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Republication of "Introduction of Recent Clinical Practice Guideline Development and Diagnostic Imaging Guidelines 2021 by the Japan Radiological Society"

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This article is the English translation from the author's previous work［Yasushi Kaji,（2022）. "Introduction of Recent Clinical Practice Guideline Development and Diagnostic Imaging Guidelines 2021 by the Japan Radiological Society" *the Journal of the Tochigi Medical Society*, 52: 63-65.（in Japanese）］. Note that figures 1 and 2 have been added for a better understanding of the content, although they are not in the original paper.

The methodology for developing clinical practice guidelines is evolving. The evaluation of evidence through a systematic review and the Grading of Recommendations Assessment, Development, and Evaluation（GRADE）system has been implemented to provide appropriate recommendations. Detailed methodologies, including conflicts of interest（COIs）management, voting, and third-party evaluation to enhance guideline reliability, are provided by the Medical Information Distribution Service（Minds）. Understanding these guideline development processes is important for physicians using the guidelines. However, no established guideline development methodology exists for diagnostic issues. By reviewing the history of diagnostic imaging guideline development in Japan, diagnosis-specific problems can be clarified. The latest "Diagnostic Imaging Guidelines 2021" covers various medical departments and presents standard imaging methods, background questions（BQs）, clinical questions（CQs）, and future research questions（FQs）. This guideline aims to promote appropriate imaging and decision making, and its dissemination is desirable to contribute to improving patient prognosis.

Keywords: clinical practice guideline, GRADE, Minds, Diagnostic Imaging Guidelines

INTRODUCTION

Clinical practice guidelines are important tools for providing standard medical care. They are not a collection of evidence. Physicians are encouraged to understand how the guidelines are developed and to use them with knowledge of their limitations. In this article, we summarize recent guideline development methods and present the guidelines for *"Diagnostic Imaging Guidelines 2021"* developed by the Japan Radiological Society based on these methods.

This article is the English translation from the author's previous work in Japanese［1］. Note that figures 1 and 2 have been added for a better understanding of the content, although they are not in the original paper.

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1. MINDS AND RECENT CLINICAL PRACTICE GUIDELINE DEVELOPMENT

The Japan Council for Quality Health Care operates the Medical Information Distribution Service (Minds), which is used to promote evidence-based medicine (EBM) [2]. Minds works to support the development of medical practice guidelines, select, and publish evaluations, promote their use, provide information for patients and the public, and support decision-making by patients and healthcare providers.

The definition of clinical practice guidelines has changed over time. According to the most recent "*Minds Practice Guideline Development Manual 2020 ver. 3.0*" [3], clinical practice guidelines are intended to support decision-making by healthcare users and providers on important health issues. It is a document that evaluates the entire body of evidence through a systematic review (SR) and provides recommendations that are considered optimal, taking into account the balance of benefits and harms. In other words, clinical practice guidelines comprise a document that provides recommendations to help patients and providers make decisions.

