Breast Cancer
DOI 10.1007/s12282-016-0674-7

The Japanese Breast Cancer Society clinical practice guidelines for screening and imaging diagnosis of breast cancer, 2015 edition

Mitsuhiro Tozaki[1] · Yoshifumi Kuroki[2] · Mari Kikuchi[3] · Yasuyuki Kojima[4] · Kazunori Kubota[5] · Hiroshi Nakahara[6] · Yoshinori Ito[7] · Hirofumi Mukai[8]

Received: 24 November 2015 / Accepted: 11 December 2015

Introduction

In the 2015 edition of Clinical Practice Guidelines for screening and imaging diagnosis of breast cancer, the major revisions were as follows;

- The recommended grade in screening CQ2 was updated.
  CQ2. Is screening mammography recommended for subjects aged 50 years or older? (Recommended from grade A to B).
- Screening CQ4 was newly described.
  CQ4. Is digital breast tomosynthesis recommended for breast cancer screening? (Recommended grade C1).
- The recommended grade in screening CQ6 was updated.
  CQ6. Is breast cancer screening with non-contrast MRI including diffusion-weighted imaging recommended? (Recommended from grade C2 to D).
- Contents of imaging diagnosis CQ3 (formerly, imaging diagnosis CQ2) were updated.
  CQ3. Is ultrasonography recommended as a tool for differential assessment of benignancy/malignancy of mass or non-mass lesions of the breast? (Mass lesions;Recommended grade B, non-mass lesions;Recommended grade C1).
- Contents of CQ and recommended grade in imaging diagnosis CQ9 have been modified.
  CQ9. Are liver ultrasonography, chest and abdominal CT, bone scintigraphy, and FDG-PET recommended as preoperative examinations?
  Liver ultrasonography, chest and abdominal CT, bone scintigraphy, and FDG-PET are recommended as preoperative examinations (staging) in patients with stage I or II initial primary breast cancer presenting with symptoms and/or findings indicative of distant metastasis and in patients with stage III initial primary breast cancer. (Recommended from grade C1 to B).
- Imaging diagnosis CQ10 has been modified with respect to the recommended grade in CQ.
  CQ10. Is imaging diagnosis recommended for evaluation of axillary lymph nodes?
  Ultrasonography is recommended for preoperative evaluation of the axillary lymph node. (Recommended from grade C1 to B).

This article is an English digested edition of the Clinical Practice Guideline of Breast Cancer 2015, published by Kanehara & Co., Ltd. Details of recommendation grades were explained in the previous report(Breast Cancer. 2015;22:1–4).

✉ Mitsuhiro Tozaki
e-tozaki@keh.biglobe.ne.jp

[1] Department of Radiology, Sagara Hospital Affiliated Breast Center, 3-28 Tenokuchi-cho, Kagoshima 892-0845, Japan

[2] Department of Radiology, Niimura hospital, Kagoshima, Japan

[3] Department of Diagnostic Radiology, National Cancer Center Hospital, Tokyo, Japan

[4] Division of Breast and Endocrine Surgery, Department of Surgery, St. Marianna University School of Medicine, Kanagawa, Japan

[5] Department of Medical Informatics, Tokyo Medical and Dental University Hospital, Tokyo, Japan

[6] Department of Radiology, Breastopia Miyazaki Hospital, Miyazaki, Japan

[7] Department of Breast Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

[8] Department of Oncology/Hematology, National Cancer Center Hospital East, Chiba, Japan

Published online: 06 April 2016

For reference

Categorization in the Japanese mammography guidelines and those of the Breast Imaging Reporting and Data System.

The Breast Imaging Reporting and Data System (BI-RADS) developed by the American College of Radiology (ACR) as a standardized quality assessment tool for drawing up imaging findings and reports is universally recognized. In Japan, the "Guidelines for Mammography" complied on the basis of the 2nd edition of BI-RADS were published in 1999. According to those guidelines, mammogram findings are finally assessed for malignancy using 5 grading categories, i.e., category 1 or 2 requiring no additional detailed examination and categories 3–5 warranting further detailed examinations.

The 5th edition of BI-RADS [1], on the other hand, is designed to provide a general flow of the breast cancer screening process as follows: lesions presenting screening-identified mammographic findings based on which malignancy cannot be negated are classified into category 0 and subjected to detailed examination performed later, i.e., additional mammography and ultrasonography at the initial screening site; if no malignant findings are noted in the detailed examination, the lesion is classified into category 1 or 2; if findings are probably benign (malignancy level: $\leq$2 %) requiring a follow-up at 6 months later, the lesion is classified into category 3; or if a higher malignancy level is suspected, the lesion is classified into category 4 or 5, warranting histopathological examination.

It is often the case in Japan at present that screening and the subsequent medical workup are conducted at different facilities, so that radiologists and other physicians at the latter sites may experience some difficulty in referring to screening mammograms. Eventually, it is considered necessary for precise control of accurate screening in Japan to classify lesions presenting findings that correspond to BI-RADS category 0 into categories 3–5. However, it is an obvious fact in this country that categorization in the worldwide spread of BI-RADS and the categorization unique to Japan are concurrently effective, causing a great deal of confusion. Inasmuch as the positive predictive value for category 3 substantially differs between these two systems, it is necessary to particularly convert pertinent data into BI-RADS categories in transmitting data generated in Japan to overseas. Furthermore, the policy in clinical practice for category 3 cases entirely differs as to whether the patient is to be followed by checkups or, otherwise, to be subjected to detailed examinations. Further measures such as terminological modifications and consensus building are considered needed in Japan.

