

The essence of the Japan Radiological Society/Japanese College of Radiology Imaging Guideline

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Abstract Diagnostic imaging is undoubtedly important in modern medicine, and final clinical decisions are often made based on it. Fortunately, Japan has the highest numbers of diagnostic imaging instruments, such as CT and MRI devices, and boasts easy access to them as well as a high level of diagnostic accuracy. In consequence, a very large number of imaging examinations are performed, but diagnostic instruments are installed in so many medical facilities that expert management of these examinations

tends to be insufficient. Particularly, in order to avoid risks, clinicians have recently become indifferent to indications of imaging modalities and tend to rely on CT or MRI resulting in increasing the number of imaging examinations in Japan. This is a serious problem from the viewpoints of avoidance of unnecessary exposure and medical economy. Under these circumstances, the Japan Radiological Society and Japanese College of Radiology jointly initiated the preparation of new guidelines for diagnostic imaging. However, the field of diagnostic imaging is extremely wide, and it is impossible to cover all diseases. Therefore, in drafting the guidelines, we selected important diseases and focused on “showing evidence and suggestions in the form of clinical questions (CQs)” concerning clinically encountered questions and “describing routine imaging

The Japan Radiological Society/Japanese College of Radiology Imaging Guideline was published in 2013.

The homepage of the Japan Radiological Society contains information about all CQs of the Japanese Imaging Guideline 2013 as an English version <http://www.radiology.jp/english/guideline.html>.

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techniques presently considered to be standards to guarantee the quality of imaging examinations”. In so doing, we adhered to the basic principles of assuming the readers to be “radiologists specializing in diagnostic imaging”, “simultaneously respecting the global standards and attending to the situation in Japan”, and “making the guidelines consistent with those of other scientific societies related to imaging”. As a result, the guidelines became the largest ever, consisting of 152 CQs, nine areas of imaging techniques, and seven reviews, but no other guidelines in the world summarize problems concerning diagnostic imaging in the form of CQs. In this sense, the guidelines are considered to reflect the abilities of diagnostic radiologists in Japan. The contents of the guidelines are essential knowledge for radiologists, but we believe that they are also of use to general clinicians and clinical radiological technicians. While the number and contents of CQs are still insufficient, and while chapters such as those on imaging in children and emergency imaging need to be supplemented, the guidelines will be serially improved through future revisions. Lastly, we would like to extend our sincere thanks to the 153 members of the drafting committee who authored the guidelines, 12 committee chairpersons who coordinated their efforts, six members of the secretariat, and affiliates of related scientific societies who performed external evaluation.

Keywords CT · MRI · Nuclear medicine · Imaging guideline · Evidence level · MINDS

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1. Evidence levels and recommendation grades

A general appraisal of the level of evidence and grading of recommendations are presented. In addition, the policy of our committee in dealing with problems encountered in the actual process of the guideline development are explained.

Basic principle of evidence ranking schemes and study design of research papers in the field of diagnostic imaging

Generally, the study design is regarded as an important factor in evidence appraisal. Randomized controlled trials (RCT) with blinding are ranked as the best evidence because their research design is the least affected by biases. According to the MINDS (Medical Information Network Distribution Service) Guide for developing Clinical Practice Guidelines 2007 of the Japan Council for Quality Health Care [1], the evidence level is highest for systematic reviews (including meta-analyses) summarizing the results of multiple RCTs, followed by one or more RCT, non-randomized controlled trials, and analytical or epidemiological studies such as cohort studies and case–control studies.

However, the RCT is a rare research design in the field of diagnostic imaging (except for clinical questions on mammographic screening for breast cancer and a few other topics). Cohort studies are also rare. In diagnostic imaging, cross-sectional studies are common since the diagnostic

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Table 1 2011 OCEBM levels of evidence (excerpts of parts related to the diagnosis)

Question	Level 1	Level 2	Level 3	Level 4	Level 5
Is this diagnostic or monitoring test accurate?	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Individual cross-sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards	Case-control studies, or poor or non-independent reference	Mechanism-based reasoning

ability (performance of the examination compared with a reference standard, e.g. sensitivity/specificity) of the modality at the time of the study is considered important. Conventional classifications of evidence were designed for clinical studies of treatment, and papers in the field of diagnostic imaging tended to be underrated due to difference in study design described above. The Oxford EMB Centre (OCEBM) proposed a method to evaluate and classify evidence according to clinical questions [2]. In this classification, evidence is evaluated by classifying clinical questions into different categories such as treatment, diagnosis, and screening. There was also an assessment method specific to diagnostic procedures, which may be applied to papers on diagnostic imaging. While the early version was difficult to use, a recent revised version was based on the concept that “the common research design on diagnosis is the cross-sectional study”, and the assessment method finally became a feasible one. Because of the absence of other relevant classification methods, the present guidelines were developed on the basis of the OCEBM Levels of Evidence.

Practical steps for evidence level appraisal

The classification workflow can be summarized as follows (See Table 1 for details).

- (1) Systematic reviews of level 2 studies are classified as level 1.

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- (2) Among cross-sectional studies, those performed with consecutive sampling, consistent reference standard, and blinding are classified as level 2, which is the highest evidence level for individual studies.
- (3) Among cross-sectional studies, those that cannot be classified as level 2 due to problems in study design (e.g., inconsistency of the reference standard) are classified as level 3.
- (4) Case-control studies are classified as level 4.

The OCEBM Levels of Evidence were introduced primarily to help busy clinicians to appraise evidence quickly. They are not suited for detailed assessment of evidence and may not be appropriate for the development of guidelines. The particular issues raised during guideline development using the OCEBM Level of Evidence, and our solutions are listed below.

- (1) Papers not focusing on imaging findings and those without a reference standard, e.g., those on technical improvements, could not be evaluated.

Many papers directly related to clinical questions used some reference standard, but some papers necessary for the understanding of recommendation grades deal with are technical matters. Such papers were included as references, but were not assigned an evidence level.

- (2) There was no mention about the level appropriate for systematic reviews/meta-analyses that collected multiple level 3 or 4 studies (cross-sectional studies that cannot be classified as level 2 due to inconsistency or ambiguousness of the reference standard or lack of consecutive selection of research subjects).

The evidence level of systematic reviews/meta-analyses, which are based on multiple pieces of evidence, is considered to be higher than that of individual papers, but it is affected by evidence levels of the original papers reviewed. In principle, the lowest evidence level of the papers included in the review was determined, and the level 1 grade higher than the lowest level was given to the systematic review/meta-analysis paper.

- (3) Regarding the research quality, consecutive sampling, consistency of the reference standard, and blinding were included in the evidence table, but other criteria (such as ambiguity of the exclusion criteria) are not mentioned in the table. In this guideline development, priority was given to

consistency of standards for leveling, and the evidence level was not changed, in principle, on the basis of items not included in the evidence table. However, items that were not included in the criteria for evidence leveling, but were considered to important (such as the difference in the research subjects from those mentioned in the CQ) were taken into consideration in the determination of the recommendation grade. (Table 1, * the following footnote is added on the original OCEBM evidence level table; levels may be graded down on the basis of study quality, imprecision, indirectness, because of inconsistency between studies, or because the absolute effect size is very small).

(4) There were several reference standards, and their accuracy varied. For example, the accuracy is considered to differ between pathological diagnoses using surgical samples and those using biopsy samples. If the reference standard varies among reports, how should the results be evaluated? Generally, the diagnostic ability of biopsy is lower than that of surgery. However, the possibility of bias is considered to increase with the lack of consistency of the reference standard. Therefore, in our guideline development, priority was given to the consistency of the reference standard, and the evidence level was not lowered due to the use of biopsy as the only reference standard if it was commonly used.

2. Determination of recommendation grades

The recommendation grades were determined according to the MINDS Guide for developing Clinical Practice Guidelines 2007 mentioned above (Table 2). It considers not only the evidence level, but also the number of studies, variation in conclusion, magnitude of clinical efficacy, clinical applicability (ability of physicians, regional characteristics, medical resources, medical insurance system), and harms and cost. Particularly, in diagnostic imaging, availability of diagnostic instruments were also taken into consideration as medical resources. In addition, factors that were not in the evidence level table, but were considered to affect the quality of evidence [mentioned in (3) of the previous section] were also evaluated in the determination of the recommendation grade.

There are particular situations requiring special consideration. Some examinations that have been used for ages, diagnostic modalities themselves were used as reference standards for the diagnosis, and there have been no study comparing them with surgical/clinical findings, or, if there are such studies, they were performed before the concept of EBM became popular and were of low quality. For example, the evidence concerning the usefulness of CT for the staging of kidney cancer is unexpectedly scarce, but the modality is in wide clinical use and is recommended in overseas guidelines. We decided that CT was considered recommendable and graded as A. Some fields with limited number of evidence, grading was made by members of each subcommittee.

Subjective elements could not be completely excluded, but we aimed to determine recommendation grades appropriate for the current clinical setting in Japan while based on evidence as much as possible.

The above is a summary of the policy of this committee in evidence level appraisal and recommendation grades in developing the present guidelines. The methods to evaluate evidence and to develop guidelines concerning diagnostic imaging may change in the future with changes in the study quality. We selected the methods that were considered to be the most feasible and valid at present.

About MINDS

- MINDS (Medical Information Network Distribution Service) is an information service provided by the Japan Council for Quality Health Care (JCQHC), a public interest incorporated foundation.
- The MINDS project has been financially supported by the Ministry of Health, Labor, and Welfare of Japan since its inception in 2002 through Grants-in-Aid for Scientific Research from 2002 to 2010 and as a consignment project since 2011.
- The aim of the MINDS project is to help medical practitioners to fully use the information related to the evidence-based medicine (EBM) in their practice. MINDS also provides patients and the public with information to help understand the basics of diseases and to share with their practitioners the up-to-date

Table 2 MINDS recommendation grades

Recommendation grade	Description
A	There is firm scientific evidence strongly recommending the procedure
B	There is scientific evidence recommending the procedure
C1	There is no scientific evidence, but the procedure is recommended
C2	There is no scientific evidence, and the procedure is disrecommended
D	There is scientific evidence suggesting ineffectiveness or harm, and the procedure is disrecommended

evidence, on which modern medical practices are based.

- MINDS functions as a guideline clearinghouse; clinical practice guidelines developed in Japan are formally evaluated by the guideline evaluation committee, and only those guidelines which meet with the quality standard are disseminated through the MINDS website.
- Some guideline developers have translated their guidelines into English to share with medical professionals abroad, and on this page, MINDS provides these English-translated clinical practice guidelines developed in Japan.

3. CT and MR systems and the state of their operation in Japan

Comparisons with foreign countries

CT and MRI play important roles in diagnostic imaging. The development of imaging devices and new imaging technology/methods has continued uninterrupted, but an involvement of physicians specializing in diagnostic imaging is necessary to draw out optimal performance and make sufficient clinical use of modalities. In Japan, however, many CT and MR systems are operated in the absence of a radiologist. Moreover, this tendency has shown no improvement for 10 years since the beginning of the survey [3].

In Japan, CT or MR systems are introduced by the judgment of medical organizations, and no political measures have been taken about the arrangement or installment conditions of medical instruments. As a result, the numbers of CT and MR systems per person are markedly higher than in foreign countries, and 60–70 % of them are in operation in the absence of a radiologist. The number of CT or MR examinations in Japan is also high on a global basis. Therefore, it is necessary to ensure the appropriateness of the implementation of imaging studies and reduce negative elements of imaging including radiation exposure.

In this chapter, the state of CT and MRI in Japan is compared with that in foreign countries, and its background is presented.

Comparisons between Japan and foreign countries

Some characteristics of medical imaging in Japan are clarified by comparison of the numbers of operating systems and examinations with those in foreign countries. Although data concerning foreign countries are limited, the OECD Health Data are frequently updated and informative. Although the latest edition is OECD Health Data 2011 [4] the values shown

in the 2009 edition were used because the numbers of both systems and examinations were available. Data not found in the OECD 2011 were supplemented from References [3, 4] concerning Japan, and the latest values shown by the OECD were used concerning foreign countries (four countries) (Table 3).

(1) Number of systems

In Japan, data concerning the number of CT systems are often limited to those about MDCT, but the number per one million people is highest among 27 countries (54.9 vs. a mean of 21.1). Actually, a considerable number of SDCT systems are in operation in Japan. According to the latest survey of medical facilities, the number of SDCT systems was 6360 in 2008, and the total with 6060 MDCT systems was 12,420 [7]. This means there were 97.4 CT systems per one million people, which is about five times the mean of various countries. The number of MR systems per population is the highest among 26 OECD countries (46.8 vs. a mean of 12.4^{*note}).

(2) Number of examinations

Data for the number of examinations are available for smaller number of countries. The number of CT annual examinations per 1000 people in Japan was the 6th among 17 countries (146 vs. a mean of 122), and that of MR examinations was the 4th (68 vs. a mean of 45). Japan belongs to the group with a high number of examinations, but the number is not impressive, considering the very high number of systems (Fig. 1).

(3) Use—number of annual examinations per system

Annual examinations per unit can be considered to be an index of usage. It could be compared among 15 countries. Contrary to the highest number of units, use of CT and MR in Japan was reverse in rank of the number of existing systems. Concerning CT, it was the 3rd from the lowest for MDCT alone (2662 vs. a mean of 6730 examinations/system) and by far the lowest when SDCT was included (1500 examinations/system). Regarding MR, the usage was the second from the lowest (1447 vs. a mean of 4665 examinations/system). For both CT and MR systems, the usage was about 1/3 of the mean of foreign countries and near the bottom.

Details of the situation of CT and MR imaging in Japan

In part 1, gross data regarding CT and MR, which can be compared easily among countries, were evaluated. Here, the state CT and MR imaging in Japan is analyzed into some more detail.

Table 3 Numbers of CT and MR units, examinations, and examinations per unit

	Population (thousands)	Units per million people		Exams/year/1000 people		Exams/year/unit	
		CT	MR	CT	MR	CT	MR
Australia	21,955	38.7	5.9	93.9	23.3	2426	3949
Austria	8363	29.3	18.4	–	–	–	–
Belgium	10,797	–	–	179.3	52.8	–	–
Canada	33,730	13.9	8.0	125.4	43.0	9022	5375
Chile	–	–	–	24.3	1.7	–	–
Czech Republic	10,492	14.1	5.7	87.5	32.3	6206	5667
Denmark	5519	23.7	15.4	83.8	37.7	3536	2448
Estonia	–	14.9	7.5	152.7	37.2	10,248	4960
Finland	5339	20.4	16.9	–	–	–	–
France	62,628	11.1	6.4	138.7	55.2	12,495	8625
Germany	81,904	–	–	–	–	–	–
Greece	11,283	33.8	21.7	–	–	–	–
Hungary	10,023	7.2	2.8	–	–	–	–
Iceland	319	34.5	21.9	156.2	75.5	4528	3447
Ireland	4462	15.3	11.9	–	–	–	–
Israel	–	9.4	1.9	122.8	15.6	13,064	8211
Italy	59,752	31.7	21.6	–	–	–	–
Japan (A)	127,510	54.9	46.8	146.1	67.8	2662	1447
Japan (B)	–	97.4	–	–	–	1500	–
Korea	48,747	37.1	19.0	93.5	13.2	2520	695
Luxembourg	494	26.3	14.2	187.0	73.9	7110	5204
Mexico	107,551	4.3	1.9	–	–	–	–
Netherlands	16,530	11.3	11.0	65.7	43.9	5814	3991
New Zealand	4316	14.6	9.7	–	–	–	–
Norway	4829	–	–	–	–	–	–
Poland	38,153	12.4	3.7	–	–	–	–
Portugal	10,632	–	–	–	–	–	–
Slovak Republic	5418	13.3	6.1	85.4	29.8	6421	4885
Slovenia	–	11.9	4.5	–	–	–	–
Spain	45,929	–	–	–	–	–	–
Sweden	9299	–	–	–	–	–	–
Switzerland	7743	32.8	–	–	–	–	–
Turkey	72,050	11.6	8.9	95.8	67.2	8259	7551
United Kingdom	60,930	7.4	5.6	–	–	–	–
United States	306,656	34.3	25.9	227.9	91.2	6644	3521
Average		21.1	12.4	121.5	44.8	6730	4665

The data concerning foreign countries were cited from the OECD Health Data (primarily the 2009 edition) [4], those concerning the number of systems in Japan from New Med Jpn (2009) [5], and those concerning the number of examinations from the Surveys of Medical Care Activities in Public Health Insurance (2009) [6]. The values in italics are data supplemented from the OECD Health Data before 2009, because the data were not presented in the 2009 edition: Belgium 2008, Denmark 2007, United Kingdom 2008, United States 2007

Also, the data for Japan (A) are the number of MDCT systems alone [5], and those for Japan (B) are the sum of MDCT + SDCT systems (cited from the Survey of Medical Institutions 2008) [7]

The number of CT examinations was also investigated in the Survey of Medical Institutions (static analysis), but the values were 30–40 % higher than those shown by the Surveys of Social, Medical, and Clinical Actions of the same years (2008 and 2011) [10]