To create guidelines that meet this definition, the methods have changed. First, to ensure unbiased development, all members of the guideline development committee are required to manage conflicts of interest (COIs), not just those responsible for developing the guidelines. Second, for a pathophysiological condition with multiple treatment options, important clinical issues are identified, with differences in the magnitude and balance of benefits and harms among the options and in which patient outcomes can be expected to be improved by providing recommendations for the options. To this end, elements of PICO or PECO (P: patients, for which patients; I or E: interventions or exposure, for which treatments, exposures, and tests; C: comparisons, controls, compared with no treatment or other methods; O: outcomes, how much the patient's outcome improves) are extracted and discussed. After evaluating the relative importance of the outcomes, the clinical question (CQ) is expressed in the form of a question using the extracted elements. An SR involves synthesizing a collection of research reports (the body of evidence) and evaluating their content. The body of evidence is the basis for answering the CQ. A systematic and exhaustive literature search is conducted, and after evaluating individual papers, all relevant papers are integrated. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system has recently been adopted as a method for evaluating data and making recommendations [4]. Specifically, the risk of bias and the indirectness of PICO are evaluated for individual studies. Inconsistency of results, imprecision of results, and publication bias are evaluated for the compilation of multiple studies. Other factors that increase the certainty of evidence include dose-response gradients, large effect sizes, and plausible residual confounding effects. The strength is determined for each body of evidence. Strengths are divided into four categories: (A) strong: high confidence in the adequacy of the effect estimate to support the recommendation, (B) medium: moderate confidence in the adequacy of the effect estimates to support the recommendation, (C) weak: limited confidence in the adequacy of the effect estimate to support the recommendation, and (D) very weak: little confidence in the adequacy of the effect estimate to support the recommendation. The strength of the evidence, balance of benefits and harms, value to the patient, cost-effectiveness, and clinical applicability are then considered in determining the level of recommendation. Recommendations are divided into two categories: strongly recommended (or not) and limited and weakly recommended (or not). The specific method of determining the recommendation should also be described, and more recently, voting, such as in the Delphi method, has been used, often accompanied by a percentage of agreement.

2. HISTORY OF DIAGNOSTIC IMAGING GUIDELINE DEVELOPMENT IN JAPAN

Around the year 2000, guidelines began to be developed for many medical specialties in Japan. In the beginning, there were no opportunities to learn systematic development methods. The first diag-

nostic imaging guidelines, developed jointly by the Japanese College of Radiology and the Japan Radiological Society in 2003, was not evidence-based because it was extremely difficult to evaluate diagnostic outcomes [5]. In 2001, Fukui *et al*. published "*Procedures for Creating Clinical Practice Guidelines ver. 4.3*," and in 2004, "*A Guide for Creating and Utilizing Clinical Practice Guidelines Based on EBM*" was published based on this document [6]. However, the main focus of these documents was treatment-related CQs, and the level of evidence (quality) was high at Level I for meta-analyses of randomized controlled trials (RCTs). Many articles on diagnostic imaging, which are mainly cross-sectional observational studies, were rated at Level IV. Although diagnostic imaging guidelines were revised in 2007 [7], some of the recommendations for diagnostic imaging did not match the perceived importance in clinical practice.

We investigated methods to appropriately evaluate the level of evidence in diagnostic articles and found that the Oxford Centre for Evidence-Based Medicine (CEBM) proposed a level of evidence for each category, including treatment or prevention, diagnosis, and prognosis. This was used in a major revision of the "*Diagnostic Imaging Guidelines 2013 edition*" [8]. Three years later, the "*Diagnostic Imaging Guidelines 2016*" [9] were published with some revisions and are available on the Minds website. Until then, however, the emphasis was on scientific evidence, and the balance of benefits and harms was left to the judgment of the authors. At that time, the target audience of the guidelines was defined as radiologists who had just obtained their certification as diagnostic radiologists. The aim of these guidelines was to enable them to perform appropriate imaging examinations in areas in which they were not proficient.

The "*Diagnostic Imaging Guidelines 2021*" [10] were developed for physicians from various clinical departments. The GRADE approach described above allows for an evaluation that does not rely solely on the level of evidence in research articles. It uses the strength of evidence in the body of evidence rather than the level of evidence in individual papers. For example, even if there are two RCT articles with high levels of evidence for a CQ, the strength of the evidence is not high if the results are conflicting. Rather, if multiple cross-sectional studies with not-so-high levels of evidence are combined to obtain results that point in the same direction, the results are considered more certain; therefore, cross-sectional studies on diagnostic imaging are also appropriately evaluated.

In the "*Diagnostic Imaging Guidelines 2016*," all PICOs were reviewed in CQ format. [9]. However, CQs with high recommendations are commonly used in clinical practice, and we debated whether it would be meaningful to include them in 2021st edition, but we decided to call them background questions (BQs) to make physicians in each specialty more aware of the importance of basic procedures. CQs are topics that are difficult to decide on in daily clinical practice, and an SR is performed. In cases where there were only a few papers that could withstand evaluation, we introduced current thinking as a future research question (FQ). By dividing the content into these three categories, it became easier to understand its strengths and weaknesses.