Screening

CQ1. Is breast cancer screening by clinical breast examination alone recommendable?

Recommendations

Screening for breast cancer by clinical breast examination alone is not recommended (Grade D).

Japan is the only country in which breast cancer screening solely based on clinical breast examination has been extensively performed. The odds ratio of a group of subjects receiving a screening within 1 year from the day on which the subject was diagnosed as having breast cancer is 0.93 (95 % CI: 0.48–1.79) and there was no mortality rate-reducing effect according to a case–control study in Japan [2].

The outcome of breast cancer is relatively favorable even in a patient who has begun treatment after subjectively noticing a palpable mass, and screening by clinical breast examination alone is thus considered to be of some definite significance including an enlightening effect, though its sensitivity is low, in a stage of social maturation which has not progressed as far as it could; however, it will not surpass imaging-based screening in terms of assessment effectiveness.

CQ2. Is screening mammography recommended for subjects aged 50 years or older or for subjects in their forties?

Recommendations

Mammographic screening for breast cancer in women aged 50 years or older is recommended (Grade B).

Mammographic screening for breast cancer in women in their forties is recommended (Grade B).

Recommendation for screening mammography in women aged 50–74 years is ranked Grade "B" in the 2009 version of the U.S. Preventive Services Task Force (USPSTF) [3]. The mortality-reducing effect in women aged 50–59 years was RR: 0.86 (95 % CI: 0.75–0.99) according to results of a meta-analysis of data from six representative randomized controlled studies, and the mortality-reducing effect in women aged 60–69 years was RR: 0.68 (95 % CI: 0.54–0.87) according to results of a meta-analysis of data from two randomized controlled studies. There was no appreciable mortality-reducing effect in women aged 70–74 years (RR: 1.12; 95 % CI: 0.73–1.72) though these data were from a single study.

Mammographic screening in women 50 years of age or older is widely conducted in Europe and the U.S.: in Japan, the Ministry of Health, Labour and Welfare issued a

circular notice to the effect that mammographic screening would be a standard method of breast cancer screening in subjects from the age of 50 or older, effective from 2000 on. In recent years, however, over-diagnosis has been and is still subject to lively controversy as a disadvantage of screening by mammography [4]. The definition thereof consists not in false positive on screening but in discovery and treatment of breast cancer that has no impact on the vital prognosis even without administering treatment. Physicians should be cognizant of the presence of over-diagnosis in conducting breast cancer screening and provide relevant information to subjects undergoing the screening.

In the USPSTF 2009 recommendation statement, screening mammography in individuals of ages between 39 and 49 years is placed as a Grade C recommendation [3]. Screening mammography is considered to have relatively high usefulness in such a subpopulation because the breast cancer incidence rate peaks in individuals in the latter half of their forties in Japan. Nationwide surveys are yet to be made, but it is infeasible under the present circumstances to directly apply in Japan those interpretations based on Europe/US data as they are; therefore, it is considered appropriate to continue the use of the current recommendations for the time being.

CQ3. Is digital mammography equally as recommendable as screen film mammography in screening for breast cancer?

Recommendations

In the screening for breast cancer, digital mammography is equally as strongly recommendable as screen film mammography (Grade A).

Currently, the use of the digital mammography method is increasing rapidly. The Digital Mammographic Imaging Screening Trial (DMIST) was designed to measure clinically important differences in diagnostic accuracy between digital and film mammography [5]. A total of 49,528 asymptomatic women presenting for screening mammography at 33 sites in the U.S. and Canada underwent both digital and film mammography. In the entire population, the diagnostic accuracy of digital and film mammography was similar (difference between methods in the area under the ROC curve, 0.03; 95 % confidence interval, −0.02 to 0.08; $p = 0.18$). However, the accuracy of digital mammography was significantly higher than that of film mammography among women under the age of 50 years (difference in the area under the curve, 0.15; 95 % confidence interval, 0.05–0.25; $p = 0.002$), women with heterogeneously dense or extremely dense breasts on mammography (difference, 0.11; 95 % confidence interval, 0.04–0.18; $p = 0.003$), and premenopausal or perimenopausal women (difference, 0.15; 95 % confidence interval, 0.05–0.24; $p = 0.002$).

CQ4. Is digital breast tomosynthesis recommended for breast cancer screening?

Recommendations

There are not sufficient grounds for recommending breast cancer screening with digital breast tomosynthesis as yet (Grade C1).

There have been many published reports of large-scale studies comparing diagnostic performance of two-dimensional (2D) mammography and digital breast tomosynthesis (DBT). A plurality of screening trials as prospective clinical studies are in progress worldwide, from which preliminary reports of two of those trials have been published. In the Oslo Tomosynthesis Screening Trial (OTST) reported from Oslo covering 12,631 women [6], comparison of a 2D mammography group and a 2D mammography+DBT group revealed that the breast cancer detection rate was increased by 27 % (or by 40 % for invasive cancer in particular) and the recall rate decreased by 15 % as a result of application of DBT. In a study reported from Italy (Screening with Tomosynthesis OR standard Mammography; STORM) in 7292 women [7], the recall rate was reduced by 17.2 %. These preliminary findings suggest the need of randomized controlled trials. Use of DBT in the screening would be anticipated for subjects with dense breasts and those with breast cancer risk. Standard criteria will have to be set up for ascertaining in what individuals DBT screening be undertaken.