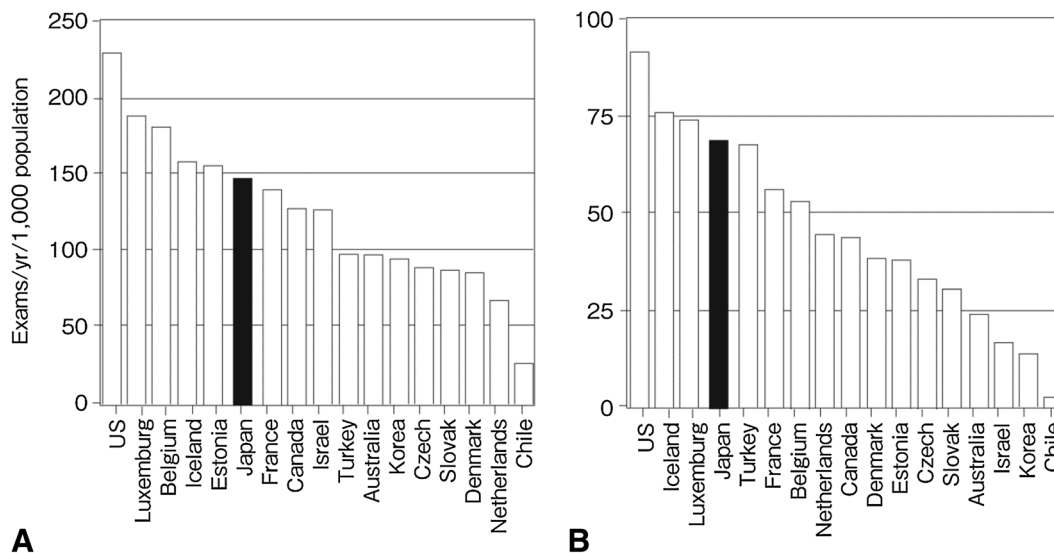


Fig. 1 Comparison of the number of examinations between Japan and foreign countries: CT (a) and MR (b). The annual numbers of examinations per 1000 people are shown. The black bars represent Japan. The mean is 121.5 for CT and 44.8 for MR. In Japan, the

numbers of CT and MR systems are distinctly high, but the number of examinations per unit is among the lowest. The data are primarily those in 2009 (see the text)

(1) Relationships with specialists in diagnostic imaging

The percentage of facilities equipped with CT or MR system with specialists in diagnostic imaging has shown no overall improvement since 2004, when the survey was initiated. Only about one third of the MDCT systems and one third of all MR systems are managed by specialists in diagnostic imaging, i.e., two thirds of the MDCT and MR systems were operating without the regular presence of specialists in diagnostic imaging [3]. In addition, there were wide differences in the percentage of facilities with specialist among machine types (Fig. 2). Images are read by specialists in diagnostic imaging, but the percentage of CT and MR images read is estimated to be 43 % from the number of additions of the reimbursement of medical fees for the management of imaging diagnosis [6]. However, the true figure is considered to be even lower, because while the examinations are included in the DPC, the addition for the management of imaging diagnosis is not.

(2) Number of examinations according to the machine type

The number of scans per system (2010) [6] varied widely. As for CT:

- MDCT with 16 or more detector rows 2799 Exams (56 %)
- MDCT with less than 16 detector rows 1120 Exams (28 %)
- SDCT 675 Exams (17 %)

As for MR:

- ≥ 1.5 T 1961 exams (67 %)
- < 1.5 T 1108 exams (33 %)

Thus, more than half of both CT and MR examinations were performed using high-performance systems. The number of SDCT systems was estimated to be 4383 from the data in 2008 [7], assuming that they have been gradually replaced by more advanced systems.

(3) Annual changes in the number of examinations and medical expenditure

The number of CT and MR examinations continued to increase [8], and about 19 million CT examinations and 10 million MR examinations were performed annually (2010). Since the frequency of imaging examinations increases with the patient’s age, the number of examinations as a whole is expected to increase at least until 2050 in Japan due to aging of the population structure despite a decrease in the total population [9].

In the medical fee reimbursement system, CT and MR are categorized together as computed tomography examinations, and the medical expenditure in this category has continued to increase and topped 500 billion yen, accounting for 60 % of the total expenditure of all diagnostic imaging modalities, in 2010 [6, 8].

Summary

The number of CT and MR systems in Japan is markedly high compared with that in foreign countries, but use is low and near the bottom. Domestically, also:

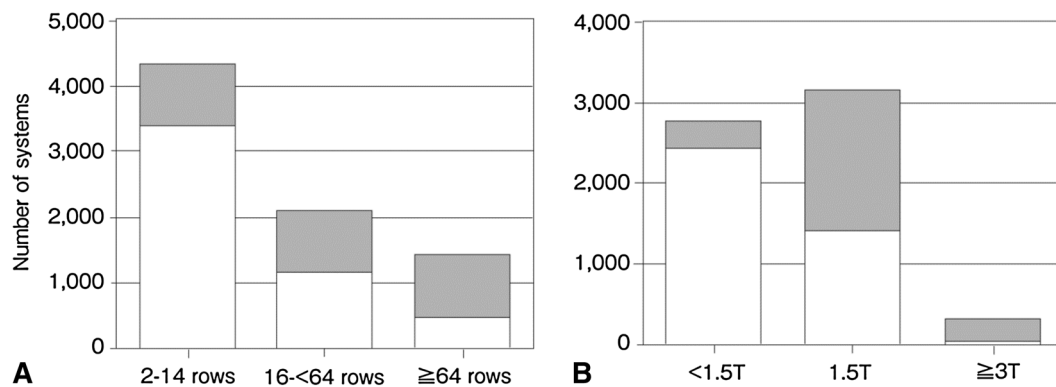


Fig. 2 Facilities with the involvement of full-time radiologist by the types of CT (a) and MR (b) systems. The shaded and white areas are the systems in operation at facilities with and without full-time radiologist, respectively. High percentages of high-performance machines are in operation with an involvement of full-time

- About two thirds of the CT (MDCT) and MR systems are operating in the absence of full-time specialist in diagnostic imaging.
- Only about 40 % of all images are estimated to be evaluated by a specialist at most.
- More than 50 % of examinations are performed using high-performance machines (MDCT with 16 or more detector rows or MR at 1.5 T or higher magnetic field strength).
- Because of the aging population, the number of examinations is expected to increase at least until 2050.

4. Improving medical services in Japan starting with radiological practice

Efficiency of medical services in Japan

When the quality of medical services in Japan is measured by international ranking, I am probably not the only one who is embarrassed by the magnitude of variation of the ranking among items. Medical services in Japan have made remarkable achievements in mean life expectancy and infant mortality rate, which are among the highest in the world. However, Japan ranks near the bottom among advanced countries in the number of physicians engaged in medical services per person (Fig. 3). The medical expenditure in Japan relative to GDP stays at the lowest level among advanced countries (Fig. 4). However, access of people to medical services is generally satisfactory, and, despite some regional differences, patients in urban regions can have access to any department of any medical organization at a low cost. Such superficial achievements are often cited as grounds for justification of the status quo, but favorably evaluating the whole on the basis of selected

radiologist, but only 35 and 36 % of all MDCT and MR systems, respectively, are in operation in the presence of a specialist [3]. A longitudinal survey [3] showed little increase in the involvement of radiologists these 10 years

items with good results permanently denies opportunities to reform weaknesses.

In reality, data that question the efficiency of medical services in Japan are abundant. First, concerning the cost, the number of visits to medical facilities per patient is highest in Japan (Fig. 5), number of beds is highest (Fig. 6), duration of hospital stay is longest (Fig. 7), and percentage of the fee of drug prescriptions in the medical expenditure is in the higher bracket (Fig. 8), among the OECD member countries. Japan ranks by far the highest in the number of CT/MRI systems installed per person (See page 6). In fact, the total number of CT examinations is high, but, as a result, the dose of medical radiation exposure is conspicuously high among the OECD member countries (discussed later). On the other hand, the degree of use of CT/MRI per unit is near the lowest (see the section, “CT and MR systems and the state of their operation in Japan,” page 5). If the total medical expenditure per person in Japan is still relatively low despite such inefficiency, it would be natural to think that it is due to low unit prices of medical services. Regarding medical performance, the ranking of Japan varies widely in mortality rate (per 100,000 people) due to major diseases (malignant neoplasms, cardiac disorders, cerebrovascular disorders) (Fig. 9) or disability-adjusted life year (Fig. 10), which is a measure of overall disease burden to society, according to the disease, and shows no overall excellence compared with foreign countries.

Problems caused by the present state to Japanese society

As observed above, there seem to be inefficient areas in medical services in Japan that need improvement. Then, what effects do such weaknesses exert on medical services in Japan? Regarding the radiological diagnosis and

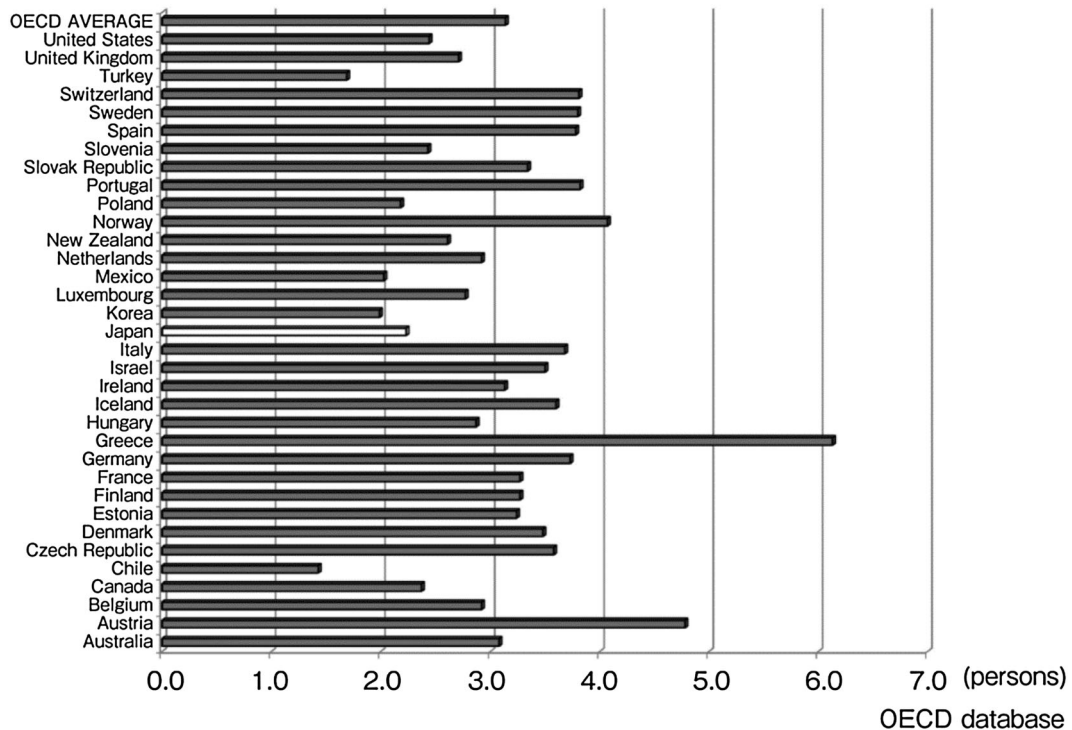


Fig. 3 Number of physicians (per 1000 people, 2010 or latest). The number of physicians is low among the OECD member countries

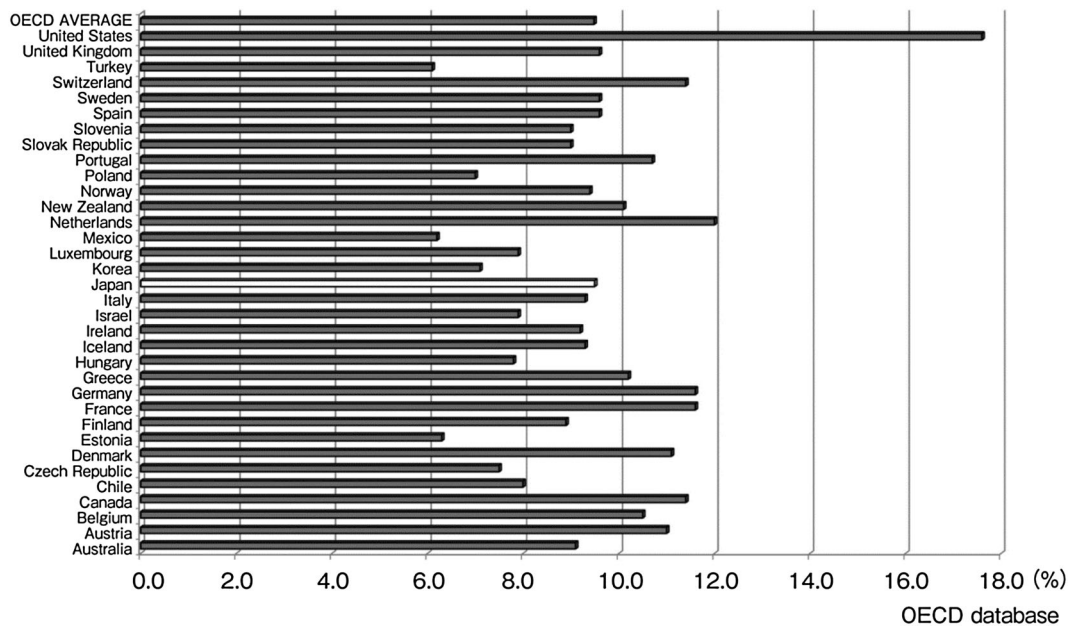


Fig. 4 Medical expenditure (relative to GDP, 2010 or latest). The medical expenditure is low among developed countries but near the average among the OECD member countries

treatment, this question boils down to an increase in medical radiation exposure, delay of implementation of necessary examinations, and deterioration of the clinical skill of physicians in various clinical departments. Because of the good access to medical services, outpatient clinics of

medical organizations (particularly, those of middle-sized or large hospitals) are always crowded above the capacity of physicians assigned to outpatient care, allowing the mocking phrase, “waiting for 2 h, treated in 5 min”. This may be partly due to the patients’ preference for large

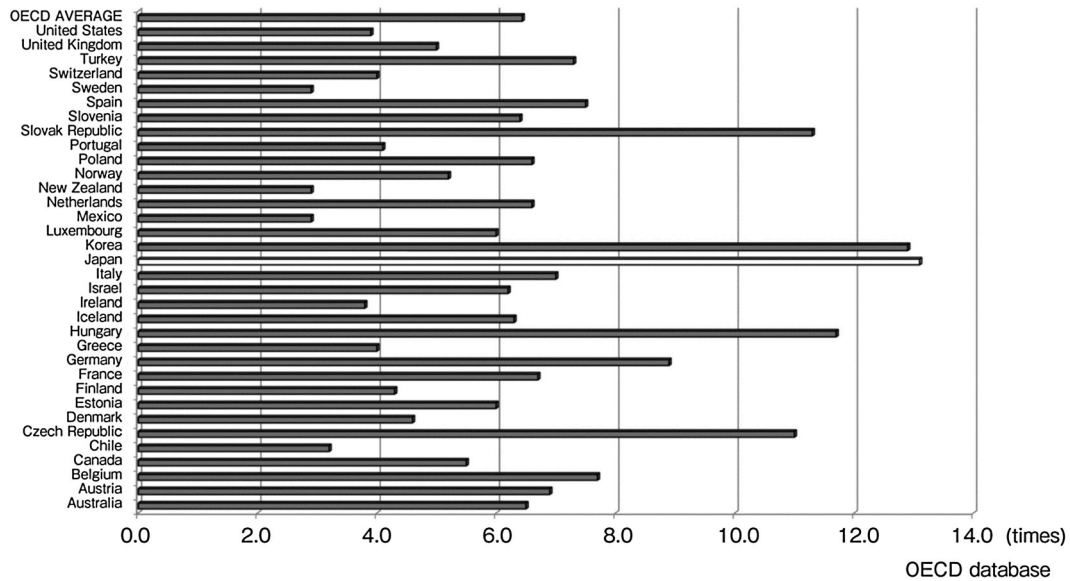


Fig. 5 Number of outpatient visits (per person, 2010 or latest). The number of outpatient visits in Japan is at the highest level