3. INTRODUCTION OF DIAGNOSTIC IMAGING GUIDELINES 2021

The "*Diagnostic Imaging Guidelines 2021*" consist of general remarks and specific sections [10]. The general remarks include important content that should be considered by all physicians ordering imaging examinations (Table 1). In each separate section, standard imaging methods are presented at the beginning of the section, followed by BQs, CQs, and FQs. Eleven areas are covered, which are listed in Table 2. In each area, representative diseases are discussed and described, including those for which standard imaging tests have been established but not yet implemented in all institutions, and those for which standard content has not yet been determined.

This section introduces the content of the urologic field, with an example of each area. In these guidelines, neoplastic diseases of the kidneys, renal pelvis, ureters, bladder, prostate, testes, and adrenal glands are mainly discussed. The standard imaging methods describe the optimal timing of dynamic contrast-enhanced CT, the amount of contrast agent injected, and the imaging conditions when a renal

Table 1. Content of general remarks

1. Evidence-Based Imaging Test Selection
2. Developing Diagnostic Imaging Guidelines
3. CT and MRI in the Radiological and Medical Services in Japan
4. Contrast Media Safety Summary of the 2018 Guidelines on the Use of Iodinated Contrast Media in Patients with Kidney Disease
5. Effects of Medical Radiation Exposure in Diagnostic Imaging and of Electromagnetic Fields in MRI
6. The Medical Accident Investigation System and Radiological and Medical Services
7. Views and Procedures for Pediatric Diagnostic Imaging

Table 2. Content of specific sections

1. Neuroradiology
2. Head and Neck
3. Chest
4. Cardiovascular
5. Digestive Organs
6. Obstetrics and Gynecology
7. Uroradiology
8. Breast
9. Musculoskeletal
10. Pediatric
11. Nuclear Medicine and Hematology