CQ5. Is breast cancer screening mammography with concomitant echography recommended?

Recommendations

There are not sufficient grounds for recommending breast cancer screening by ultrasonography as yet (Grade C1).

Mammography is an effective method of breast cancer screening with a proven mortality rate-reducing effect, but it cannot be denied that the effectiveness of mammography is relatively low in cases of dense breasts and in young women. At present, however, ultrasonography lacks rational grounds for its effectiveness and is not recommended as a tool for population-based (organized) screening [8, 9]. Its application as an ancillary optional screening tool for mammographic screening of dense breast cases and young women is expected. In such instances, nevertheless, subjects to be examined should be given an explanation about the disadvantages such as the potential need for an expensive complete medical workup.

CQ6. Is breast cancer screening with non-contrast MRI including diffusion-weighted imaging recommended?

Recommendations

As it cannot be said that there are sufficient scientific grounds for breast cancer screening with non-contrast MRI, including diffusion-weighted imaging, it is not recommendable to implement such a program (Grade D).

Greater improvement of diagnostic performance of non-contrast MRI may be expected as compared to mammography, but no comparative high-level evidence trial has as yet been conducted. Radiographic methods and diagnostic criteria in diffusion-weighted imaging should be standardized in order to use diffusion-weighted imaging for breast cancer screening. The ground for demonstrating the usefulness of diffusion-weighted imaging in cases of asymptomatic non-palpable lesions subject to screening is insufficient at present [10]. Therefore, breast cancer screening with non-contrast MRI, including diffusion-weighted imaging, cannot be recommended.

CQ7. Is FDG-PET recommended for breast cancer screening?

Recommendations

FDG-PET is not recommendable for breast cancer screening (Grade D).

There has been no evidence shown to enable a definitive judgment as to whether screening with FDG-PET has any breast cancer mortality rate-reducing effect or not. Furthermore, the breast cancer detection rate by screening with FDG-PET is lower than that by the current breast cancer screening with mammography combined with clinical breast examination [11]. In addition, a FDG-PET is extremely expensive, and this procedure has the disadvantage of entailing systemic exposure. Therefore, FDG-PET is not useful as a screening method for breast cancer.

Diagnosis

CQ1. Is diagnostic mammography recommended in young women?

Recommendations

Diagnostic mammography performed with meticulous care may be considered, although there are as yet no sufficient scientific grounds for application of diagnostic mammography in young women (Grade C1).

Application of this procedure in the clinical practice setting should be judged taking into consideration the lower breast cancer incidence rate for women under 30 or 35 years of age as compared to women in their forties or fifties, and also with an understanding of the merits and drawbacks of this diagnostic modality [12, 13].

CQ2. Is ultrasonography recommended as a means for breast cancer detection in the clinical practice setting?

Recommendations

Ultrasonography is recommended for patients in whom mammography and palpation have failed to detect abnormalities (Grade B).

Relatively not much importance has been attached to ultrasonographic diagnosis in Europe and the U.S., both of which have a long history of mammography; however, ultrasonography is gradually being seen in a new light in recent years with the improvement of ultrasonographic diagnostic apparatus and diagnostic techniques.

It has been reported that a large-scale multicenter prospective study using ultrasonography and mammography for breast cancer screening (Study ACRIN6666) demonstrated that discoveries of breast cancer increased by 1.1–7.2 persons per 1000 and the false positive rate also increased as a result of concomitant application of ultrasonography [14]. In Japan as well, concomitant application of ultrasonography in breast cancer screening is currently being investigated and a large-scale clinical study [15] is in progress. The study is probably the largest randomized clinical study in the world, with more than 75,000 subjects enrolled besides introduction of the accuracy control of ultrasonography. Results of the study will strongly influence the future trend of breast ultrasonography.

CQ3. Is ultrasonography recommended as a tool for differential assessment of benignancy/malignancy of mass or non-mass lesions of the breast?

Recommendations

The performance of ultrasonography is recommended for diagnostic differentiation between benign and malignant mass lesions of the breast (Grade B).

The performance of ultrasonography with meticulous care may be considered although there is no sufficient

scientific ground as yet for diagnostic differentiation between benign and malignant non-mass lesions. (Grade C1).

The BI-RADS for Ultrasound [16] provides information to enable standardization of terms of imaging findings and homogeneous diagnosis, and it has been reported that the true positive ratio is 71.3 %, the positive predictive value 67.8 %, and the negative predictive value 92.3 % in the diagnostic differentiation between benignancy and malignancy of solid masses of the breast [17, 18]. However, although the diagnostic validity is high for masses greater than a certain size, there are noticeable differences in interobserver findings as to small lesions where the accuracy of diagnosis is in no way high [19, 20]. Further improvement of accuracy through the further technical development of instruments/apparatus with microlesions in view and introduction of new applications is expected.