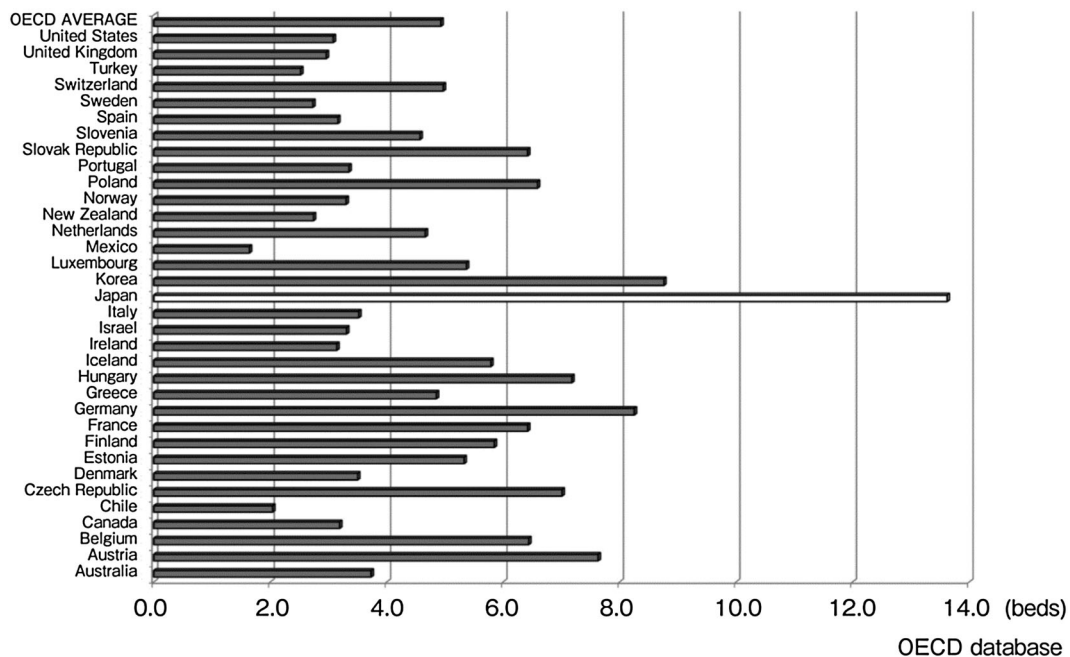


Fig. 6 Number of beds (relative GDP, 2010 or latest). The number of beds in Japan is by far the highest

hospitals, but I would venture to say, taking the risk of misunderstanding, that the low cost of each visit is a cause of the high frequency of patient consultations (i.e., high patient-regulated demand). As a result, in hospital outpatient clinics, each physician must examine 50 or more patients until evening without even taking lunch. An outpatient physician is required to reach some conclusion about the diagnosis and treatment within 10 min for each patient on the initial visit. The physician makes a medical

interview, performs physical examinations, determines an examination plan, explains the plan to the patient, obtains consent, explains the results to the patient coming back after the examinations, shows possible diagnoses, explains the treatments, obtains consent, and performs them, all within 10 min. The fact that medical actions are performed in Japan in such a short time can never be understood by physicians in Western countries. If the situation is explained to them, they would reply that it is impossible to

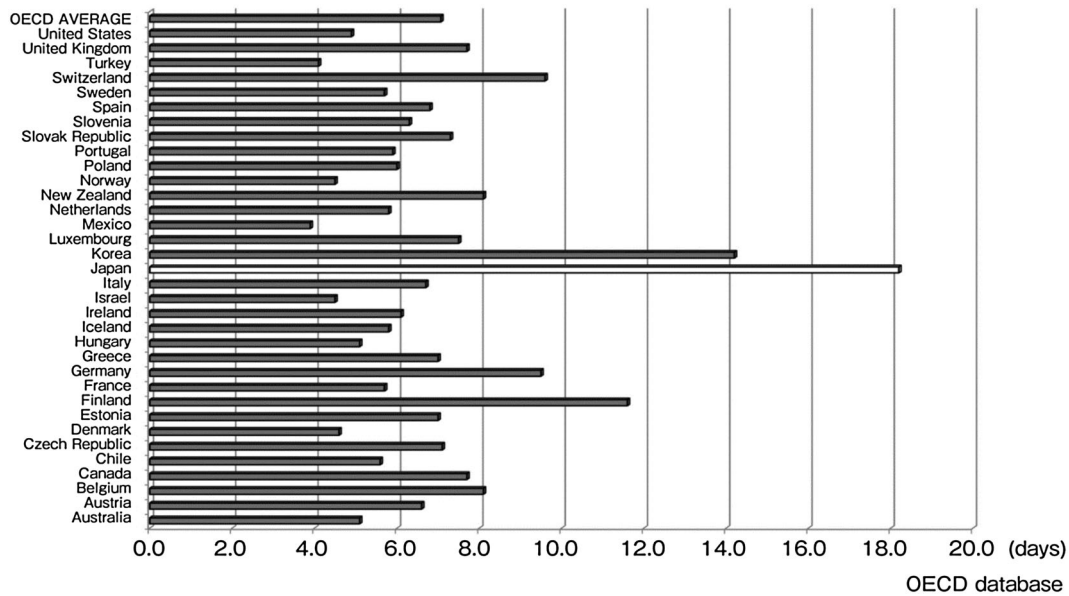


Fig. 7 Mean duration of hospital stay (due to all diseases, 2010 or latest). The mean duration of hospital stay is long and at the top level among the OECD member countries

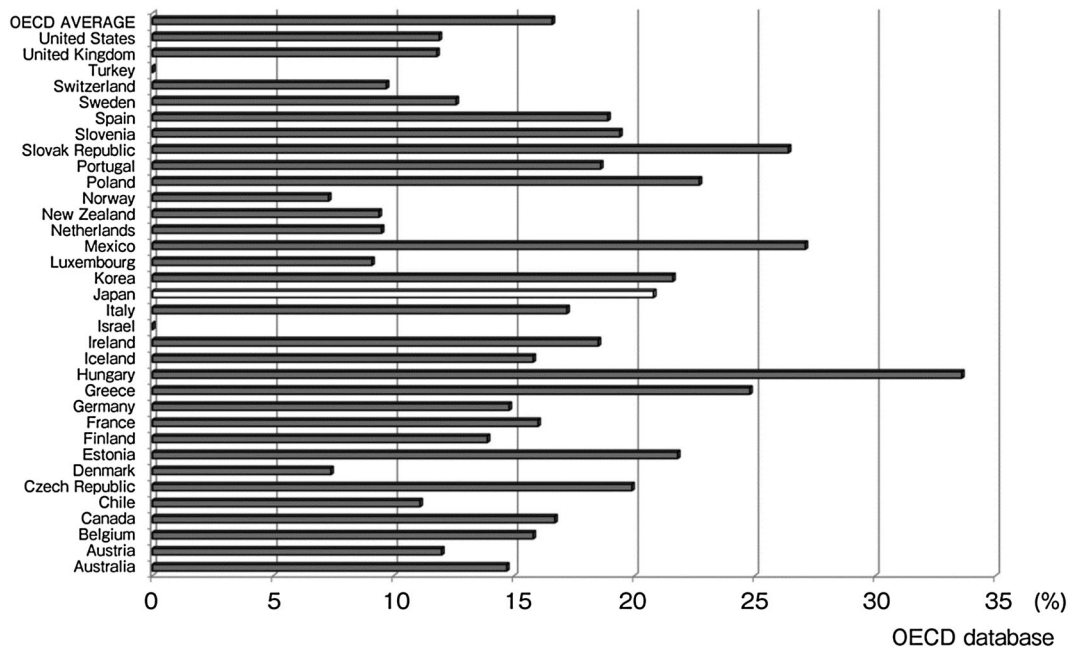


Fig. 8 Expenditures for drugs and medical expendables (relative to total medical expenditure, 2010 or latest). The expense for drugs is in the higher brackets

perform the diagnosis and treatment in such a short time (without mistakes). As patients demand increasingly higher quality of medical services, their tolerance to medical errors is diminishing, and physicians inevitably rely on imaging diagnostic modalities such as CT and MRI to reach quickly some conclusion or treatment plan without overlooking problems. The physicians are also prompted to

eliminate buds of medical errors, though their possibility may be low, by resorting to roughly targeted treatments such as the prophylactic administration of anti-influenza virus agents or antibiotics even when spontaneous cure is expected. For patients on revisits, administrations are continued, and follow-up examinations are repeated, without carefully talking to them or reevaluating the

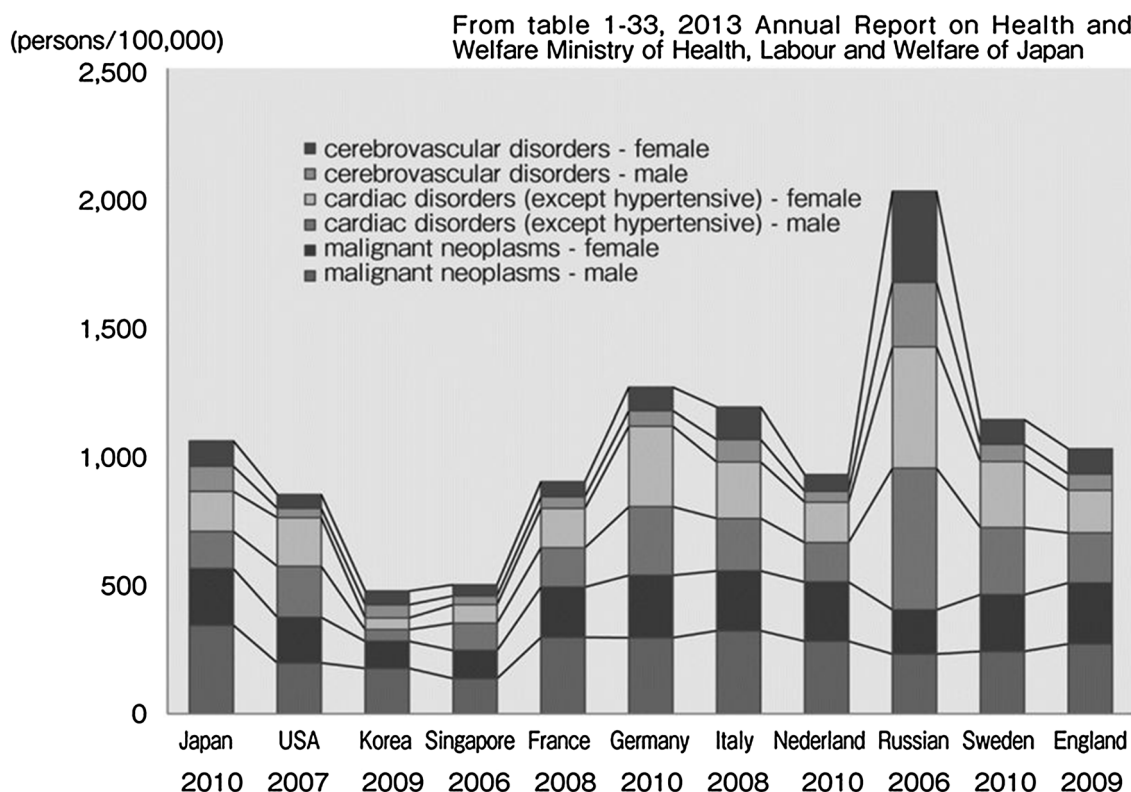


Fig. 9 Mortality rate (by gender and cause of death) 2010 or latest. The ranking of Japan in the mortality rate varies by disease. The mortality rate due to cerebrovascular disorders, cardiac disorders, and malignant neoplasms combined ranks in the middle level among

developed countries, disorders, cardiac disorders, and malignant neoplasms combined ranks in the middle level among developed countries

prescriptions. Thus, in busy outpatient clinics, radiological examinations, which are originally supportive diagnostic procedures, have been transformed to low-cost automatic diagnostic devices. The medical fee reimbursement system may also be promoting orders by conditional reflex. The fees for outpatient care are paid on a fee-for-service basis, and payments are made even when a physician orders examinations without carefully evaluating their indications, possibly contributing to an increase in examinations that are unlikely to be necessary. However, if such practice becomes routine, waiting time for necessary examinations is prolonged. Also, if the number of examinations increases, the number of outpatient visits increases further, because, due to extreme busyness of the laboratory and physicians, the examination results are presented on another day. In addition, for diagnostic devices to be always available, even small medical facilities are required to install them. This results in an increase in the number of installations of CT/MR devices, and installation of devices in unnecessary numbers leads to low level of use and poor maintenance. Efforts to increase the degree of use under such circumstances result in hospital-induced demand, i.e.,

the use of devices in patients for whom the examination may be unnecessary and even the general public.

The trap of cost increase due to uniform control of medical fees and necessity of redistribution of resources for improvements in efficiency

As observed above, the efficiency cannot be improved as expected from attempts to reduce the cost by universal compression of medical fees. We call this paradox the “trap of cost increase due to uniform control of medical fees”. Unquestionably, the national budget allocated to medical services is limited, and the state finance is in a critical state due to long-standing economic stagnation. If such uncontrolled increases in the number of imaging examinations continue, the government would reasonably be tempted to cut the budget uniformly for diagnostic imaging. Indeed, fees for CT and MR examinations have been repeatedly cut at each revision of fees for medical services. However, many studies in Japan and abroad have demonstrated that the policy to universally reduce reimbursement of medical fees is a double-edged sword that

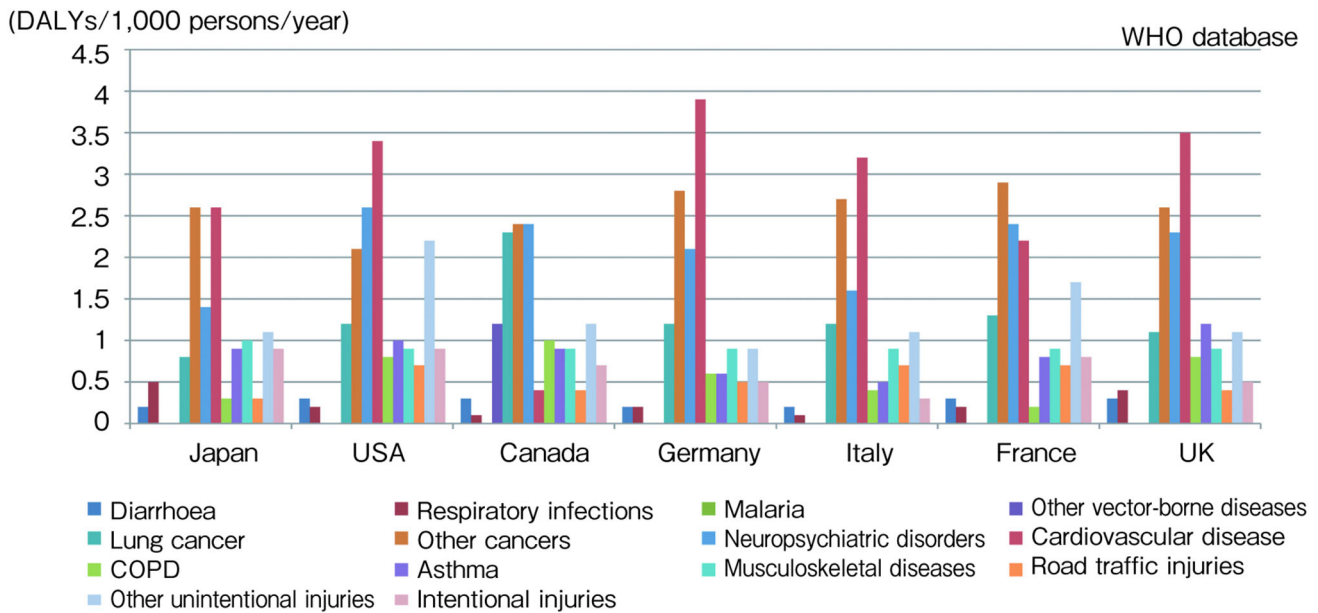


Fig. 10 Disease burden according to the disability-adjusted life year (2004). The disability-adjusted life year, calculated as the sum of the number of years potentially lost due to early death caused by disease and the number of years of healthy life lost due to health damage or disability due to disease, is an index of disease-related loss (burden) of society. It is frequently used to evaluate the order of priority for improvements in public hygiene or medical services in general.

Burden to society is larger as the value is higher. The ranking of Japan in developed countries varies among diseases, e.g., respiratory diseases, malignant tumors, and cardiovascular disorders, and shows no striking difference. The superiority of the effects of medical intervention to diseases in Japan is not obvious compared with other countries

ironically invites rises in the medical cost by provoking demands [11–13]. In Japan, also, such uniform compression of fees for examinations and drugs is accompanied by the risk of promoting excessive use of drugs and diagnostic tools including CT. If apparently wasteful medical expenditures are difficult to eradicate in Japan, the medical administration may be caught in the “trap of cost increase due to uniform control of medical fees”. In taking measures to improve the efficiency of medical services, it is necessary to evaluate the causes of the excessive use of drugs and diagnostic devices as mentioned above and to remove fundamental causes. In advanced countries such as Japan, the days when the efficiency of medical services was measured simply in terms of quantity are gone. We are in the era of quality-oriented assessment of medical services. Regarding radiological services, policies that ensure the highest payment when (1) a roadmap to mildly invasive and accurate diagnoses with minimum radiation exposure is drawn by a specialist in diagnostic imaging, (2) examinations are performed using appropriate and quality-controlled devices and (3) protocols, (4) diagnoses are made properly by qualified specialists in diagnostic imaging, (5) treatments based on such diagnoses are carried out, and (6) patients are rehabilitated through the shortest process are awaited to be implemented. We consider it necessary to redistribute medical resources to apply proper incentives for movements in such a direction.

Excessive examinations and increases in medical radiation exposure

When imaging modalities are appropriately used in clinical practice, this is helpful to specialists in diagnostic imaging. In fact, the use of radiation including CT is undoubtedly making great contributions to improvements in health of the people, but the excessive use of radiation for reasons mentioned above is considered to cause adverse effects. The paper by Barrington de Gonzales that appeared in *Lancet* in 2004 showed that diagnostic radiation is used most frequently in Japan among the OECD member countries and that the associated risk of carcinogenesis is also estimated to be high [14]. As this report was featured in a Japanese newspaper [15], people began to foster anxiety over medical radiation exposure, and, responding to the public mindset, the Japan Radiological Society issued an announcement concerning this problem. In Japan, anxiety over health damage due to low-dose radiation exposure is growing further, particularly after the accident of the nuclear power plants in Fukushima. However, medical radiation exposure plays a greater role than nuclear power plants in low-dose exposure in daily life of all Japanese people, and we are obligated to respond to this anxiety. A symposium on medical radiation exposure was held at the 63rd Annual Meeting of the Japan Radiological Society in 2004, when the paper by Gonzales et al.

attracted attention, and the results were summarized by the chairman [16]. The following are excerpts of the parts of the summary related to the goals of future actions by radiologists.

