitors. However, metastatic recurrences must be carefully monitored in the MIBC setting. Follow up after radical cystectomy is classified as per: (i) pT2 or less and pN0; and (ii) pT3 or greater or any pT N1–3 disease, according to the risk of progression.

Conclusions

The main changes in the 2019 revision of the Clinical Practice Guidelines for Bladder Cancer were explained. Guidelines should be updated based on the current evidence, and updates carried out without delay. The hope is that this guideline will be assessed by many urologists and will be the cornerstone for the next revision.

Acknowledgments

This guideline was funded by the guideline committee of the Japanese Urological Association and was developed in

Table 6 Follow-up strategy after radical cystectomy for MIBC†,‡

Postoperative years		1 year	2–3 years	4 years	5 years	After 5 years (60 months)
pT2 or less and N0	Blood test CT§, cytology	Every 3 months Post 3, 6, and 12 months	Every 6 months Every 6 months	Every 6 months Every 12 months	Every 6 months Every 12 months	Monitoring cancer recurrence is considered for each case Cytology is used for urinary tract recurrence
pT3 or high or any pT N1–3	Blood test CT§, cytology	Every 3 months	Every 6 months	Every 6 months	Every 6 months	Kidney and upper urinary tract are followed by US and blood test annually Blood test of vitamin B_{12}, metabolic disorder, renal function etc. is recommended annually for a lifetime

†If the bladder is preserved by chemoradiotherapy, basically, it is advisable to follow up after total cystectomy shown in this table, in addition to examining the timetable for high-risk NMIBC follow up shown in Table 5. ‡The follow up in this table is a typical follow-up protocol, and it is desirable to make appropriate corrections based on clinical judgment, such as the patient's condition, medical condition, pathological findings and the presence or absence of perioperative chemotherapy. §It is desirable to carry out CT urography during CT to evaluate the upper urinary tract.

cooperation with the Japanese Society of Radiation Oncology. We also thank the Japan Medical Library Association responsible for literature searches and Igakutosho Shuppan for publication-related support. Following the revision of this guideline, our thanks also go out to each of the individuals who participated in the drafting and the external evaluation committee for performing assessments of the content.

Research collaborators – Nobuyuki Sekita: Department of Radiology, Funabashi Central Hospital; Hiroshi Juri and Yuki Inada: Department of Radiology, Osaka Medical College; Takashige Abe: Department of Urology, Hokkaido University Graduate School of Medicine; Hideo Fukuhara: Department of Urology, Kochi University, Kochi Medical School; Yukio Naya: Department of Urology, Teikyo University Chiba Medical Center; Satoshi Mutoh: Department of Urology, Juntendo University School of Medicine; Shigehisa Kitano: Department of Experimental Therapeutics, National Cancer Center Hospital; Takashi Kobayashi: Department of Urology, Graduate School of Medicine, Kyoto University; Teruo Inamoto: Department of Urology, Osaka Medical College; Makito Miyake: Department of Urology, Nara Medical University; Junichi Inokuchi: Department of Urology, Graduate School of Medical Sciences, Kyushu University; Tetsutaro Hayashi: Department of Urology, Graduate School of Biomedical Sciences, Faculty of Medicine, Hiroshima University; Takahiro Kojima: Department of Urology, Faculty of Medicine, University of Tsukuba; Katsuyoshi Hashine: Department of Urology, Shikoku Cancer Center; Toshiki Kijima: Department of Urology, Tokyo Medical and Dental University; Yoshiyuki Matsui and Tomohiko Hara: Department of Urology, National Cancer Center; Shingo Hatakeyama: Department of Urology, Hirosaki University Graduate School of Medicine; Yoshiaki Yamamoto: Department of Urology, Graduate School of Medicine, Yamaguchi University; Shintaro Narita: Department of Urology, Akita University School of Medicine; Tomoyasu Tsushima: Department of Urology, Okayama Medical Center; Takafumi Miura: Department of Urology and Chief of Palliative Care, Secomedic Hospital; Takeru Shiroiwa: Center for Outcomes Research and Economic Evaluation for Health, National Institute of Public Health.

External evaluation committee members – Mototsugu Oya: Department of Urology, Keio University School of Medicine; Momokazu Gotoh: Department of Urology, Graduate School of Medicine Program in Function Construction Medicine, Nagoya University; Haruki Kume: Department of Urology, Faculty of Medicine, The University of Tokyo; Yasutomo Nasu: Department of Urology, Okayama University Graduate School of Medicine, Dentistry and pharmaceutical Sciences.

Patient representative – Katsuyuki Tsunemune: Chief Officer of General Incorporated Association, Sojin-Kai.

The costs of the development of these guidelines were covered by the business operating expenses of the Japanese Urological Association.

Conflict of interest

This guideline has been prepared for the purpose of social contribution, and the recommendations are purely scientifically based. Although there are potential conflicts of interest through lectures between individual members and companies, and so on, self-reports on conflicts of interest for all members involved in the preparation of this guideline should be submitted to the Japanese Urological Association Conflict of Interest Committee. It was carefully deliberated and determined that there were no material conflicts of interest. The conflicts of interest of each committee member is managed by the Japanese Urological Association and published on the Japanese Urological Association website.

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