Further, terms for non-mass lesions are not clearly defined in BI-RADS. For example, a hypoechoic area may be placed under the category of non-mass lesions in Japan while it is frequently classified as an ill-defined hypoechoic mass overseas [21]. There are only limited reports dealing with categorization of non-mass lesions at present [22, 23], so that terminological assessments and multicenter studies seem to be needed to provide a highly reproducible categorization scheme. Particularly, the necessity to check and improve consistency between the Japanese guideline and BI-RADS is considered as extremely urgent.

CQ4. Is flow imaging in ultrasonography recommendable for diagnostic differentiation between benignancy and malignancy of mass lesions?

Recommendations

Flow imaging in ultrasonography performed with meticulous care may be considered although there is no sufficient scientific ground as yet for diagnostic differentiation between benign and malignant mass lesions (Grade C1).

Flow imaging (a general term for tumor vascularity, Doppler, contrast enhanced ultrasonography, etc.) is installed as a standard device in virtually all breast echography systems but there are no established diagnostic criteria. Further, examination by flow imaging involves measurement errors due to performance and setting of the system parameters or variations in the operator's technical skill that cannot be disregarded. Such errors are magnified particularly when studying microlesions. Necessary requirements remain, such as improvement of precision of the apparatus, standardization of the settings, and accuracy control of the examination technique [24].

CQ5. Is elastography in ultrasonographic examination recommendable for diagnostic differentiation between benignancy and malignancy of mass lesions?

Recommendations

Elastography performed with meticulous care in ultrasonographic examination may be considered although there are no sufficient scientific grounds for diagnostic differentiation between benignancy and malignancy of mass lesions as yet (Grade C1).

Tissue elasticity imaging is a novel technology most deserving of special mention in the latest diagnostic ultrasonographic instrumentation. Elastography is a new technique, the use of which has rapidly become widespread in recent years, and many recent prospective clinical study reports have shown the usefulness of the elasticity score as well as of the elasticity index, and indicated that specificity was improved by concomitant elastography in ultrasonographic examination of women in whom a medical workup was recommended as a result of screening. This modality has been being recognized as a clinically useful technique [25–28]. However, the problem of operator dependency is also a point at issue [29], so there are matters yet to be resolved such as verification of the extent of operator dependency involvement.

Furthermore, ultrasound elastography utilizing acoustic radiation force impulse (ARFI) technology and a technique whereby the propagation velocity of shear waves generated within a tissue is measured have been reported in recent years [30–35]. This technique is expected to entail less operator dependency and is currently under assessment for clinical usefulness. In the future, usefulness of the following three techniques, each applied alone or two or more applied in combination, will have to be assessed and verified: elasticity imaging that allows manual strain analysis, elastography utilizing ARFI, and hardness analysis using shear wave velocity.

CQ6. Are CT and MRI recommended in determining diagnosis and treatment policies for intra-breast lesions?

Recommendations

1. MRI is recommended in determining diagnosis and treatment policies for intra-breast lesions (Grade B).
2. CT is not recommended in determining diagnosis and treatment policies for intra-breast lesions (Grade D).

It is rather uncommon that MRI is performed in determining diagnosis and treatment policies for intra-breast

lesions in the clinical practice setting where the indication for biopsy is determined according to categorization of respective examination procedures in the case of a lesion identified by mammography or ultrasonography and the lesion is subjected to imaging-guided biopsy. However, MRI obviously has higher diagnostic performance than mammography and ultrasonography and is considered useful in such cases where it is difficult to decide definitively on the indication for biopsy due to inconsistencies among clinical findings and mammographic and ultrasonographic findings or where it is difficult to perform imaging-guided biopsy by mammography or ultrasonography. In the EUSOBI guideline as well, evaluation of lesions of which diagnosis by mammography or ultrasonography is inconclusive constitutes an indication for MRI [36].

Meanwhile, there is no published study demonstrating superiority in diagnostic performance of CT to mammography and ultrasonography. The grounds, on which the verification of the usefulness of CT in determining the diagnosis and treatment policies for intra-breast lesions can be based, are therefore insufficient. Furthermore, CT has a major drawback in that any attempt to conduct a dynamic study for kinetic analysis of lesions will eventually lead to increased exposure to X-rays, so that performance of CT for determining diagnosis and treatment policies for intra-breast lesions cannot be recommended.

CQ7. Are CT and MRI recommended for diagnosing the extent of breast cancer?

Recommendations

1. MRI is recommended for diagnosing the extent of breast cancer (Grade B).
2. CT may be more effective than conventional clinical findings, mammography and ultrasonography in diagnosing the extent of breast cancer prior to breast-conserving surgery in patients in whom MRI cannot be performed (Grade C1).

It has been documented in many papers that the diagnostic validity of MRI breast cancer extent assessment is higher as compared to mammography and ultrasonography. In recent years, however, a report has appeared demonstrating no significant difference in the percentage of cases requiring reoperation (19 vs 19 %) between a group of MRI-examined patients ($n = 816$) and a non-MRI-examined patient group ($n = 807$) [37]. It has been pointed out, nevertheless, that the percentage of cases requiring reoperation substantially varies among medical institutions [38] and that information gained by MRI scanning with the patient in the prone position may not be correctly reflected in breast-conserving surgery. Subsequently, an additional report has been published indicating the usefulness of preoperative MRI in a study that employed the percentage of cases requiring reoperation as an endpoint [39] as well as a report not indicating the usefulness of preoperative MRI [40], so further accumulation of pertinent data is anticipated.