(1) To carry out a large-scale fact-finding investigation about the clinical practice of radiology, evaluate its significance, and transmit the results in Japan and abroad. To call for cooperation in such actions to related scientific societies/organizations and the government.

(2) To urge the medical society to make judgments in consideration of patients' radiation exposure without sacrificing appropriate diagnostic information in performing radiological diagnosis.

(3) To make efforts in the QC/QA and improvements/development of imaging procedures and instruments in consideration of reduction of patients' radiation exposure.

(4) To initiate the evaluation for appropriate recording of medical radiation exposure in individual patients.

(5) To make the medical staff engaged in radiological diagnosis capable of specifically and appropriately explain medical radiation exposure, its risk, and safety measures to the patients, their families, and medical staff of other departments.

(6) To prompt and promote research on low-dose exposure, which is important to improve the understanding of the risk of low-dose radiation exposure, in cooperation with related scientific societies/organizations.

Today, more than 8 years after the proposal, regarding the fact-finding investigation of radiological diagnosis and treatment, attempts to understand the true state of clinical practice of radiology including questionnaire surveys are being made by the Japan Radiological Society and Japanese College of Radiology. Also, efforts to reduce the exposure dose including the application of iterative reconstruction to CT are continued through the industry-academia-government cooperation. However, the goals have not been sufficiently achieved. We consider that a large-scale fact-finding survey on radiological practice primarily by the Japan Radiological Society or by an external agency consisting of not only a group of experts including radiologists but also the administration and general people, who are recipients of medical services, is necessary in an early stage. Along with analysis of the present state, the urge for the preparation of an environment of medical services in which indications of radiological examinations are evaluated by specialists in diagnostic imaging, appropriate examination plans using appropriate machines are determined, prompt and appropriate diagnoses are made, and life-long recording of radiation exposure of individual patients is implemented is considered to be growing.

Medical services in Japan, which appear to be making considerable achievements at a low cost, also have

inefficient areas and may be improved further by their correction. If radiological practice accounts for a large part of this inefficiency, we are bound to be more serious in improving the situation.

After this section, we show the examples of clinical questions (CQ) in each organ (or region), such as brain and nervous system, head and neck, and thoracic region.

CQ15 What imaging modalities are appropriate for normal pressure hydrocephalus?

Recommendation grade; B CT, MRI

Recommendation grade; C1 Brain perfusion SPECT

CT and, particularly MRI, which are morphological imaging techniques, are recommended because they can delineate morphological abnormalities characteristic of idiopathic normal pressure hydrocephalus (iNPH) and are useful for its discrimination from other disorders that cause cognitive impairment including Alzheimer's disease.

Brain perfusion SPECT is also useful for discrimination of iNPH from other disorders and may be worth considering.

Background/objective

While iNPH is "a treatable dementia", the symptoms of which can be alleviated by CSF shunt surgery, its differentiation from other disorders that cause similar symptoms is a prerequisite for evaluating indications for this treatment. Various reports are observed concerning neuroimaging of iNPH. In this section, the usefulness of neuroimaging techniques for the diagnosis of iNPH is evaluated.

Comments

(1) *Basic morphological changes in iNPH* In iNPH, characteristic findings described as "disproportionately enlarged subarachnoid-space hydrocephalus: DESH" are observed, and they are useful for discrimination from other diseases presenting as ventricular dilation associated with brain atrophy. In addition to ventricular dilation with an Evans index (maximum width between the frontal horns of the lateral ventricles/maximum transverse internal diameter of the skull at the same level) exceeding 0.3, the findings indicate uneven distribution of the subarachnoid space, i.e., narrowing at the high convexity and longitudinal fissure of the cerebrum and widening at the sylvian fissure and basilar cistern (Fig. 11). According to a prospective cohort study performed in Japan to clarify the clinical significance of these findings (study of idiopathic normal pressure hydrocephalus on neurological improvement: SINPHONI), their validity was confirmed by an 80 % response rate to



Fig. 11 Normal pressure hydrocephalus. On coronal T2-weighted image, ventricular dilation, narrowing of high-convexity sulci, enlargement of the sylvian fissures, and decreases in the callosal angle are observed

VP shunt [17]. In addition, an epidemiological study in Japan has demonstrated the presence of elderly people who show morphological changes similar to those in DESH, though they are asymptomatic (asymptomatic ventriculomegaly with features of iNPH on MRI: AVIM), and caution is necessary in the diagnosis [18].

(2) *CT* Generally, CT exceeds MRI in few respects. However, it is possible to evaluate morphological abnormalities in DESH and other disorders such as local dilation of cerebral sulci, narrowing of the posterior half of the cingulate sulcus, and sharpened callosal angle by preparing coronal and sagittal images using multi-planar reconstitution technique due to improvements in special resolution associated with increases in detector rows [19, 20].

(3) *MRI* Changes around the ventricles and in deep white matter are not essential for the diagnosis of iNPH and are also observed in other disorders [17, 19, 21]. While the flow void phenomenon of the cerebral aqueduct is frequently observed in iNPH, it is a non-specific finding also noted in other diseases causing cognitive dysfunction [19, 21, 22]. The measurement of the CSF flow rate by phase contrast MRI has been reported to be sensitive for the diagnosis of iNPH [23, 24], but its diagnostic value has not been established. Although changes in the diffusion anisotropy ratio and diffusion coefficient in the cerebral white matter observed on diffusion tensor and diffusion-weighted imaging and a decrease in the *N*-acetyl aspartate/creatine (NAA/Cr) ratio detected by 1H-MRS are useful for discrimination of iNPH patients from normal individuals, they

are also observed in other dementing disorders, and their diagnostic value remains unsettled [21, 25, 26]. It is possible to evaluate objectively findings reflecting DESH, i.e., dilation of the lateral ventricles and sylvian fissures and narrowing of the high-convexity subarachnoid space, by statistical image analysis [27, 28].

(4) *Brain perfusion SPECT* On brain perfusion SPECT, decreases in the blood flow are observed not only around the corpus callosum and sylvian fissure, but also in the cerebral cortex in various patterns, i.e., anterior-dominant, posterior-dominant, and diffuse [29]. Statistical image analysis suggests relative increases in the blood flow in the high-convexity and median regions in addition to decreases in the blood flow, presumably reflecting a decrease in the subarachnoid space and an increase in the density of the gray matter due to DESH [30]. Such findings have been reported to be useful for discrimination of iNPH from other dementing disorders including Alzheimer's disease [29, 30].

Index words and secondary materials used as references

A search of PubMed was performed using “idiopathic normal pressure hydrocephalus”, “CT”, “MRI”, “SPECT”, “scintigraphy”, “cisternography”, “cerebral blood flow”, “MR spectroscopy”, and “imaging” as keywords. The Japanese Society of NPH iNPH Treatment Guidelines Preparation Committee eds: iNPH Treatment Guidelines, 2nd edition was also used as a reference.

CQ17 What imaging modalities are appropriate when an intraocular tumor is suspected?

Recommendation grade; B MRI
Recommendation grade; C1 CT

MRI is recommended because it shows higher tissue contrast than CT.

CT has a high detection power for calcification and is useful for the diagnosis of retinoblastoma, so its use for the initial diagnosis may be considered. However, the regular and frequent use of CT for the follow-up after treatment or its use for screening of children for retinoblastoma is not recommended.

Background/objective

Regarding orbital/ocular disorders, CT is often performed in patents with orbital trauma and those who cannot be sedated. Before the 1990s, CT was used frequently for the examination of orbital/ocular disorders, but MRI has become widely available today, and the frequency of CT examinations for intraocular tumors has decreased due to

X-ray exposure and the lack of tissue contrast. In this section, CT and MRI are compared to evaluate what imaging modalities should be selected for typical intraocular tumors (retinoblastoma frequently affecting children and malignant melanoma frequently affecting adults).

Comments

(1) *Retinoblastoma* Of the retinoblastomas, 95 % are diagnosed by the age of 5 years, and 56–72 % are detected due to leukocoria. Since the prognosis of retinoblastoma is markedly affected by the early diagnosis and treatment, diagnostic imaging is important. Retinoblastoma is characteristically accompanied by calcification (≥ 90 %), and CT, which has a higher detection power for calcification than MRI or ultrasonography, is useful for its diagnosis [31–34]. However, some question about the use of CT as the first choice in consideration of X-ray exposure in the neonatal period/early childhood [35, 36]. As there is a report that the detectability of calcification of retinoblastoma is about 96 % by CT, 95 % by ultrasonography, and 89 % even by MRI if sequences sensitive for calcification such as T2 star-weighted imaging are added [36], CT may not be indispensable for the diagnosis of retinoblastoma. Also, there are retinoblastomas that show no clear mass formation or calcification, and such lesions are difficult to diagnose without MRI or ultrasonography [31]. At the very least, frequent CT examination for the follow-up after treatment for retinoblastoma or the use of CT for screening of children for retinoblastoma is not recommended.

Retinoblastoma presents a hyperdense image on CT, and contrast enhancement is observed in 27.5 % of the patients, but it is a non-specific finding [32, 33]. Also, the prognosis of retinoblastoma is affected by the presence or absence of choroidal invasion, optic nerve invasion, intracranial infiltration, and dissemination. While choroidal and optic nerve invasion can also be evaluated by CT, it can better be evaluated by MRI with high tissue contrast, and ultrasonography is superior for the evaluation of minute extraocular infiltration [31–34, 37]. If a tumor infiltrates the vitreous body and subretinal space, it may cause retinal detachment, and the differentiation between the tumor and subretinal effusion becomes necessary. MRI is more effective than CT for this purpose [31–34]. The administration of an iodine-based contrast medium is necessary for the CT evaluation of tumor invasion, and MRI should be considered first line also from the viewpoint of X-ray exposure.

Bilateral retinoblastoma occurs in 25 %, and trilateral retinoblastoma (retinoblastoma involving the bilateral retinae and the pineal body or suprasellar region) occurs in 5–15 %, of the patients with hereditary retinoblastoma. MRI is superior to CT for the evaluation of intracranial

infiltration of the tumor, presence or absence of suprasellar or pineal lesions, and dissemination [31, 35].

Diseases that exhibit white pupil and need discrimination from retinoblastoma include persistent hyperplastic primary vitreous (PHPV) and Coats' disease. This differentiation can be made by MRI with high tissue contrast [31, 34].

(2) *Malignant choroidal melanoma* Choroidal melanoma tends to be hyperdense on CT and shows mild-moderate contrast enhancement on contrast-enhanced CT [38–40]. While the tumor can also be delineated by CT, MRI with high tissue contrast is superior. Melanoma in particular often emits characteristic signals on MRI [32, 39, 40] (Fig. 12). MRI and ultrasonography surpasses CT in the evaluation of extraocular infiltration of tumors [32, 39, 41]. They are also more effective than CT for the separation and discrimination of associated retinal detachment from tumor [39, 40]. Although melanomas 2 mm or less in diameter are reportedly difficult to delineate by CT or MRI [38, 40], they may be visualized by MRI due to the recent development of MRI techniques and coils and the increased availability of MRI with a static magnetic field of 1.5 T or above. There is no evidence for recommending CT as the first choice imaging modality when malignant choroidal melanoma is suspected.

Index words and secondary materials used as references

A search of PubMed was performed using “retinoblastoma”, “uveal melanoma”, “ocular tumor”, “CT”, and “MRI” as keywords. The Japan Radiological Society and



Fig. 12 Ocular tumor (malignant melanoma) T2-weighted image. A mass, which is hypointense compared with the surrounding vitreous body, is observed in the medial region of the right eye ball (rightwards arrow). It was a malignant melanoma of the choroid

Japanese College of Radiology eds.: Guidelines for Diagnostic Imaging 2003 was also used as a reference.

CQ42 Is MRI appropriate for the diagnosis of mediastinal tumors?

MRI is useful for the diagnosis of cystic lesions of the mediastinum and may also provide additional information concerning solid tumors of the mediastinum.

It is also very useful for the diagnosis of posterior mediastinal tumors and is recommended.

Background/objective

Usually, CT is used first for the imaging diagnosis of mediastinal tumors. MRI (Fig. 13) may be performed after CT, but its necessity or usefulness has not been sufficiently evaluated. The effectiveness of MRI for the diagnosis of mediastinal tumors was evaluated.

Comments

Mediastinal tumors are classified into anterior, middle, and posterior mediastinal lesions. They are also classified into cystic and solid lesions according to the internal properties. The site of origin and internal properties must be taken into consideration in discussing the usefulness of MRI.

There have been few reports directly comparing the usefulness of CT and MRI in mediastinal tumors. According to comparison of the diagnostic ability of CT

and MRI for anterior mediastinal tumors [42], the diagnostic accuracy was 84 and 81 % for thymoma, 45 and 15 % for thymic cancer, 67 and 33 % for teratoma, 36 and 27 % for malignant germ cell tumor, and 55 and 40 %, respectively, for malignant lymphoma. In these anterior mediastinal solid tumors, CT shows equal or higher diagnostic ability compared with MRI. Particularly, for the diagnosis of teratoma, CT is significantly superior to MRI. Cystic masses of the mediastinum such as thymic, bronchial, and esophageal cysts are known to show a wide variety of densities and signals on plain CT and T1-weighted MRI due to bleeding or protein content [43, 44], making the diagnosis difficult, but, according to the above report, the diagnostic accuracy for thymic cysts was 46 % by CT and 71 % by MRI, being significantly higher for MRI [42]. In a report comparing the delineability of various findings of thymic epithelial tumors by CT and MRI [45], the visualization rate was 18 and 75 % for the peritumoral capsule, 13 and 43 % for intratumoral septa, and 5 and 17 %, respectively, for intratumoral hemorrhage, indicating higher delineation power of MRI. Fibrotic septa that separate the tumor or a capsule around the tumor visualized by MRI have been reported to suggest low-malignancy thymoma. There is also a report that stage III thymoma could be differentiated by dynamic MRI [46]. By a study evaluating the correlation between MRI findings and the WHO histological classification of thymic epithelial tumors [47], encapsulated, distinctly-bordered, round tumors were reported to suggest type A thymoma, and tumors with intratumoral hypointense areas on T2-

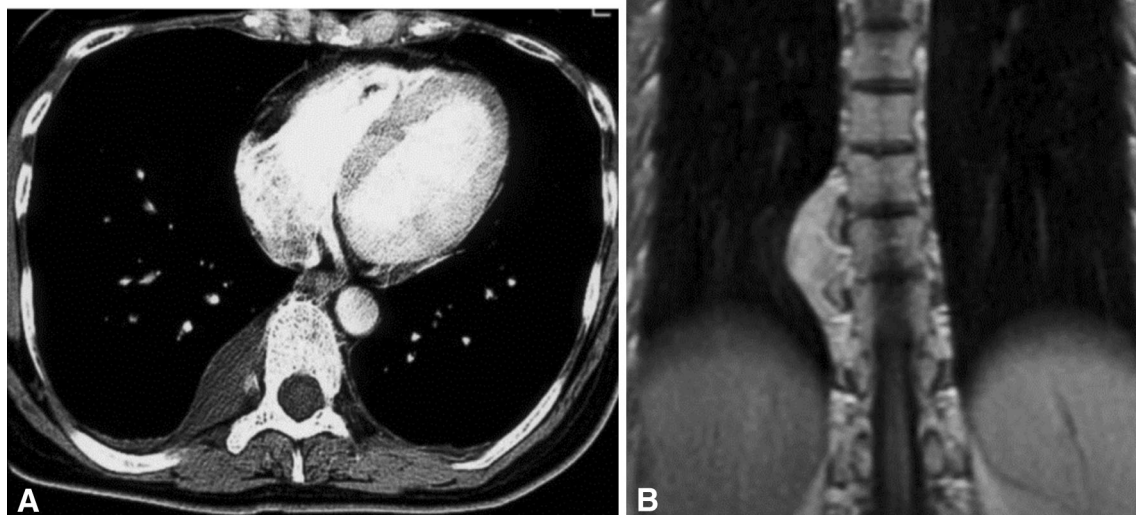


Fig. 13 Gangliocytoma. **a** Contrast-enhanced CT: a mass is observed in the posterior mediastinum (right paravertebral region). Contrast enhancement is moderate, and the interior is nearly homogeneous.

b Coronal T1-weighted MRI: The vertical extent of the tumor is easy to evaluate by MRI. The lesion is a long and thin tumor showing wide-based spread involving multiple vertebral bodies

weighted image or mediastinal lymph node enlargement to suggest thymic cancer. It is difficult to diagnose the WHO histological classification from MRI findings in other tumor types. Chemical shift imaging has been reported to be useful for the discrimination between thymoma and thymic hyperplasia [48].

Since CT and MRI are equally useful for the evaluation of great vessel invasion of thymic epithelial tumors [45], the invasiveness of the tumor may be evaluated by MRI if contrast-enhanced CT is impossible due to iodine allergy.

Most masses arising in the posterior mediastinum are neurogenic tumors such as schwannoma, neurofibroma, gangliocytoma, paraganglioma, and neuroblastoma, and MRI is useful for the evaluation of the relationships of the tumor with the nerves and intervertebral foramen (Fig. 13) [49]. Recently, it has become possible to readily prepare MPR images using volume data of CT and to reconstruct images other than transverse views. While the superiority of MRI is diminishing, there is no report comparing the usefulness of CT and MRI concerning posterior mediastinal tumors.