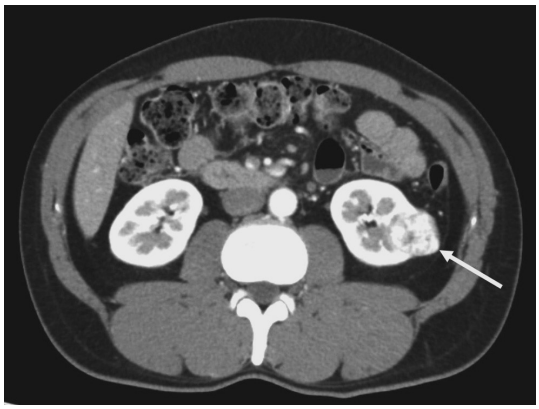
Fig. 1a

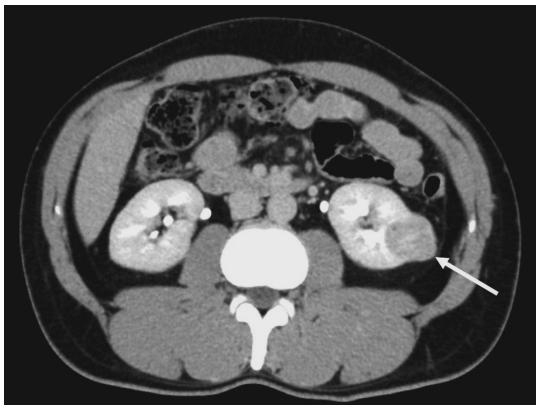
Fig. 1b

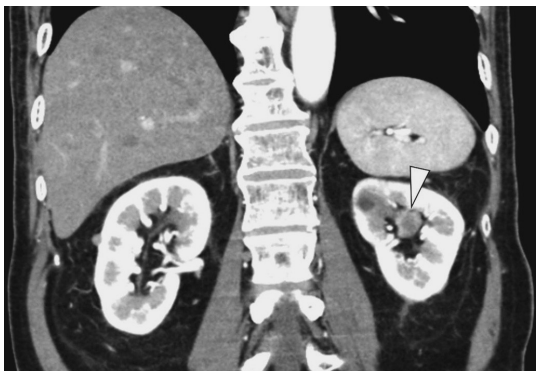
Fig. 1c

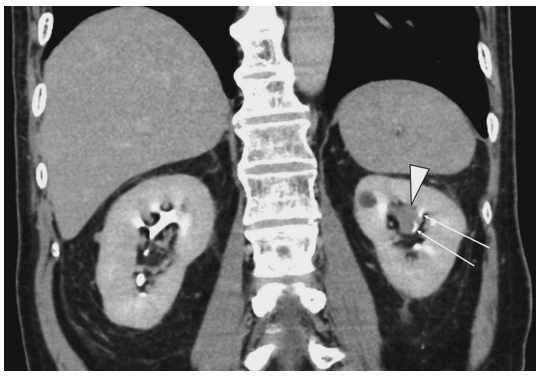
Fig. 1d

Figure 1. Findings of dynamic contrast-enhanced CT in patients with renal cell carcinoma and renal pelvic carcinoma
Renal cell carcinoma is typically enhanced in the corticomedullary phase (a, arrow), showing washout in the renal parenchymal phase (b, arrow). In contrast, renal pelvic carcinoma shows weak enhancement in the corticomedullary phase (c, arrowhead). In the excretory phase (d), urine mixed with contrast (small arrow) can be identified lateral side of the tumor (arrowhead), indicating that the tumor's primary location is in the renal pelvis.

tumor is suspected, as well as details on simplifying these procedures during follow-up. Urologic infectious diseases, such as pyelonephritis, usually do not require imaging, but CT may be performed if the disease is unresponsive to antimicrobial therapy. In addition, the important phase of renal dynamic contrast CT is different when suspecting renal cell carcinoma arising from the renal parenchyma and when suspecting urothelial carcinoma arising from the renal pelvis or ureters (Fig. 1). Detailed imaging techniques are also described for other urologic organs. It is important to emphasize that the appropriate imaging technique depends on what is suspected at the time the examination is ordered. The clinician needs to clarify "what is suspected from the patient's history and examination," confirm that "a positive (or negative) imaging result will significantly alter management," and then order an imaging study with sufficient information. This allows the radiologist or radiologic technologist to select

Table 3. Key questions of uroradiology

BQ 68	Is DMSA scintigraphy recommended to detect renal scarring?
BQ 69	Is contrast-enhanced CT recommended to evaluate solid renal masses?
BQ 70	Which imaging examinations are recommended for staging renal cancer?
BQ 71	Is CT recommended when a urothelial tumor of the upper urinary tract is suspected?
BQ 72	Is MRI recommended to determine the invasion depth of bladder cancer?
BQ 73	Is MRI recommended for the local staging of prostate cancer?
BQ 74	Is bone scintigraphy recommended for prostate cancer staging and post-treatment follow-up?
BQ 75	Which imaging examinations are recommended for staging testicular tumors?
BQ 76	Which imaging examinations are recommended for the posttreatment evaluation of a testicular tumor?
BQ 77	Which imaging examinations are recommended to diagnose adrenal adenomas?
CQ 17	Is omitting contrast-enhanced MRI recommended when MRI is performed to detect clinically significant prostate cancer in patients with incipient disease?
FQ 16	In which cases is MRI recommended to differentiate renal mass lesions?