There is no certain evidence at present to indicate that breast MRI scanning should be performed as a routine preoperative examination in cases of breast-conserving surgery. The usefulness of preoperative MRI as evaluated using the percentage of cases requiring reoperation as an endpoint is currently subject to worldwide controversy. However, it is unquestionably clear that MRI is superior to any other imaging examinations in respect of accuracy of diagnosis of the extent of breast cancer.

It is a noticeable characteristic feature of medical practice in Japan that contrast enhanced CT has been frequently adopted in the evaluation of the extent of breast cancer [41]. However, it has been reported that CT and MRI are virtually comparable in terms of diagnostic specificity but the former is significantly lower in sensitivity and in accurate diagnosis rate [42, 43]. Contrast enhanced CT may have potential usefulness in preoperatively diagnosing the extent of breast cancer in patients in whom MRI cannot be performed due to claustrophobia, implanted metal devices, or adverse reactions to contrast medium.

CQ8. Is MRI recommended for detecting multifocal breast cancer undetectable by mammography and ultrasonography?

Recommendations

MRI is recommended for detecting multifocal breast cancer which is undetectable by mammography and ultrasonography (Grade B).

The usefulness of MRI in detecting multifocal breast cancer that cannot be detected by mammography and ultrasonography has been recognized from early on in Europe and the U.S. Therefore, stress has been placed on the need for an MRI-guided biopsy from the first half of the 1990s, and the procedure is stated as an essential technique in the European and U.S. guidelines [36, 44]. A unicenter study with MRI-guided biopsy in Japan showed that the frequency with which breast cancer was detected was 33 % (34/102) [45]. Currently, measures to cope with lesions detectable only by MRI should be examined since MRI-guided biopsy is not included in the category of techniques acceptable for national health insurance reimbursement in this country.

CQ9. Are liver ultrasonography, chest and abdominal CT, bone scintigraphy, and FDG-PET recommended as preoperative examinations?

Recommendations

1. Liver ultrasonography, chest and abdominal CT, bone scintigraphy, and FDG-PET are not recommended as preoperative examinations (staging) in patients with stage I or II initial primary breast cancer presenting with no symptoms or findings indicative of distant metastasis (Grade C2).
2. Liver ultrasonography, chest and abdominal CT, bone scintigraphy, and FDG-PET are recommended as preoperative examinations (staging) in patients with stage I or II initial primary breast cancer presenting with symptoms and/or findings indicative of distant metastasis and in patients with stage III initial primary breast cancer (Grade B).

The usefulness of bone scintigraphy, liver ultrasonography, and FDG-PET as preoperative examinations (staging) of stage I to II initial primary breast cancer with low incidence of distant metastasis is insignificant. However, bone scintigraphy, liver ultrasonography, and FDG-PET (including PET/CT) may be considered in such patients who present with metastasis-related clinical manifestations such as localized bone pain or abdominal symptoms or who show blood biochemical test abnormalities such as elevation of alkaline phosphatase and hepatic dysfunction as well as in patients with stage III or more advanced breast cancer with a high risk of distant metastasis [46–48].

CQ10. Is imaging diagnosis recommended for evaluation of axillary lymph nodes?

Recommendations

1. Ultrasonography is recommended for preoperative evaluation of the axillary lymph node (Grade B).
2. Application of CT or PET solely for the purpose of evaluating axillary lymph nodes is basically not recommended because scientific grounds for their application seem to be insufficient (Grade C2).

Sporadic reports have described the superior diagnostic sensitivity of axillary lymph node evaluation by means of ultrasonography, CT, or FDG-PET, and the accurate diagnosis rate with these modalities is higher as compared to palpation. All these procedures have relatively high image-diagnostic specificity and therefore are considered amply applicable in the clinical setting [49, 50]. Nevertheless, omitting sentinel node biopsies solely on account of negative findings in diagnostic imaging should be avoided, as well as the selection of axillary regional lymphadenectomy just because of positive findings in diagnostic imaging. There are no ample grounds for recommending the application of CT or FDG-PET, besides ultrasonography, for the sole purpose of axillary lymph node evaluation [51, 52].

CQ11. Is imaging diagnosis more useful than a clinical breast examination in interpreting therapeutic responses to neoadjuvant chemotherapy?

Recommendations

Evaluation by imaging diagnosis is more recommended than clinical breast examination in interpreting therapeutic responses to neoadjuvant chemotherapy. However, no conclusions have been reached yet as to the selection of the proper modality or modalities, and the proper evaluation protocol (Grade B).

Recognition of imaging diagnosis is emerging as a tool for early prediction of clinical responses to neoadjuvant chemotherapy and has obviously greater usefulness than a clinical breast examination [53]. However, the accuracy control of image-diagnosis instruments in evaluating neoadjuvant chemotherapy is still not sufficient. Studies are currently in progress regarding not merely dimensional but also morphologic changes in tumors, changes in image pattern, changes on diffusion-weighted imaging, and the like, so that no conclusions have been reached yet as to selection of the proper modality (or modalities) and appropriate evaluation protocol. Study of the results of further investigations will clarify the usefulness and techniques of imaging modalities, timing of image evaluation, and so on.