Index words and secondary materials used as references

A search of PubMed was performed using “MRI”, “thymoma”, “thymic epithelial tumor”, “lymphoma”, “mediastinum”, and “mediastinal tumor” as keywords.

CQ49 What imaging modalities are appropriate for the diagnosis of acute pulmonary thromboembolism?

Recommendation	Contrast-enhanced CT of the chest grade; A
Recommendation	Pulmonary perfusion scintigraphy, grade; B lower extremity venous ultrasound, lower extremity venous CT

CT is recommended as there is strong evidence supporting its usefulness. Pulmonary perfusion scintigraphy is also useful and recommended. These examinations may be performed alone or in combination. Lower extremity venous ultrasound or CT is useful and recommended for the diagnosis of deep venous thrombosis.

Background/objective

To diagnose efficiently pulmonary thromboembolism, appropriate selection of examinations and evaluation of the results are necessary. In Western countries, the diagnostic utility has been established on the basis of the results of a number of studies [50–52] and the selection of examinations based on the clinical probability is recommended, but this method has not been widely accepted in Japan [53].

Here, the value of contrast-enhanced CT (of the chest, lower extremity), pulmonary perfusion scintigraphy, and lower extremity venous ultrasound in the diagnostic procedure are evaluated.

Comments

Pulmonary thromboembolism requires prompt and accurate diagnosis because a delay of treatment may result in aggravation of the condition and even death, but the selection of examinations and evaluation of the results differ according to the patient’s condition (Fig. 14).

If a patient suspected to have pulmonary thromboembolism exhibits a state of circulatory collapse, emergent CT should be performed and treatment started after a definitive diagnosis. Other thoracic disorders that need to be differentiated including aortic dissection and pericardial effusion can also be diagnosed. If emergent CT cannot be performed, right heart strain is assessed by transthoracic echocardiography, and, if acute pulmonary thromboembolism is clinically suspected, anticoagulant therapy is evaluated. In such situations, CT should be performed as early as possible to confirm the diagnosis (Fig. 15).

If the hemodynamic status is stable, the clinical probability should be evaluated according to the patient’s clinical information. This evaluation is made by clinicians, but radiologists must also be informed of the results. The Wells score [54] is the best known evaluation method.

If the clinical probability is moderate or low, D dimers are assayed first. If the D dimer level is normal, pulmonary thromboembolism can be excluded, and no further examination or treatment is necessary. If the D dimer level is higher than the normal range, CT or, depending on the situation, pulmonary perfusion scintigraphy should be performed. If both examinations are negative, no treatment is required.

If, on the other hand, the clinical probability is high, the D dimer level, associated with a low negative predictive value, is not useful, so CT should be performed first, with pulmonary perfusion scintigraphy depending on the situation. According to a multicenter progressive study reported in 2006 (prospective investigation of pulmonary embolism diagnosis II: PIOPED II) [55], the negative predictive value in this group was low at 60 %, and additional examinations (pulmonary perfusion scintigraphy, lower extremity venous ultrasound) should be considered, if the thrombus cannot be confirmed by CT.

Which of CT and pulmonary perfusion scintigraphy should be used is controversial, but the greatest advantage of CT is its high availability [56]. Emergency pulmonary perfusion scintigraphy can be performed at few facilities. Also, CT has many advantages such as that it can delineate

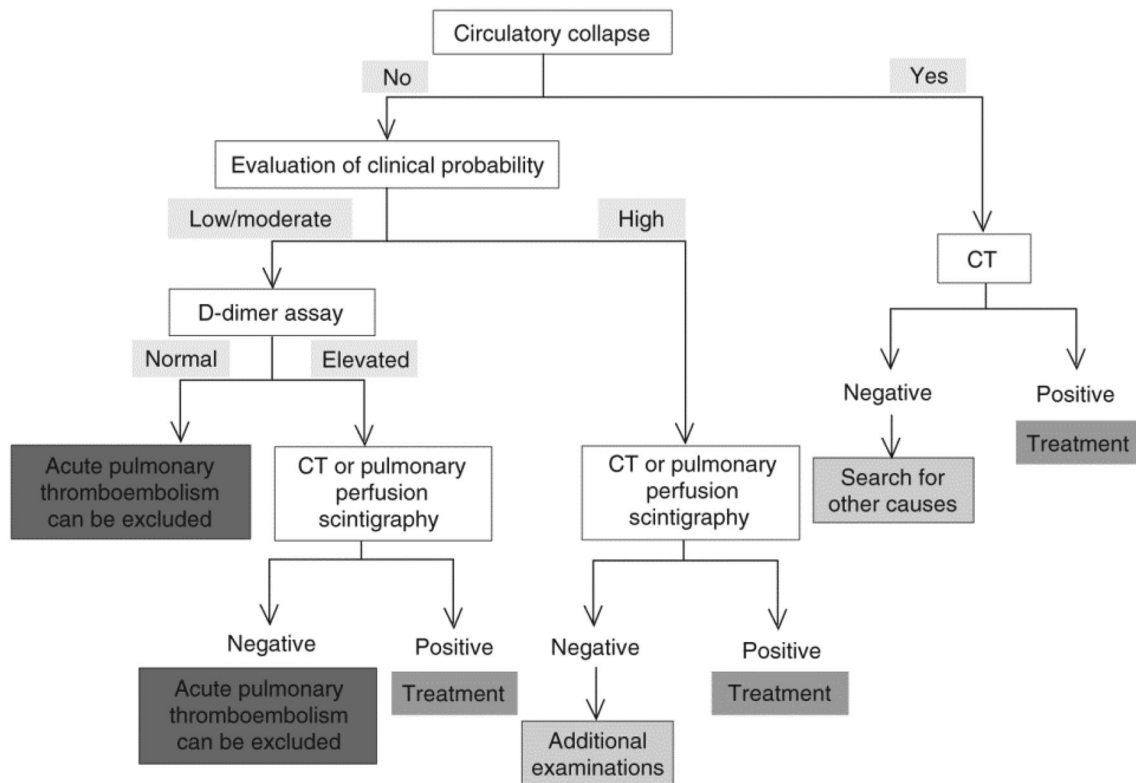


Fig. 14 Diagnostic procedure for patients suspected of having acute pulmonary thromboembolism

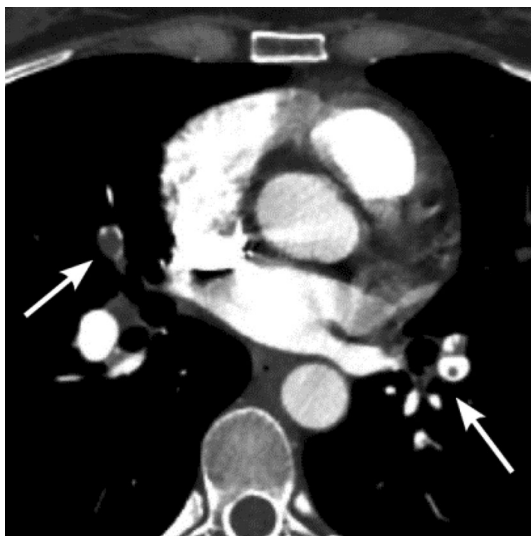


Fig. 15 Acute pulmonary thromboembolism contrast-enhanced CT of the chest. Many unenhanced thrombi (*rightwards arrow*) are observed in the bilateral pulmonary arteries. Thrombi are imaged as if they are floating in the pulmonary artery characteristically in acute pulmonary thromboembolism. The right ventricle is dilated

the thrombus itself and that aortic, pulmonary, and thoracic lesions can be diagnosed, so it is usually the first choice. However, while the exposure has been reduced in recent

CT devices, presently the exposure is lower by pulmonary perfusion scintigraphy [57]. Therefore, pulmonary perfusion scintigraphy should be considered in examination of young patients and for repeated follow-up examinations. Pulmonary perfusion scintigraphy is recommended in patients with a history of adverse reactions to the contrast agent and those with renal dysfunction. Also, as pulmonary perfusion scintigraphy shows a high negative predictive value, this less invasive modality is recommended for patients with a low clinical probability and normal chest plain radiographs.

More than 90 % of the thrombi that cause pulmonary thromboembolism are lower extremity venous thrombi, and the evaluation of the lower extremity veins is necessary for the determination of the therapeutic approach including the necessity of an inferior vena cava filter. Lower extremity venous ultrasound and CT venography, in which the pelvic region and lower extremities are imaged in the delayed phase of pulmonary artery CT, are diagnostic methods for lower extremity venous thrombosis. In the PIOPED II [55], the sensitivity for the diagnosis of pulmonary thromboembolism was reported to have improved from 82 to 90 % by the inclusion of CT venography in the diagnostic procedure. However, it must be remembered that the inclusion of CT venography significantly increases the exposure. Caution is needed, particularly in young women.

Since the diagnostic accuracy is considered comparable between lower extremity venous ultrasound and CT venography, the former is more desirable if possible [50].

Index words and secondary materials used as references

A search of PubMed was performed using “pulmonary embolism”, “diagnosis”, and “guideline” as keywords. The JCS Joint Working Group: Guidelines for the diagnosis, treatment, and prevention of pulmonary thromboembolism and deep vein thrombosis [53] were also used as a reference.

CQ62 Which modalities are appropriate for detecting early hepatocellular carcinoma in patients with chronic liver disease?

Gd-EOB-MRI has a high diagnostic ability for early hepatocellular carcinoma. There have been few reports on the diagnostic ability of Sonazoid contrast-enhanced ultrasonography for early hepatocellular carcinoma.

Background/objective

Recently, with the development of imaging diagnostic devices and new contrast agents, the evaluation of targets other than the blood flow has become possible, and small lesions have begun to be detected frequently in patients with chronic liver disease. Early hepatocellular carcinoma, which is an unclear nodule 20 mm or less in diameter representing a hypovascular well-differentiated hepatocellular carcinoma, exhibits diverse features on imaging studies due to changes in the portal and arterial blood flows in the nodule in the course of its multistage development. Generally, the disease is often treated in the stage of hypovascular well-differentiated hepatocellular carcinoma, which is an early hepatocellular carcinoma dedifferentiated from a dysplastic nodule (DN), and further dedifferentiated and hypervascularized well-differentiated hepatocellular carcinoma. It is important to have knowledge of findings on contrast-enhanced ultrasonography, dynamic MDCT, and Gd-EOB-MRI and their diagnostic performance in early hepatocellular carcinoma.

Comments

(1) *Scientific statement* In 30 nodules of early hepatocellular carcinoma diagnosed by hepatectomy, ROC analysis of the diagnostic abilities of dynamic MDCT and Gd-EOB-MRI showed that the Az value, sensitivity, and NPV were significantly higher by Gd-EOB-MRI (0.98–0.99, 94–97, and 96.8–98.1 %) than by dynamic MDCT (0.87, 58–68, and 80.7–84.4 %, respectively), that the specificity

and PPV showed no significant difference, but that the diagnostic performance of Gd-EOB-MRI for early hepatocellular carcinoma was significantly higher than that of dynamic MDCT (Table 4) [58].

Also, of the 15 nodules of well-differentiated hepatocellular carcinoma 2 cm or less in diameter diagnosed by biopsy, 67, 40, and 60 % were diagnosed by Sonazoid contrast-enhanced ultrasonography, dynamic MDCT, and Gd-EOB-MRI, respectively, as hepatocellular carcinoma (a nodule showing contrast enhancement in the arterial phase and washout in the portal-venous phase or a nodule showing contrast enhancement in the arterial phase, low signal intensity in the hepatocyte phase of Gd-EOB-MRI, and hypodensity in the Kupffer phase of Sonazoid contrast-enhanced ultrasonography). The diagnostic abilities of Gd-EOB-MRI and Sonazoid contrast-enhanced ultrasonography for well-differentiated hepatocellular carcinomas 2 cm or less in diameter have been reported to be higher than that of dynamic MDCT. However, of these 15 nodules, five were considered to be hypovascular, and three of them showed hypoattenuation in the portal-venous phase of MDCT, only one of them showed hypoecho in the Kupffer phase of Sonazoid contrast-enhanced ultrasonography, and four of them showed hypointensity in the hepatocyte phase of Gd-EOB-MRI. Thus, the evidence concerning the relative diagnostic abilities of these modalities for hypovascular well-differentiated hepatocellular carcinoma is insufficient [59].

In a multicenter joint research participated in by 15 facilities regarding the diagnostic ability for hepatocellular carcinoma 2 cm or less in diameter, nodule-by-nodule ROC analysis of 279 hepatocellular carcinomas showed that the sensitivity of Gd-EOB-MRI (38–55.4 % for lesions 10 mm or less in diameter, 71.1–87.3 % for those 10–20 mm in diameter) was higher than that of dynamic MDCT (26.1–47.3 % and 65.7–78.4 %, respectively) [60]. According to another report on the diagnostic performance for hepatocellular carcinomas 2 cm or less in diameter, the sensitivities of Sonazoid contrast-enhanced ultrasonography (67.6 %) and Gd-EOB-MRI (76.5 %) were higher than that of MDCT (52.9 %), but the differences were not significant (Table). However, in the above two reports, the evaluation was not restricted to well-differentiated hepatocellular carcinoma [61].

From these observations, Gd-EOB-MRI is considered to have higher diagnostic ability than MDCT for early hepatocellular carcinoma. Presently, there is no report providing evidence sufficient for the evaluation of the diagnostic ability of Sonazoid contrast-enhanced ultrasonography or its comparison with that of MDCT or Gd-EOB-MRI.

(2) *Comments* Early hepatocellular carcinoma is a well-differentiated hepatocellular carcinoma presenting as an

Table 4 Abilities of imaging modalities to detect early hepatocellular carcinoma in chronic liver disease patients: early hepatocellular carcinoma findings and advantages and disadvantages of each modality

Imaging findings						
	Non-contrast phase	Contrast-enhanced early phase	Contrast-enhanced late phase	Advantages	Disadvantages	Notes
Sonazoid contrast-enhanced ultrasonography		Shows various echo patterns due to slight changes in the blood flow [59, 74]	Hypoecho in Kupffer phase: 54–67 % [59, 74] DN and early HCC are isoechoic with hepatic parenchyma but become hypoechoic in the Kupffer phase through the process of dedifferentiation	Simple and mildly invasive Applicable also to kidney dysfunction patients No exposure Real-time evaluation of hepatic blood flow possible	Presence of dead angles Detection power affected by the patient's physique and technician's skill	Detection power for blood flow of hepatic nodules is significantly higher than dynamic CT or MRI with relatively fixed imaging timing [65, 70]
Dynamic MDCT	Hypoattenuation nodule: 43–47 % [58, 59, 71]	Early-phase contrast enhancement: 0–60 % [58, 61, 62, 66]	Hypoattenuation nodule: 40–73 % [58, 59, 71]	Wide availability of MDCT with 16 or more detector rows Essential for qualitative diagnosis and determination of therapeutic approach, plays primary role in imaging diagnosis	Exposure The use of a contrast agent is difficult in some patients with kidney dysfunction	
EOB Primovist MRI	Hyperintensity T2-signals: 10–32 % Fat-containing nodules: 26–53 % [58, 71, 72, 74]	Arterial-phase contrast enhancement: 0–67 % [58, 61, 62, 66, 67]	Hypointensity in delayed phase: 47–68 % Low signal intensity in hepatocyte phase: 79–92 % [58, 59, 61, 62, 66, 71, 72]	Capable of collecting blood flow information and evaluating hepatocyte function, has high diagnostic power	Insufficient availability of MRI systems with sufficient diagnostic power of 1.5 T or higher Difficult to perform in some patients with implanted metallic devices or kidney dysfunction	Hepatocyte phase is significantly useful for detecting small HCC [67], EOB uptake ratio is useful for discrimination between well-differentiated HCC and DN [73]

unclear nodule 20 mm or less in diameter. It shows poor tumor angiogenesis and is hypovascular. Its biological malignancy is low, it rarely shows intrahepatic metastasis or vascular invasion, and its prognosis is favorable [62, 63]. In hepatocellular carcinoma, the portal and arterial blood flows in the nodule change in the process of multistage tumorigenesis. In early hepatocellular carcinoma, the arterial blood flow is deficient, but becomes richer with decreases in the portal blood flow through the process of dedifferentiation. A tumor in which hypervascular areas develop in the nodule (nodule-in-nodule) is biologically a small advanced hepatocellular carcinoma even if it is histologically well-differentiated hepatocellular carcinoma. Some such lesions cause local intrahepatic metastasis or vascular invasion and may have a poor prognosis [64]. Therefore, diagnosing the disease in the stage of hypovascular early hepatocellular carcinoma is considered to contribute to a better prognosis.

For hyperarterialized moderately or more differentiated hepatocellular carcinoma, various imaging modalities show similar diagnostic performance, but it tends to be higher in Gd-EOB-MRI than in dynamic MDCT [65]. The degree of malignancy of nodules evaluated by CT with intra-arterial contrast injection and signal intensity in the hepatocyte phase of Gd-EOB-MRI are correlated with the degree of malignancy of borderline lesions, and the early liver cancer type was more markedly hypointense and detected more frequently than the DN type. Hepatocyte phase Gd-EOB-MRI very sensitively delineates changes in an early stage of multistage carcinogenesis of lesions from DN to early hepatocellular carcinoma compared with conventional diagnostic methods and has an excellent diagnostic ability for early hepatocellular carcinoma [66].