BQ: background question, CQ: clinical questions, FQ: future research question

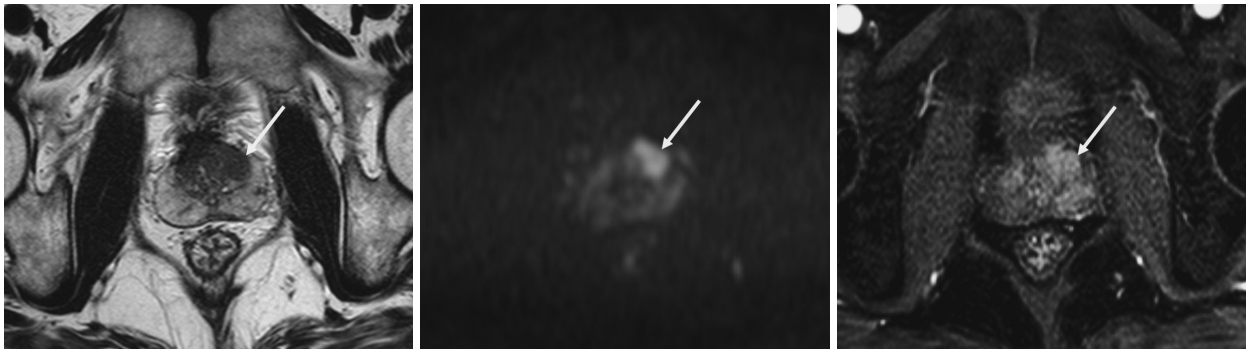

Fig. 2a Fig. 2b Fig. 2c

Figure 2. Typical MRI findings in patients with prostate peripheral zone cancer
Prostate peripheral zone cancer typically presents with low signal intensity on T2-weighted images (a, arrow), high signal intensity on diffusion-weighted images (b, arrow), and early enhancement on dynamic contrast-enhanced MRI (c, arrow). In this case, the combination of T2-weighted and diffusion-weighted imaging findings is highly suggestive of prostate cancer, without contrast-enhanced imaging.

the appropriate imaging method.

Table 3 shows the content of uroradiology with regard to the key questions (BQs, CQs, and FQs) in clinical practice, which comprise the main part of each section. CQ17 is presented as an example. Following the procedure described above, we formulated the CQ: "Is it recommended to omit contrast-enhanced MRI when MRI is performed to detect clinically significant prostate cancer in patients with incipient disease?" The detection of prostate cancer by MRI has been based on the integration of information from T2-weighted images, diffusion-weighted images, and dynamic contrast-enhanced images. Recently, however, it has become known that diffusion-weighted MRI has a higher diagnostic performance, and an increasing number of papers have examined the diagnostic performance of both T2-weighted and diffusion-weighted MRIs, and the results have been favorable (Fig. 2). If there is no significant decrease in diagnostic performance when contrast-enhanced MRI is omitted, the risk of adverse drug reactions from contrast administration, the time and effort required for contrast administration and imaging, and the cost of the contrast agent can all be reduced to zero. With this background, we took up this topic as a CQ, conducted an SR after a literature search, and prepared a recommendation statement in accordance with the procedure. We then discussed whether the recommendation was appropriate or not, and finally decided on the recommendation statement by voting with the participation of review committee members from a

closely related department of urology. As a result, it was concluded that a weak recommendation for CQ would be made if the facility was able to "perform imaging under appropriate conditions using a 3 Tesla MRI system," had "an experienced diagnostician," and could "perform prostate biopsy using appropriate techniques." As a third-party evaluation, the content of all areas, with all BQs, CQs, and FQs described, was sent to the relevant medical societies for their comments. The final manuscript was published in September 2021, after the necessary revisions were made. Currently, not only the Japanese version but also the English version is available to the public, and anyone can access it from the Japan Radiological Society website [11, 12].

CONCLUSION

We have outlined recent methods for creating guidelines for clinical practice and presented the contents of the "*Diagnostic Imaging Guidelines 2021*." When using the guidelines, it is important to understand how they were developed so that they can be used appropriately. Even if guidelines have been developed, if they are not used, patient outcomes will not improve. We urge those who read this paper to spread the word that the "*Diagnostic Imaging Guidelines 2021*" are also available online.

Disclosure of COI

The author has no financial conflicts of interest disclose concerning this review paper.

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