CQ12. Is FDG-PET recommended at least for detecting postoperative recurrence and metastasis of breast cancer in patients suspected to have some signs of recurrence?

Recommendations

FDG-PET is recommended for detecting postoperative local recurrence and metastasis in breast cancer patients with positive clinical test findings (Grade B).

FDG-PET is not recommended as a post-breast surgery routine examination. However, FDG-PET is commonly performed as a tool for identifying metastasis and determining treatment policies in patients suspected to have recurrence from physical findings, other imaging examinations, or tumor markers and in those with a proven local recurrence: FDG-PET is considered useful in such patient groups [54–56].

CQ13. Is biopsy recommended in cases of distant recurrence?

Recommendations

1. A biopsy is recommended in the case of a lesion likely to be a distant recurrence lesion which cannot be concluded to be of breast cancer origin (Grade A).
2. Biopsies performed with meticulous care may be considered, though lacking in sufficient scientific grounds as yet, in the case of a lesion likely to be a distant recurrence lesion which can be concluded to be of breast cancer origin where ER, PgR, and HER2 of the primary lesion are unknown or where relevant laboratory test data are not really reliable (Grade B).

Whilst a biopsy should be considered in the case of a lesion which cannot be definitively identified as being a distant recurrence of a breast cancer lesion, treatment may be brought forward without conducting a biopsy if the lesion is conclusively a distant recurrence lesion and if immunohistochemical data concerning the primary lesion are reliable. However, a biopsy of the distant recurrence lesion may have to be considered whenever feasible if ER, PgR, and HER2 data at the initial surgery are unknown or not considered reliable [57–60].

In conducting a biopsy, the benefits and disadvantages should be fully taken into account and patient pain and complications must be minimized. A biopsy should be performed only when the patient has been given an adequate explanation of his/her disease condition and in cooperation with other related departments. Since facilities available for the safe conduct of biopsies of distant recurrence lesions are limited, such a facility should be entrusted with carrying out the biopsy without hesitation if the current facility lacks any of the capability or capacity for carrying out biopsies.

Compliance with ethical standards

Conflict of interest Yoshinori Ito received a research funding from Novartis, Chugai, Parexel, Esai, Sanofi, Taiho, EPS, Dai-ichi-sankyo, and Boehringer-ingelheim, and received manuscript fees from Chugai, Esai and Novartis.

References

1. Breast imaging reporting and data system (BI-RADS) atlas. 5th ed. Reston: American College of Radiology; 2013.
2. Kanemura S, Tsuji I, Ohuchi N, Takei H, Yokoe T, Koibuchi Y, et al. A case control study on the effectiveness of breast cancer screening by clinical breast examination in Japan. Jpn J Cancer Res. 1999;90(6):607–13.
3. Screening for breast cancer:U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2009;151(10):716–726.
4. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening:an independent review. Lancet. 2012;380(9855):1778–86.
5. Pisano ED, Gatsonis C, Hendrick E, Yaffe M, Baum JK, Acharyya S, Digital Mammographic Imaging Screening Trial(DMIST)Investigators Group, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med. 2005;353(17):1773–83.
6. Skaane P, Bandos AI, Gullien R, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. Radiology. 2013;267(1):47–56.
7. Ciatto S, Houssami N, Bernardi D, et al. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM). Lancet Oncol. 2013;14(7):583–9.
8. Teh W, Wilson AR. The role of ultrasound in breast cancer screening. A consensus statement by the European Group for Breast Cancer Screening. Eur J Cancer. 1998;34(4):449–50.
9. Gartlehner G, Thaler K, Chapman A, Kaminski-Hartenthaler A, Berzaczy D, Van Noord MG, et al. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. Cochrane Database of Syst Rev 2013;(4): CD009632. doi:10.1002/14651858.CD009632.pub2.
10. Tozaki M, Fukuma E. 1H MR spectroscopy and diffusion weighted imaging of the breast:are they useful tools for characterizing breast lesions before biopsy? AJR Am J Roentgenol. 2009;193(3):840–9.
11. Kojima S, Zhou B, Teramukai S, Hara A, Kosaka N, Matsuo Y, et al. Cancer screening of healthy volunteers using whole-body 18F-FDG-PET scans: the Nishidai clinic study. Eur J Cancer. 2007;43(12):1842–8.
12. Bassett LW, Ysrael M, Gold RH, Ysrael C. Usefulness of mammography and sonography in women less than 35 years of age. Radiology. 1991;180(3):831–5.
13. Osako T, Iwase T, Takahashi K, Iijima K, Miyagi Y, Nishimura S, et al. Diagnostic mammography and ultrasonography for palpable and nonpalpable breast cancer in women aged 30–39 years. Breast Cancer. 2007;14(3):255–9.
14. Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, ACRIN 6666 Investigators, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. JAMA. 2008;299(18):2151–63.
15. Ishida T, Suzuki A, Kawai M, Narikawa Y, Saito H, Yamamoto S, et al. A randomized controlled trial to verify the efficacy of the use of ultrasonography in breast cancer screening aged 40-49 (J-START): 76 196 women registered. Jpn J Clin Oncol. 2014;44(2):134–40.
16. American College of Radiology. BI-RADS:ultrasound, 2nd ed. In:Breast imaging reporting and data system:BI-RADS atlas, 5th ed. Reston:American College of Radiology; 2013.
17. Costantini M, Belli P, Lombardi R, Franceschini G, Mulè A, Bonomo L. Characterization of solid breast masses:use of the sonographic breast imaging reporting and data system lexicon. J Ultrasound Med. 2006;25(5):649–59.
18. Hong AS, Rosen EL, Soo MS, Baker JA. BI-RADS for sonography:positive and negative predictive values of sonographic features. AJR. 2005;184(4):1260–5.
19. Abdullah N, Mesurolle B, El-Khoury M, Kao E. Breast imaging reporting and data system lexicon for US:in-terobserver agreement for assessment of breast masses. Radiology. 2009;252(3):665–72.
20. Raza S, Chikarmane SA, Neilsen SS, Zorn LM, Birdwell RL. BI-RADS 3, 4, and 5 lesions: value of US in management—follow-up and outcome. Radiology. 2008;248(3):773–81.