In early hepatocellular carcinoma, portal venous and arterial blood in the tumor decreases (Nakajima O: Morphogenesis and progression of liver cancer [67]). Therefore, the tumor is hypovascular and is expected to be hypoechoic compared with non-tumoral areas on perfusion imaging of Sonazoid contrast-enhanced ultrasonography, but no consistent results have been obtained concerning the findings or diagnostic ability of the modality due to the slightness of blood flow changes. Also, in early hepatocellular carcinoma, the contrast of Kupffer cells is reduced equally or more mildly compared with non-tumoral areas [68], and not many lesions are visualized as defects in the Kupffer phase of Sonazoid contrast-enhanced ultrasonography. Therefore, there is presently no report of a high evidence level concerning the diagnostic ability of Sonazoid contrast-enhanced ultrasonography for early hepatocellular carcinoma or comparison of its diagnostic performance with other modalities. However, ultrasonography including that using Sonazoid contrast enhancement is occasionally performed periodically in patients with

chronic liver disorders, and early hepatocellular carcinoma is often delineated as a hypoechoic nodule by reflecting fatty change of cancer cells. The frequency of detection of such hypoechoic nodules has been reported to be 40 % in small hepatocellular carcinomas 10–15 mm in diameter [69], and the detection of such lesions often lead to the diagnosis of early hepatocellular carcinoma. MDCT and Gd-contrast-enhanced dynamic MRI themselves have high detection sensitivity for arterial blood flow, but the evaluation of hypovascular early hepatocellular carcinoma requires precise judgment and is often difficult. Reports of their diagnostic performance also vary widely.

In the papers cited in this CQ, no consensus has been reached regarding the diagnostic ability of Sonazoid contrast-enhanced ultrasonography. While the sensitivity of Gd-EOB-MRI for early hepatocellular carcinoma tends to be higher than that of MDCT, it must be noted that MRI systems capable of high-quality dynamic study were used in the studies cited in this article and that MRI systems with a low magnetic field strength or deficient in diagnostic ability are inappropriate for diagnosing early hepatocellular carcinoma. Such MRI systems capable of high-quality dynamic study are not as widely available as ultrasonographs or MDCT devices, and, in practice, dependence on ultrasonography or dynamic MDCT is unavoidable in follow-up imaging studies.

Index words and secondary materials used as references

A search of PubMed was performed using “early hepatocellular carcinoma”, “CT”, “EOB MRI”, and “sonazoid ultrasonography” as keywords. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 update was also used as a reference.

CQ73 Which imaging modalities are appropriate as for the reliable diagnosis of liver hemangiomas?

Recommendation grade; A	Extracellular gadolinium contrast-enhanced dynamic MRI
Recommendation grade; B	EOB contrast-enhanced MRI, contrast-enhanced dynamic CT
Recommendation grade; C1	Ultrasonography and contrast-enhanced ultrasonography

MRI including extracellular gadolinium contrast-enhanced dynamic MRI is the most reliable and is strongly recommended. EOB contrast-enhanced MRI and contrast-enhanced dynamic CT also have a sufficient diagnostic ability and are recommended to be performed. The diagnostic performance of ultrasonography is improved by the use of a contrast agent, and the modality should be considered.

Background/objective

Cavernous hemangioma is the most frequent benign tumor of the liver. It is sometimes difficult to discriminate from primary liver cancer in patients with chronic liver disease and liver metastasis in tumor-bearing patients. It is often detected incidentally also in healthy individuals. Since it rarely ruptures or transforms into a malignant disease, unnecessary treatment can be avoided if it is definitively diagnosed by a minimally invasive and highly accurate method. This also avoids invasive procedures and cost of unnecessary additional examinations or follow-up.

Comments

A majority of liver hemangiomas are cavernous hemangiomas, which are benign liver diseases that form localized liver masses due to tumorous growth of large and small vascular lumens, in which flattened endothelial cells are arranged. In the interior of vascular lumens, degeneration such as new and old thrombus formation, necrosis, scars, fibrosis, and calcification is observed. As degeneration advances, the lesion becomes sclerosed hemangioma. It is necessary to diagnose liver hemangioma using imaging modalities by understanding these tissue architectures and degeneration [75].

Until the early 1990s, liver hemangiomas were occasionally diagnosed definitively by angiography [76], but invasive angiography has been completely obviated as a diagnostic procedure due to the recent development of less invasive imaging techniques. Similarly, while radionuclide studies using ^{99m}Tc -labeled erythrocytes used to be performed, it has fallen into disuse due to the unsatisfactory accuracy [76] and difficulty of diagnosing small hemangiomas. The performance of ultrasound devices began to improve since the late 1980s with improvements in the detection sensitivity for hemangiomas [77], but their differentiation from malignant tumors was not easy by ultrasonography without contrast enhancement. In the late 1980s, MRI became increasingly available, and its usefulness for the diagnosis of liver hemangiomas was reported [77–80]. According to comparisons of ultrasonography with non-contrast CT and MRI performed in this period, MRI showed higher detection sensitivity [77–79]. Thereafter, there was also a report that non-contrast MRI was superior to contrast-enhanced CT [81]. From the early 1990s, the development of helical CT and high magnetic field strength MRI progressed, and contrast-enhanced dynamic study became possible with both CT and MRI, resulting in marked improvements in the diagnostic ability for liver hemangioma [82, 83] and reports of

[84]. In this period, Doppler ultrasonography was reported to be useful for the diagnosis of liver hemangioma [85], but the procedure has not been established as a method for the definitive diagnosis. Recently, also, with the introduction of contrast-enhanced ultrasonography, more detailed analysis of the hemodynamics of liver hemangiomas has become possible, causing improvements in the diagnostic performance of ultrasonography [86–88]. However, the reliability of contrast-enhanced ultrasonography for the diagnosis of liver hemangioma has not been securely established due to the presence of dead angles, difficulty in simultaneous evaluation of multiple lesions, and variability of the results depending on the examiner's skill and the patient's physique. In MRI, many hemangiomas show hyperintensity on T2-weighted imaging, and lesions about 4 mm in diameter has become detectable. On gadolinium contrast-enhanced MRI, usual staining type hemangiomas, in which marginal nodular staining extends internally with time, account for about 70 % of the lesions [80, 89]. Some hemangiomas are those with arteriportal (AP) shunts, early enhancing type hemangiomas, which show intense enhancement of the whole lesion from the early phase of contrast enhancement, and delayed staining hemangiomas, which show partial dot-like staining (bright-dot sign) or only pale staining in the margin until the late phase of contrast enhancement. With improvements in the understanding of these atypical findings [89], it has become possible to diagnose liver hemangiomas with a high level of confidence. Moreover, radiation exposure cannot be ignored on contrast-enhanced multiphase CT [90], and, particularly, on secondary examination of hemangiomas incidentally detected in healthy individuals, MRI with the benefit of no radiation exposure even on contrast-enhanced multiphase imaging, is recommended. Recently, EOB Primovist contrast-enhanced MRI has begun to be performed widely for close evaluation of liver masses, but it often fails to present clear hyperintensity of blood pools in the late to delayed phase of contrast enhancement, its diagnostic ability for small hemangiomas is considered to be limited [91–93].

Index words and secondary materials used as references

A search of PubMed was performed using “liver”, “hemangioma”, “diagnosis”, “CT”, “US”, “MRI”, “angiography”, “scintigraphy”, and “EOB” as keywords.

CQ86 Is contrast-enhanced CT appropriate for diagnosis and assessment of severity in acute pancreatitis?

Contrast-enhanced CT is strongly recommended for the diagnosis and severity assessment of acute pancreatitis.

Background/objective

Acute pancreatitis is classified as acute abdomen. It is acute inflammation of the pancreatic parenchyma and is divided into mild cases that can be managed by conservative treatment and severe cases in which inflammation is not localized in the pancreatic parenchyma, but spreads to tissues and organs not only around, but also distant from, the pancreas, and fatal complications such as systemic circulatory insufficiency, multiple organ failure, and severe infections develop due to systemic inflammatory response syndrome (SIRS). Imaging modalities play an important role in the evaluation of complications affecting the whole body as well as the state of the pancreas itself. If the disease follows a serious course, the mortality rate is very high, and the assessment of disease severity is closely related to the appropriateness of the selection of treatments [94].

Comments

Acute pancreatitis is frequently manifest as an edematous pancreas and responds to conservative treatments. However, about 20 % of the cases are classified as severe acute pancreatitis, showing systemic inflammatory changes and subsequently developing various complications, with a high mortality rate [94]. If the diagnosis of acute pancreatitis cannot be confirmed, or if the cause of pancreatitis cannot be identified by clinical findings, blood tests, and urinalysis, CT should be performed readily.

CT provides objective images of a wide area of the body without being affected by gas in the gastrointestinal tract or adipose tissue in the abdominal wall or cavity and is suitable for the evaluation of not only pancreatic necrosis and changes around the pancreas, but also complications

extending to other parts [95–98]. CT is used for the severity assessment as well as diagnosis of acute pancreatitis as mentioned below, and contrast-enhanced CT is recommended, if possible. If the condition is mild edematous pancreatitis, the only findings on contrast-enhanced CT are homogeneous delineation of the pancreatic parenchyma, normal-sized or only mildly enlarged pancreatic parenchyma itself (Fig. 16), and slight hyperdensity of the adipose tissue around the pancreas [94]. Local edema extends along the mesentery, mesocolon, and hepatoduodenal ligament to the abdominal cavity, and typical CT findings are enlargement of the pancreas, increased fat density in tissues around the pancreas to the retroperitoneal cavity (primarily, the anterior pararenal space), mesocolon, and mesentery proper, exudate retention (Fig. 17), pseudocyst formation, heterogeneous density of the pancreatic parenchyma, pancreatic necrosis (Fig. 18), fat necrosis of the retroperitoneal cavity and mesentery, hematoma, and pancreatic rupture on injury. Gas in and around the pancreas is often caused by fistula formation to the intestine or infection by gas-producing microorganisms (Fig. 19). In more distant areas, bilateral pleural effusion and atelectasis may also occur [99]. Indications of contrast-enhanced CT should be evaluated in consideration of the history of allergy to contrast agents and renal function.

The criteria for assessment of severity in acute pancreatitis by the Ministry of Health, Labour, and Welfare (2008) consist of nine prognostic factors and also mention the contrast-enhanced CT grade as an independent item. These assessment criteria are also adopted in the guidelines for the management of acute pancreatitis: JPN guidelines 2010, and the disease is judged to be severe when the prognostic factor score is 3 or higher, or the contrast-enhanced CT grade is 2 or higher. Since the presence or absence of pancreatic necrosis and extrapancreatic spread

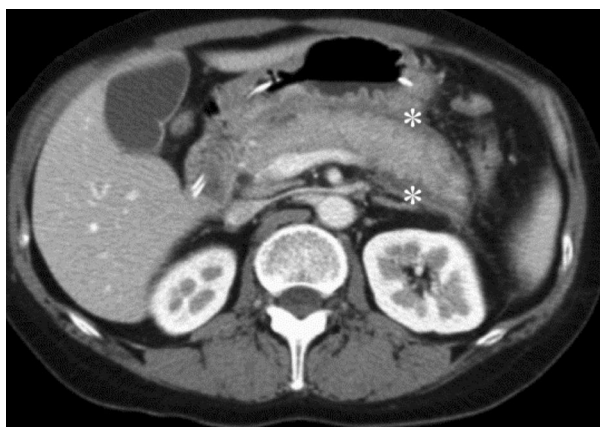


Fig. 16 Acute edematous pancreatitis (CT Grade 1). On contrast-enhanced CT, the entire pancreatic parenchyma is enlarged, but no clear hypo-enhanced area is noted. Effusion (*asterisk*) is observed

degree of extrapancreatic spread	anterior pararenal space	base of the mesocolon	lower pole of the kidney
hypo-enhanced area of pancreas			
localized in a segment of, or around, the pancreas	*		
involving 2 segments			
occupying 2 entire segments or wider			

□ Grade 1 ■ Grade 2 ■ Grade 3
Severe when CT Grade ≥ 2

around the pancreas, and a diagnosis of acute pancreatitis with a CT Grade of 1 can be made

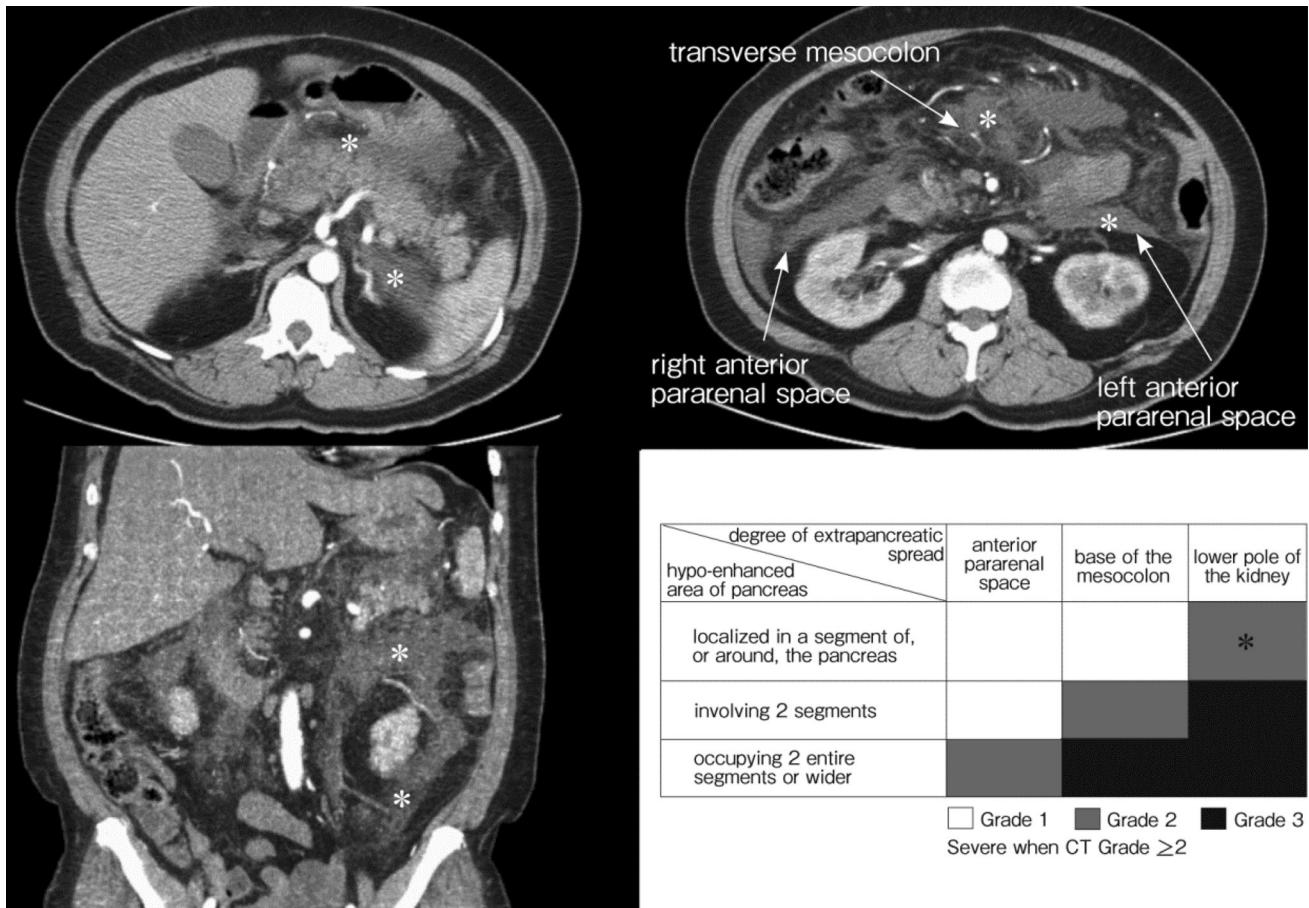


Fig. 17 Severe acute pancreatitis (CT Grade 2). While the entire pancreatic parenchyma is enlarged, no clear hypo-enhanced area is noted. Fat necrosis (*asterisk*) is observed in the transverse mesocolon

and anterior pararenal space and extends beyond the lower pole of the kidney. A diagnosis of severe acute pancreatitis of CT Grade 2 can be made

of inflammation are closely related to the frequency of the occurrence of complications and mortality rate [94, 100], these factors are incorporated in the contrast-enhanced CT grade. For contrast-enhanced CT grading, the pancreatic parenchyma is divided into three segments for convenience, i.e. the head, body, and tail, poorly enhanced areas are regarded as necrotic areas, and the extent of necrotic areas is reflected in the grade. Also, the extent of extra-pancreatic spread of inflammation is added to the assessment as another factor, and the grade elevates as inflammation extends to the anterior pararenal space, to the base of the mesocolon, and to areas beyond the lower pole of the kidney. Advantages of contrast-enhanced CT are its usefulness for the diagnosis of complications such as pseudocysts, abscesses, mesenteric hemorrhage, non-obstructive mesenteric ischemia, false aneurysms, and portal thrombosis [97, 98] and its excellence in delineation of pancreatic duct stenosis due to small pancreatic cancers [101], which may cause acute pancreatitis, in addition to the evaluation of the area of intra- and extra-pancreatic spread mentioned above.

Index words and secondary materials used as references

A search of PubMed was performed using “acute pancreatitis”, “CT”, and “computed tomography” as keywords. Committee for Revision and Publication of the Guidelines for the Management of Acute Pancreatitis: JPN guidelines 2010 ed: Guidelines for the Management of Acute Pancreatitis: JPN guidelines 2010, third edition, 2010 was also used as a reference.

CQ99 Which imaging modalities are appropriate for postoperative follow-up of colorectal cancer?

- Recommendation grade; Contrast-enhanced CT
B
- Recommendation grade; MRI (rectal cancer), PET (PET/CT)
C1

Contrast-enhanced CT is recommended. While the evidence is insufficient, MRI and PET/CT are also useful in some patients and may be considered.

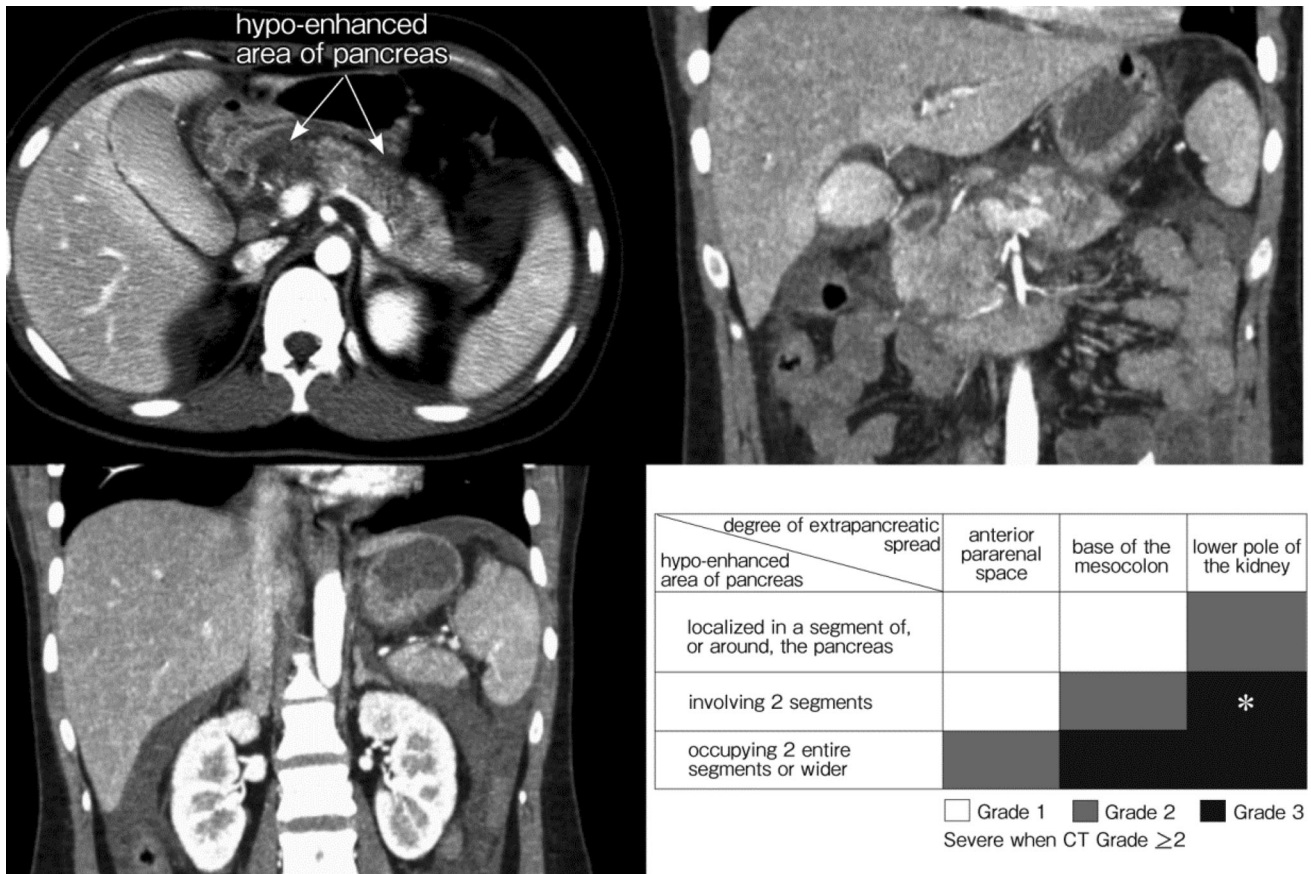


Fig. 18 Severe acute pancreatitis (CT Grade 3). The entire pancreatic parenchyma is enlarged, and hypo-enhanced areas are observed in the body and tail of the pancreas. Fat necrosis (*asterisk*) extends beyond

the lower pole of the kidney, and a diagnosis of severe acute pancreatitis of CT Grade 3 can be made

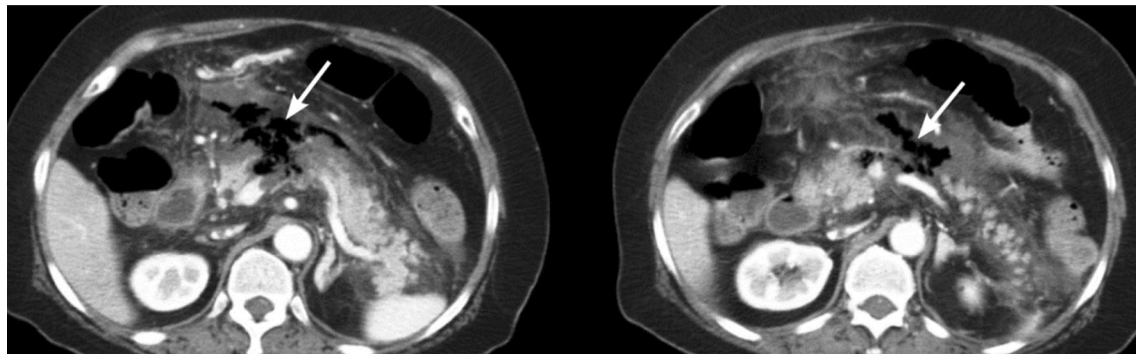


Fig. 19 Infectious pancreatic necrosis. The head of the pancreas is enlarged, and hypo-enhanced areas are observed in the body. Gas (*rightwards arrow*) is noted in the area of necrosis, and infectious pancreatic necrosis was demonstrated by FNA

Background/objective

While the therapeutic results of cancer of the digestive tract are improving, the recurrence rate of advanced cancer remains high. Local recurrence, lymph node metastasis, and metastasis to other organs may be detected early by designed, careful postoperative surveillance. Which imaging modalities are useful for postoperative surveillance of

colorectal cancer was evaluated on the basis of the literature.

Comments

Regarding the method for postoperative surveillance of colon cancer, multiple randomized controlled trials (intensive vs. non-intensive) and their meta-analysis have been

Table 5 Postoperative surveillance methods for colorectal cancer recommended by the JSCCR Guidelines for the Treatment of Colorectal Cancer and international guideline

	JSCCR Guidelines (Stage I mp, Stage II)	JSCCR Guidelines (Stage III)	ASCO	ESMO
Medical interview	Every 3 months for the first 2.5 years and every 6 months thereafter	Every 3 months for the first 3 years and every 6 months thereafter	Every 3–6 months for the first 3 years and every 6 months thereafter	When appropriate
Tumor marker (CEA)	Every 3 months for the first 2.5 years and every 6 months thereafter	Every 3 months for the first 3 years and every 6 months thereafter	Every 3 months (started after the end of chemotherapy in patients undergoing 5FU adjuvant chemotherapy)	When there are symptoms suggestive of recurrence
Chest X-ray	Every 6 months for the first 3 years and annually thereafter	Every 6 months	Chest X-ray is not recommended	When there are symptoms suggestive of recurrence
Chest CT	When necessary	Annually Chest X-ray may be omitted when chest CT is performed	Annually	When there are symptoms suggestive of recurrence
Abdominal US	After 6, 18, and 30 months	After 6, 18, 30, 42, and 54 months	No mention	Annually for 3 years after surgery
Abdominal CT	Annually	Annually	Annually	When there are symptoms suggestive of recurrence
Pelvic CT (rectal cancer)	After 1, 2, 3, and 5 years	Every 6 months for the first 2 years and annually thereafter	Considered for previously unirradiated patients	Not recommended to be performed periodically
Colonoscopy	1 and 3 years after surgery ^a	1, 2, and 3 years after surgery ^a	3 years after surgery and every 5 years thereafter ^b	Every 5 years

^a For the evaluation of anastomotic recurrence, when necessary

^b Flexible sigmoidoscopy performed every 6 months in rectal cancer patients non-irradiated for 5 years

carried out internationally, and the early detection of recurrence was shown to be possible with an improvement in the prognosis in the intensive group [102]. In Western countries, guidelines have been issued successively since 2005, and the Guidelines for the Treatment of Colorectal Cancer prepared for the standardization of the diagnosis and treatment of colorectal cancer were published in Japan, but the surveillance method varies among the guidelines (Table 5).

According to a follow-up study of colorectal cancer patients after curative resection by the Japanese Society for Cancer of the Colon and Rectum, recurrence occurred within 3 years after surgery in 80 % or more, and within 5 years after surgery in 95 %, but more than 5 years after surgery in less than 1 %, of all patients. Recurrence was observed most frequently in the liver, followed by the lung, and locally in the colon. This suggests that surveillance should be continued over 5 years after surgery at shorter intervals during the first 3 years.

The detection rate for resectable lung metastases on postoperative surveillance of colon cancer patients with plain chest radiography is low at about 1 %, and the

modality is not recommended in Western countries for periodic follow-up. Moreover, as it is possible today to scan from the thoracic to pelvic region in one session by multislice CT, the importance of plain chest radiography in surveillance has decreased

According to the ASCO Guidelines, annual thoracoabdominal CT scans are recommended for 3 years after surgery in groups at high-risk for recurrence. The guidelines also recommend that pelvic CT should be considered, particularly for previously unirradiated patients after surgery for rectal cancer. There is a report that the discrimination between post-surgical scarring and recurrent lesions is difficult and that baseline pelvic CT images early after surgery are useful for this purpose [103]. Also, if intrapelvic recurrence is suspected, diffusion-weighted MRI, EUS, and PET/CT of the pelvic region have been reported to be useful [104–108]. The ESMO Clinical Practice Guidelines recommend thoracoabdominal CT examination every 6–12 months over 3 years after surgery for the high-risk group. According to the guidelines, the usefulness of other imaging modalities has not been demonstrated, and

they should be applied only to patients in whom recurrence is suggested by symptoms.

The usefulness of periodic colonoscopy has not been established due to the low incidence of anastomotic recurrence after surgery for colon cancer [109]. In rectal cancer, however, the local recurrence rate is higher than in colon cancer, and there has been a report recommending colonoscopy for surveillance [110]. Recently, the availability of CT-colonography (CTC), which can be performed more easily than colonoscopy, is increasing. The sensitivity and specificity of CTC for the diagnosis of local recurrence of colorectal cancer are reportedly 81.8 and 93.1 %, respectively [110], and contrast-enhanced CTC is expected to be useful for future colorectal cancer surveillance.

See CQ69 for liver metastasis of colorectal cancer.

Index words and secondary materials used as references

A search of PubMed was performed using “colorectal cancer”, “surveillance”, “recurrent”, and “postoperative” as keywords. The ASCO Guidelines 2005, ESMO Clinical Practice Guidelines 2010, NCCN Guidelines 2012, and the Japanese Society for Cancer of the Colon and Rectum ed: JSCCR Guidelines for the Treatment of Colorectal Cancer 2009 were also used as references.

CQ 115 Is diagnostic imaging useful for the diagnosis of uterine sarcoma?

Recommendation grade; B Staging: MRI and CT
Recommendation grade; C1 Qualitative diagnosis: MRI

MRI is recommended for the qualitative diagnosis of uterine sarcoma, although the evidence level is not high. Dynamic contrast-enhanced MRI may also be performed, as it may contribute to the diagnosis. For staging uterine sarcoma, the evaluation by MRI or CT is recommended.

Background/objective

Uterine sarcoma is often difficult to diagnose by cytological examination or biopsy, and it is often problematic to distinguish benign degenerated uterine leiomyomas and uterine sarcomas. Carcinosarcoma is recently considered to be metaplasia of endometrial cancer; however, it is included as uterine sarcoma in many retrospective studies and also included in this evaluation. The usefulness of diagnostic imaging for the preoperative diagnosis and staging of uterine sarcoma is evaluated.

Comments

Ultrasonography, which is the first imaging modality of choice in the gynecologic disorders, was suggested to be useful for the differentiating between uterine leiomyoma and sarcoma in early reports [111], but this could not be confirmed in subsequent studies [112]. MRI has high soft tissue contrast and is useful for the differential diagnosis of uterine masses. Sarcoma was reported to be a large mass with heterogeneous signal intensity due to hemorrhage and necrosis [113]. However, Cornfeld et al. reported that there is no objective criteria in the differentiation between benign and malignant uterine mesenchymal tumors by MRI [114]. Diffusion-weighted imaging is a recent developed technique in which malignant lesions tend to show high intensity because of high cellularity and allows quantitative evaluation by the measurement of the apparent diffusion coefficient (ADC). The diagnostic performance for uterine sarcoma was improved by the measurement of the ADC [115–118] and further accumulation of cases is awaited.

The clinical course and treatment of uterine sarcoma vary with the histological type. Reported MRI features of each histological type helps the diagnosis, although no reports with high evidence level exists due to rarity and lack of large-scale studies of uterine sarcomas. The presence of hemorrhage and necrosis which can be evaluated by MRI signals give clues to the diagnosis of uterine leiomyosarcoma [119] (Fig. 20). Contrast-enhanced MRI is useful for the evaluation of necrosis, and the accuracy has been reported to be improved by dynamic contrast-enhanced MRI with the measurement of LDH isozymes [120]. Endometrial stromal sarcoma exhibits various invasion patterns, and MRI findings such as bands of low signal intensity on T2-weighted imaging and continuous tumor extent along the blood vessels and the ligaments are informative [121]. Carcinosarcoma is difficult to differentiate from uterine body cancer; however, on MRI it is a large mass that dilates the uterine cavity and shows characteristic MRI features such as heterogeneous hyperintensity on T2-weighted imaging, early and persistent enhancement and/or gradual and delayed strong enhancement [122, 123].

Although the clinical staging of uterine sarcoma used to be made similarly to uterine body cancer, a new staging system was established by the FIGO in 2009. The diagnosis of uterine sarcoma may be difficult, however, MRI and CT are recommended for the assessment of local and distant metastasis.

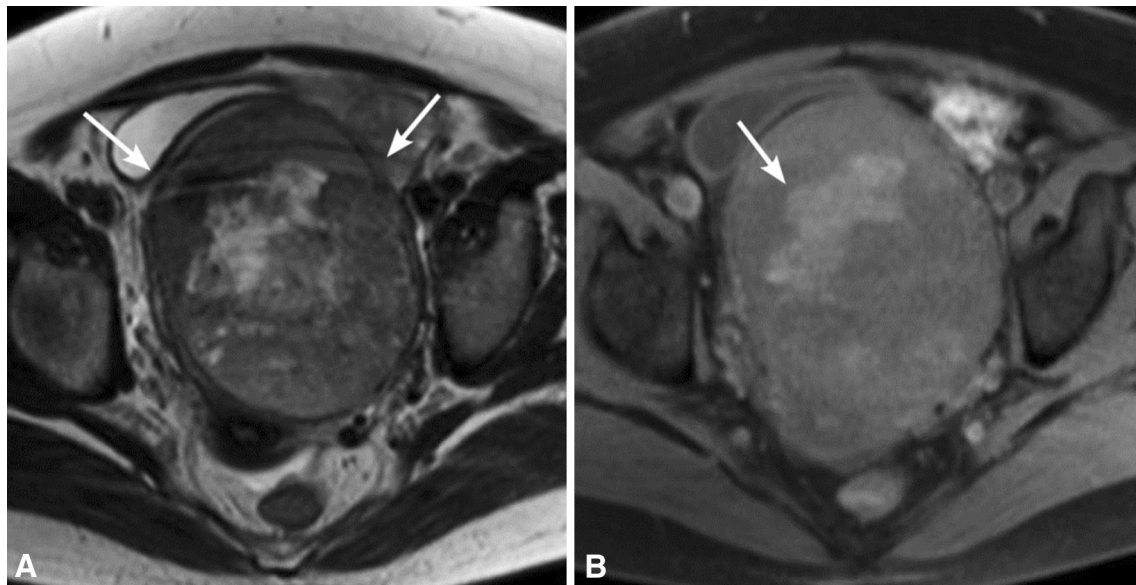


Fig. 20 Uterine leiomyosarcoma. **A** T2-weighted image: a heterogeneously hyperintense mass is observed in the myometrium of the uterine body (*rightwards arrow*). **B** T1-weighted image: Irregular T1

hyperintensities are presented in the mass (*rightwards arrow*), suggesting hemorrhage due to necrosis, and leiomyosarcoma is likely based on the images

Index words and secondary materials used as references

A search of PubMed was performed using “uterine sarcomas”, “endometrial stromal sarcomas”, “uterine leiomyosarcomas”, “uterine carcinosarcomas”, and “diagnostic imaging” as keywords.

CQ123 Is contrast-enhanced CT appropriate for the evaluation of solid renal masses?

Recommendation grade; A	Contrast-enhanced CT (judgment of whether or not a renal mass is solid)
Recommendation grade; B	Dynamic CT (qualitative differentiation of solid renal masses)

Contrast-enhanced CT is strongly recommended for the judgment of whether or not a renal mass is solid.

Dynamic CT is recommended, because clear cell renal cell carcinoma, which accounts for 70–80 % of renal cell carcinomas, can be identified and because a homogeneous appearance suggests a benign entity not requiring surgery.