21. Wang LC, Sullivan M, Du H, Feldman MI, Mendelson EB. US appearance of ductal carcinoma in situ. Radiographics. 2013;33(1):213–28.
22. Tozaki M, Fukuma E. Category assessment based on 3D volume data acquired by automated breast ultrasonography. Jpn J Radiol. 2012;30(2):185–91.
23. Ko KH, Hsu HH, Yu JC, Peng YJ, Tung HJ, Chu CM, Chang TH, Chang WC, Wu YC, Lin YP, Hsu GC. Non-mass-like breast lesions at ultrasonography: feature analysis and BI-RADS assessment. Eur J Radiol. 2015;84(1):77–85.
24. Schroeder RJ, Bostanjoglo M, Rademaker J, Maeurer J, Felix R. Role of power Doppler techniques and ultrasound contrast enhancement in the differential diagnosis of focal breast lesions. Eur Radiol. 2003;13(1):68–79.
25. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology. 2006;239(2):341–50.
26. Cho N, Moon WK, Kim HY, Chang JM, Park SH, Lyou CY. Sonoelastographic strain index for differentiation of benign and malignant nonpalpable breast masses. J Ultrasound Med. 2010;29(1):1–7.
27. Raza S, Odulate A, Ong EM, Chikarmane S, Harston CW. Using real-time tissue elastography for breast lesion evaluation. J Ultrasound Med. 2010;29(4):551–63.
28. Leong LC, Sim LS, Lee YS, Ng FC, Wan CM, Fook-Chong SM, et al. A prospective study to compare the diagnostic performance of breast elastography versus conventional breast ultrasound. Clin Radiol. 2010;65(11):887–94.
29. Yoon JH, Kim MH, Kim EK, Moon HJ, Kwak JY, Kim MJ. Interobserver variability of ultrasound elastography: how it affects the diagnosis of breast lesions. AJR Am J Roentgenol. 2011;196(3):730–6.
30. Nakashima K, Shiina T, Sakurai M, Enokido K, Endo T, Tsunoda H, Takada E, Umemoto T, Ueno E. JSUM ultrasound elastography practice guideline: breast. J Med Ultrasonics. 2013;40:359–91.
31. Meng W, Zhang G, Wu C, Wu G, Song Y, Lu Z. Preliminary results of acoustic radiation force impulse (ARFI) ultrasound imaging of breast lesions. Ultrasound Med Biol. 2011;37(9):1436–43.
32. Tozaki M, Isobe S, Sakamoto M. Combination of elastography and tissue quantification using the acoustic radiation force impulse (ARFI) technology for differential diagnosis of breast masses. Jpn J Radiol. 2012;30(8):659–70.
33. Tozaki M, Isobe S, Fukuma E. Preliminary study of ultrasonographic tissue quantification of the breast using the acoustic radiation force impulse (ARFI) technology. Eur J Radiol. 2011;80(2):e182–7.
34. Berg WA, Cosgrove DO, Doré CJ, Schäfer FK, Svensson WE, Hooley RJ, et al. Shear-wave elastography improves the specificity of breast US: the BE1 multinational study of 939 masses. Radiology. 2012;262(2):435–49.
35. Tozaki M, Saito M, Benson J, Fan L, Isobe S. Shear wave velocity measurements for differential diagnosis of solid breast masses: a comparison between virtual touch quantification and virtual touch IQ. Ultrasound Med Biol. 2013;39(12):2233–45.
36. Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European Society of Breast Imaging. Eur Radiol. 2008;18(7):1307–18.
37. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. Lancet. 2010;375(9714):563–71.
38. Jeevan R, Cromwell DA, Trivella M, Lawrence G, Kearins O, Pereira J, et al. Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics. BMJ. 2012;345:e4505.
39. Obdeijn IM, Tilanus-Linthorst MM, Spronk S, van Deurzen CH, de Monye C, Hunink MG, et al. Preoperative breast MRI can reduce the rate of tumor-positive resection margins and reoperations in patients undergoing breast-conserving surgery. AJR Am J Roentgenol. 2013;200(2):304–10.
40. Wang SY, Kuntz KM, Tuttle TM, Jacobs DR Jr, Kane RL, Virnig BA. The association of preoperative breast magnetic resonance imaging and multiple breast surgeries among older women with early stage breast cancer. Breast Cancer Res Treat. 2013;138(1):137–47.
41. Akashi-Tanaka S, Sato N, Ohsumi S, Kimijima I, Inaji H, Teramoto S, Akiyama F. Evaluation of the usefulness of breast CT imaging in delineating tumor extent and guiding surgical management: a prospective multi-institutional study. Ann Surg. 2012;256(1):157–62.
42. Uematsu T, Yuen S, Kasami M, Uchida Y. Comparison of magnetic resonance imaging, multidetector row computed tomography, ultrasonography, and mammography for tumor extension of breast cancer. Breast Cancer Res Treat. 2008;112(3):461–74.
43. Shimauchi A, Yamada T, Sato A, Takase K, Usami S, Ishida T, et al. Comparison of MDCT and MRI for evaluating the intraductal component of breast cancer. AJR Am J Roentgenol. 2006;187(2):322–9.
44. American College of Radiology. ACR practice guideline for the performance of contrast-enhanced magnetic resonance imaging (MRI) of the breast. Reston: American College of Radiology; 2014.
45. Tozaki M, Yamashiro N, Sakamoto M, Sakamoto N, Mizuuchi N, Fukuma E. Magnetic resonance-guided vacuum-assisted breast biopsy: results in 100 Japanese women. Jpn J Radiol. 2010;28(7):527–33.
46. Brennan ME, Houssami N. Evaluation of the evidence on staging imaging for detection of asymptomatic distant metastases in newly diagnosed breast cancer. Breast. 2012;21(2):112–23.
47. Riegger C, Herrmann J, Nagarajah J, Hecktor J, Kuemmel S, Otterbach F, et al. Whole-body FDG PET/CT is more accurate than conventional imaging for staging primary breast cancer patients. Eur J Nucl Med Mol Imaging. 2012;39(5):852–63.
48. Koolen BB, Vrancken Peeters MJ, Aukema TS, Vogel WV, Oldenburg HS, van der Hage JA, et al. 18F-FDG PET/CT as a staging procedure in primary stage II and III breast cancer: comparison with conventional imaging techniques. Breast Cancer Res Treat. 2012;131(1):117–26.
49. Alvarez S, Añorbe E, Alcorta P, López F, Alonso I, Cortés J. Role of sonography in the diagnosis of axillary lymph node metastases in breast cancer: a systematic review. AJR Am J Roentgenol. 2006;186(5):1342–8.
50. Esen G, Gurses B, Yilmaz MH, Ilvan S, Ulus S, Celik V, et al. Gray scale and power Doppler US in the preoperative evaluation of axillary metastases in breast cancer patients with no palpable lymph nodes. Eur Radiol. 2005;15(6):1215–23.
51. Quon A, Gambhir SS. FDG-PET and beyond: molecular breast cancer imaging. J Clin Oncol. 2005;23(8):1664–73.
52. Cooper KL, Harnan S, Meng Y, Ward SE, Fitzgerald P, Papaioannou D, et al. Positron emission tomography (PET) for assessment of axillary lymph node status in early breast cancer: a systematic review and meta-analysis. Eur J Surg Oncol. 2011;37(3):187–98.
53. von Minckwitz G, Kümmel S, Vogel P, Hanusch C, Eidtmann H, Hilfrich J, German Breast Group, et al. Intensified neoadjuvant chemotherapy in early-responding breast cancer: phase III randomized GeparTrio study. J Natl Cancer Inst. 2008;100(8):552–62.
54. Siggelkow W, Rath W, Buell U, Zimny M. FDG PET and tumour markers in the diagnosis of recurrent and metastatic breast cancer. Eur J Nucl Med Mol Imaging. 2004;31(Suppl 1):S118–24.