Background/objective

For the diagnosis of solid renal tumor, the lesion must first be confirmed as a solid mass. Next, the discrimination of whether the lesion is benign or malignant is made. Angiomyolipoma (AML) and renal cell carcinoma (RCC) are the most important differential diagnoses in consideration of their frequency. If the lesion is malignant, it is also desirable to provide information concerning the histological type. Recently, from the viewpoint of molecular

targeted treatment, the differentiation between clear cell RCC and other histological types is important. The usefulness of contrast-enhanced CT for the definitive diagnosis of solid renal mass and differentiation between benign and malignant diseases is evaluated below.

Comments

For the qualitative diagnosis of whether a renal mass is solid or cystic, it is important to perform contrast-enhanced as well as non-contrast CT to examine enhancement characteristics. Formerly, the lesion was judged to be solid when the CT value increased by 10 HU or more between before and after contrast enhancement [124], but, after the advent of helical CT, contrast enhancement is considered definitive with an increase in the CT value of 20 HU or more in consideration of the effect of pseudoenhancement [125]. Also, while the qualitative diagnosis of masses 10 mm or less in diameter is difficult at a slice thickness of 5 mm, the ability to qualitatively diagnose masses 5–10 mm in diameter is markedly improved by the use of thin slices of about 3 mm [126]. If a cyst is strongly suspected after non-contrast CT, usual contrast-enhanced CT (nephrographic phase) suffices. However, if a solid mass is suspected, dynamic CT is recommended to discriminate benign and malignant lesions.

For the discrimination of benign and malignant lesions, AML and RCC are the most important differential diagnoses. AML can usually be diagnosed by the detection of fat density at non-contrast CT, which is more accurate than contrast-enhanced CT for this purpose [127]. The reported

threshold of fat density at non-contrast CT has varied widely from -10 to -40 HU, but the diagnostic ability for AML has recently been reported to be maximum at a threshold of -10 HU [127]. On the other hand, contrast-enhanced CT is useful for the diagnosis of solid tumors except for classic AML that contains fat density. Particularly, the homogeneity and pattern of contrast enhancement at dynamic CT are useful.

First, lesions that show heterogeneous marked enhancement in the corticomedullary phase of dynamic CT can be nearly identified as clear cell RCC, which confirms the malignancy (Fig. 21) [128–135]. Generally, malignant lesions present with heterogeneous contrast enhancement due to hemorrhage or necrosis. In contrast, lesions that are homogeneous at dynamic CT are often benign. For example, AML with minimal fat (fat poor AML, hyperattenuating type) shows a homogeneous appearance after contrast as it consists mostly of muscle components [136, 137] (Fig. 22). This type of AML accounts for about 5 % of all AML and is characterized by hyperdensity (more than 45 HU) compared with the renal parenchyma at non-contrast CT and hypointensity at T2-weighted MRI [136]. Benign tumors such as leiomyoma, metanephric adenoma, and small oncocytoma are also homogeneous on contrast enhanced imaging. Particularly, those that are hyperdense at non-contrast CT and show homogeneous contrast enhancement (hyperattenuating homogeneously enhancing masses) are likely to be benign [137]. However, as malignant tumors such as papillary renal cell carcinoma



Fig. 21 Clear cell RCC contrast-enhanced CT (corticomedullary phase). A mass that shows heterogeneous marked enhancement is observed in the left kidney (*rightwards arrow*). The image is consistent with clear cell RCC



Fig. 22 AML with minimal fat contrast-enhanced CT (nephrographic phase). A homogeneous solid mass (*rightwards arrow*) is observed in the left kidney. It was AML with minimal fat

may also exhibit similar appearances, confirmation by biopsy is recommended [137].

There have been a number of reports that histological classification of RCC is also possible by dynamic CT. RCC has three major histological types: Clear cell type, chromophobe type, and papillary type. Although reports have varied in the dose or infusion rate of the contrast agent, scanning timing, and number of scans, clear cell RCC shows heterogeneous marked enhancement in the corticomedullary phase (about 30 s after the beginning of the contrast agent administration) and show fading in the nephrographic (after about 80–100 s) and early excretory (after about 180–300 s) phases [128–135]. In chromophobe RCC, homogeneous moderate contrast enhancement is observed in the corticomedullary phase, but it diminishes thereafter [128, 129, 132, 135]. Papillary RCC shows only slight contrast enhancement in the corticomedullary phase and is usually gradually enhanced homogeneously to the early excretory phase [128, 130, 132, 134, 135, 138]. These differences in the enhancement pattern reflect angiogenesis of the tumor [128, 139]. Thus, these three major histological types are distinguishable from one another. However, it is important to note that the imaging appearance of oncocytoma resembles those of clear cell and chromophobe RCCs [128, 132–134, 140, 141] and that of metanephric adenoma also resembles that of papillary RCC [128].

Index words and secondary materials used as references

A search of PubMed was performed using “renal”, “tumor”, “CT”, “assessment”, “characteristics”, “differentiation”, “pathologic correlation”, “renal cell carcinoma”,

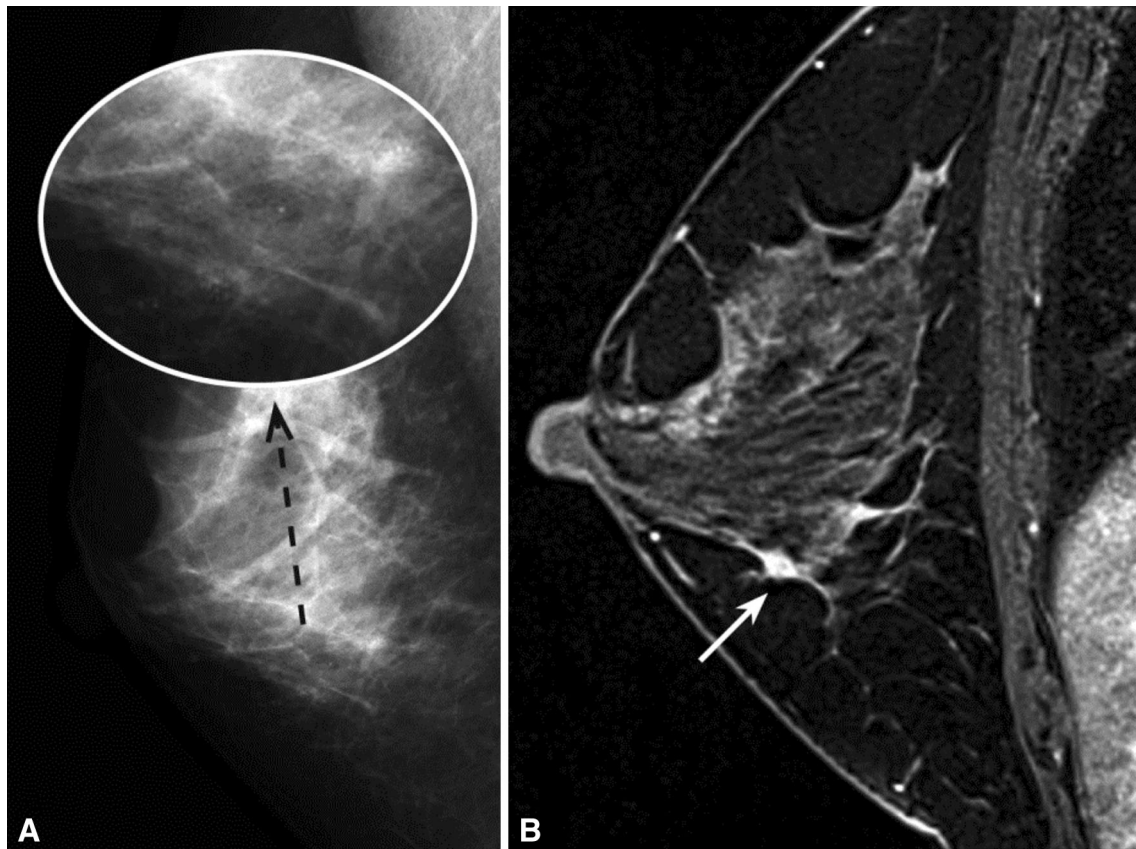


Fig. 23 Calcified lesions of microinvasive carcinoma and MRI. Microcalcification was noted in the L region on screening mammography (a). No abnormality was noted on ultrasonography, but MRI

(b) showed enhancement in the area of calcification (*rightwards arrow*). Surgery was performed after SVAB, and a diagnosis of microvascular carcinoma was made

and “angiomyolipoma” as keywords. The American College of Radiology guidelines (Israel GM et al.: American College of Radiology ACR Appropriateness Criteria® Clinical Condition: Indeterminate Renal Masses. Available at: <http://www.acr.org//media/ACR/Documents/AppCriteria/Diagnostic/IndeterminateRenalMasses.pdf>) was also used as a reference.

CQ132 Is MRI appropriate for the qualitative diagnosis of calcified breast lesions without corresponding abnormalities on ultrasonography?

While scientific evidence is insufficient, implementing MRI as a means for the selection of the therapeutic approach may be considered.

Background/objective

With the increase in the screening rate using mammography, patients in whom calcified lesions requiring further evaluation are detected have been increasing. In Japan, if no abnormality is noted by ultrasonography, stereotactic

vacuum-assisted breast biopsy (SVAB) is performed, but its indications are unclear, and as the availability of the device remains insufficient as it can only be performed at limited facilities. Also, the usefulness of MRI for the evaluation of calcified lesions is controversial, and the position of MRI in the diagnosis and treatment of calcified lesions has not been established (Fig. 23). The usefulness of MRI for the evaluation of calcified lesions was evaluated.

Comments

Reports on the usefulness of MRI for the evaluation of calcified lesions began to appear in the late 1990s, but as the ability of MRI in the qualitative diagnosis of calcified lesions was insufficient, the benefit of MRI was refuted [142]. In the 2000s, the diagnostic ability of MRI was improved due to technical developments, and the recent changes in the clinical procedures associated with the introduction of SVAB have led to increases in reports recommending MRI [143–145].

According to major reports on the ability of MRI for the qualitative diagnosis of calcified lesions published after 2000, the sensitivity was 73–90 %, specificity was 76–100 %, positive predictive value was 73–92 %, negative predictive value was 71–97 %, and the accuracy was 74.5–96 % [143–147]. Only three reports from Japan clearly mentioned that no abnormality was noted on ultrasonography [143–145], and ultrasonography was not mentioned or was not performed in the other reports. The categories of target calcification and diagnostic criteria by MRI also varied among reports.

Among the possible roles of MRI in the diagnosis of calcified lesions, it is expected to be most useful for the selection between SVAB and observation for calcified lesions with no abnormality on ultrasonography. While there have been positive reports that observation is possible if there are no malignant findings on MRI [144, 145], a recent meta-analysis [148] presented a negative view that the negative predictive value of MRI is not sufficiently high to justify avoidance of SVAB.

In conclusion, MRI is not a modality that can replace SVAB, but as it may help with the selection of the therapeutic approach, its implementation may be considered.

Index words and secondary materials used as references

A search of PubMed was performed using “MRI”, “breast”, “screening mammography”, and “microcalcification” as keywords.

CQ150 Is MRI appropriate for the diagnosis of meniscus/cruciate ligament tears of the knee?

MRI is useful for the selection of patients for arthroscopic treatment. It should be performed in combination with clinical examination by an orthopedist.

Background/objective

MRI is frequently used for the diagnosis of tears of the menisci and cruciate ligaments, which are intra-articular structures of the knee. Physical examination by orthopedists is also regularly performed, and some orthopedists undervalue MRI. While arthroscopy is regarded as the most reliable diagnostic method, it is more invasive and expensive than MRI, so MRI is preferable to diagnostic arthroscopy. The usefulness of MRI for the diagnosis of meniscus/cruciate ligament tears was evaluated.

Comments

There have been a number of studies that evaluated the usefulness of physical examination by orthopedists for the

diagnosis of meniscus/cruciate ligament tears of the knee using arthroscopy as a reference standard. According to meta-analyses of these studies, the diagnostic ability varied in individual physical test [149–151], and it was improved by a composite physical examination [149]. There have also been many studies that evaluated the diagnostic ability of MRI (Figs. 24, 25) using arthroscopy as a reference standard. According to a meta-analysis by Oei et al. [152], the sensitivity and specificity of MRI were 93 (92–95) and 88 (85–91) % for the medial meniscus tears, 79 (74–84) and 96

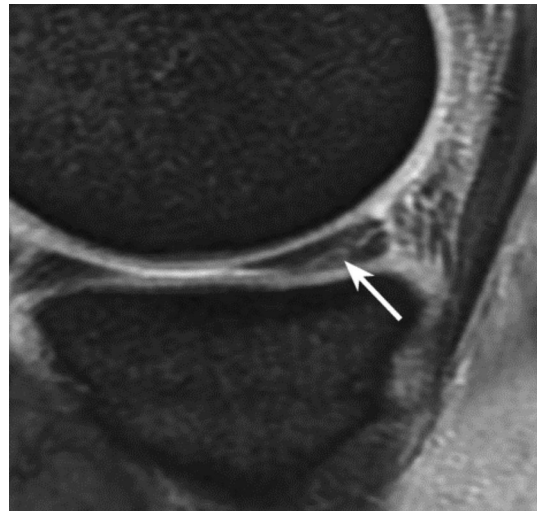


Fig. 24 Horizontal tear of the medial meniscus. Sagittal T2*-weighted image. Linear hyperintensity (*rightwards arrow*) extending to the inferior surface is observed in the posterior horn of the medial meniscus

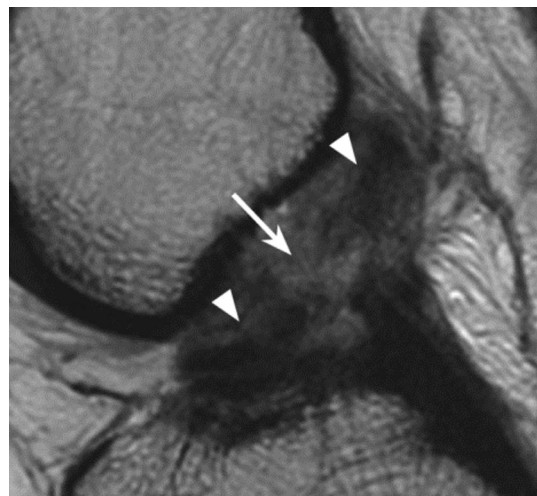


Fig. 25 Complete tear of the anterior cruciate ligament. Sagittal T2-weighted image. The continuity of the anterior cruciate ligament is interrupted in the middle part (*rightwards arrow*) with its fragments swelling, increased in signal intensity, and luxated (*blackup pointing triangle*)

(95–97) % for the lateral meniscus tears, 94 (92–97) and 94 (93–96) % for the anterior cruciate ligament tears, and 91 (83–99) and 99 (99–100) % for the posterior cruciate ligaments tears, respectively. By a meta-analysis by Crawford et al. [153], the sensitivity, specificity, and accuracy of MRI were 91.4, 81.1, and 86.3 % for medial meniscus tears, 76.0, 93.3, and 88.8 % for lateral meniscus tears, and 86.5, 95.2, and 93.4 % for anterior cruciate ligament tears, respectively. MRI shows high diagnostic performance for meniscus/cruciate ligament tears, but its sensitivity is the lowest for lateral meniscus tears, so more attention to subtle findings is necessary in the lateral meniscus than in the medial meniscus or cruciate ligaments. The MR units used in the reports were diverse from 0.1 to 1.5 T systems, but there have been reports suggesting no marked difference in the diagnostic ability according to the magnetic field strength [154, 155]. It must be noted that arthroscopy is not perfect as a reference standard due to some defects: the accuracy is dependent on the examiner's skill, there are areas difficult to examine such as the peripheries and posterior segment of the meniscus, and only the surface of intra-articular clinical structures can be examined.

Regarding whether or not MRI should be performed after clinical examination by an orthopedist, there have been many studies using arthroscopy as a reference standard, most of which suffered a limitation that only patients with clinically suspected meniscus or ligament tears were included. There have been reports that the diagnostic ability of clinical examination were comparable to, or higher than, that of MRI, suggesting a supplemental diagnostic rule of MRI [156–162]. On the other hand, there have also been reports that the diagnostic ability of MRI was higher than that of clinical examination, or that the diagnostic ability was improved by performing MRI [163, 164]. It has also been reported that MRI could reduce the need of diagnostic arthroscopy in 27.3–51.4 % of the patients [165–167]. Vincken et al. [167] evaluated 293 patients who underwent MRI and arthroscopy after orthopedist's examination, observed that the sensitivity and specificity for the selection of patients requiring arthroscopic treatment were 93.2 and 79.2 %, respectively, and 87.3 and 88.4 % after adjustment for verification bias, and concluded that MRI was useful for the selection of patients for arthroscopic treatment.

For the diagnosis of meniscus/cruciate ligament tears, it is recommended to perform MRI in combination with clinical examination by an orthopedist rather than alone. It is useful for reducing diagnostic arthroscopy and selecting patients who require arthroscopic treatment.

Index words and secondary materials used as references

A search of PubMed was performed using “knee”, “meniscus injury”, “meniscus tear”, “ligament injury”,

“ligament tear”, “MRI”, and “arthroscopy” as keywords. Medina LS and Blackmore C eds: Evidence-Based Imaging: Optimizing Imaging in Patient Care 2011 was also used as a reference.

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