55. Eubank WB, Mankoff D, Bhattacharya M, Gralow J, Linden H, Ellis G, et al. Impact of FDG PET on defining the extent of disease and on the treatment of patients with recurrent or metastatic breast cancer. AJR Am J Roentgenol. 2004;183(2):479–86.
56. Yap CS, Seltzer MA, Schiepers C, Gambhir SS, Rao J, Phelps ME, et al. Impact of whole-body 18F-FDG PET on staging and managing patients with breast cancer: the referring physician's perspective. J Nucl Med. 2001;42(9):1334–7.
57. Simmons C, Miller N, Geddie W, Gianfelice D, Oldfield M, Dranitsaris G, et al. Does confirmatory tumor biopsy alter the management of breast cancer patients with distant metastases? Ann Oncol. 2009;20(9):1499–504.
58. Thompson AM, Jordan LB, Quinlan P, Anderson E, Skene A, Dewar JA, Breast Recurrence in Tissues Study Group, et al. Prospective comparison of switches in biomarker status between primary and recurrent breast cancer:the breast recurrence in tissues study (BRITS). Breast Cancer Res. 2010;12(6):R92.
59. Amir E, Miller N, Geddie W, Freedman O, Kassam F, Simmons C, et al. Prospective study evaluating the impact of tissue confirmation of metastatic disease in patients with breast cancer. J Clin Oncol. 2012;30(6):587–92.
60. Houssami N, Macaskill P, Balleine RL, Bilous M, Pegram MD. HER2 discordance between primary breast cancer and its paired metastasis:tumor biology or test artefact? Insights through metaanalysis. Breast Cancer Res Treat. 2011;129(3):659–74.