Original Article

Comparison of Diagnostic Performance and Confidence between Contrast-Enhanced Computed Tomography Scan and Non-Contrast-Enhanced Computed Tomography Plus Abdomen Ultrasound for Hepatic Metastasis in Patients with Breast Cancer

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Abstract

Background: The purpose of this study was to compare the performance between noncontrast-enhanced computed tomography (NECT) plus abdominal ultrasound (US) (NECT + US) with contrast-enhanced computed tomography (CECT) for the detection of hepatic metastasis in breast cancer patient with postsurgical follow-up. **Methods:** A total of 1470 patients without already diagnosed hepatic metastasis were included. All patients underwent US and multiphase CECT including the NECT. Independent reviewers analyzed images obtained in four settings, namely, abdominal US, NECT, NECT + US, and CECT and recorded liver metastases using a 5-grade scale of diagnostic confidence. Sensitivity, specificity (diagnostic performance), and area under the receiver operating characteristic curve (AUC, diagnostic confidence) were calculated. Interoperator agreement was calculated using the kappa test. **Results:** Reference standards revealed no metastases in 1108/1470 patients, and metastasis was detected in 362/1470 patients. Abdominal US ($P < 0.01$) and NECT ($P = 0.01$) significantly differed from CECT, but NECT + US did not significantly differ from CECT in terms of sensitivity ($P = 0.09$), specificity ($P = 0.5$), and AUC ($P = 0.43$). After an additional review of abdominal US, readers changed the diagnostic confidence scores of 106 metastatic lesions diagnosed using NECT. Interobserver agreements were good or very good in all four settings. Additional review of abdominal US with NECT allowed a change in the therapeutic plan of 108 patients. **Conclusion:** Abdominal US + NECT showed better diagnostic performance for the detection of hepatic metastases than did NECT alone; its diagnostic performance and confidence were similar to those of CECT.

Keywords: Breast cancer, hepatic metastasis, noncontrast-enhanced computed tomography, ultrasonography

Introduction

Contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) are currently the only imaging modalities that offer the highest diagnostic potential for the assessment of liver metastases in patients with breast cancer.[1-5] Recently, application of CECT has been extended to the follow-up of benign lesion (hepatic cysts, pancreatic cysts, etc.) or cancer after surgery; however, the application of CECT has been limited by an increase in the number of patients with poor renal function because of an increase in the life expectancy and by allergies to contrast media (CMs).[6,7] Moreover, application of MRI is limited to initial follow-up examination because of its high cost or limited accessibility of equipment.

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Noncontrast-enhanced computed tomography (NECT), an alternative modality for examining the entire abdominopelvic cavity without CMs, has been confirmed to show a lower diagnostic performance than CECT, especially for hepatic metastasis.[8,9] To supplement the detection of hepatic metastasis, additional abdominal ultrasound (US) can be considered. Although abdominal US is less accurate than CECT, previous studies have shown that it is moderately accurate and is the first modality for screening hepatic metastasis because it is a reliable, easily available, low-cost, and noninvasive imaging modality.[4,5]

To our knowledge, no published studies have compared the usefulness of NECT + abdominal US (NECT + US) versus CECT for the follow-up of patients with breast cancer. We hypothesize that NECT + US and CECT will demonstrate equivalent efficacy for the diagnosis of hepatic metastasis during follow-up of patients with breast cancer. Replacing CECT would result in reduced patient complications, even with the low-risk profile of intravenous iodinated CMs. And considering the high volume of examinations within this patient population, such equivalency could result in significant benefits to both the health-care system and patients.

The aim of this study was to compare the diagnostic performances of NECT + US and CECT in hepatic metastasis during postsurgical follow-up for breast cancer.

Materials and Methods

Patients

This retrospective study was approved by our Institutional Review Board (approval number: 2020-218), which waived the need for informed consent.

Between June 2008 and December 2015, registered diagnostic radiologists examined 1830 consecutive patients (1811 women; mean age, 59 years; age range, 46–88 years) were enrolled in this study. Enrolled patients were referred to our institution for abdominal US for the detection of liver metastases during postsurgical follow-up (interval range, 8–52 months; mean, 56.2 months) of pathologically proven breast cancer. Patients who are already diagnosed hepatic metastasis were excluded from this study when design stage. We included only patients who underwent CECT scan including noncontrast scan within 3 months (280 patients excluded) after abdomen US.

Exclusion criteria were previous treatment of hepatic metastases by radiofrequency ablations or surgical procedures (18 patients); pathological or fibroscan-based diagnosis of liver cirrhosis or chronic liver disease (56 patients); and presence of primary hepatic tumors including hepatocellular carcinoma or intrahepatic cholangiocarcinoma (6 patients). Finally, 1470 patients (1459 women; mean age ± standard deviation [SD], 57 ± 10.5 years; range, 46–85 years) were finally included in the study [Figure 1].

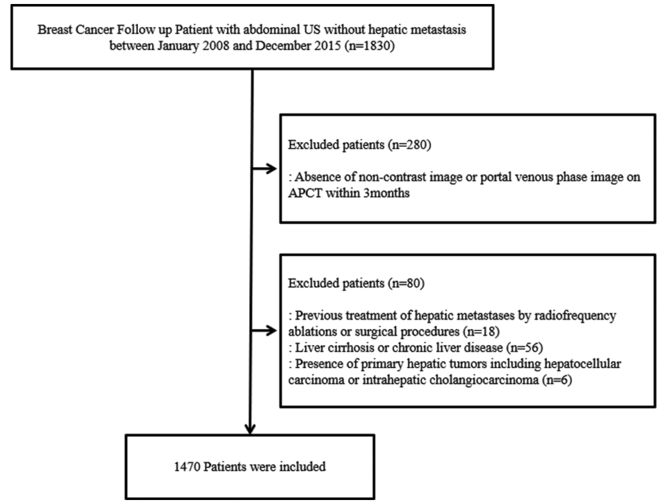

Figure 1: Flow diagram illustrating selection of the study population

Ultrasound and computed tomography examination

Ultrasound and computed tomography technique

Four experienced radiologists, who were aware of the patients' clinical histories, performed gray-scale US scanning. Computed tomography (CT) examinations were performed using one of the five different scanners available at our institution: SOMATOM Sensation 64, SOMATOM Definition, SOMATOM Force, SOMATOM AS-Edge, and SOMATOM Definition Flash (Siemens Healthcare, Forchheim, Germany). More detailed US and CT scanning techniques are described in Appendix 1.

Ultrasound and computed tomography evaluation

US images and CT images were reviewed on screen using a PACS viewer (INFINITT PACS; Infinitt Healthcare, Seoul, Korea) by two independent readers among four performed US with >5 years of experience in abdominal US and abdominopelvic CT scan. Discrepant interpretations between the readers of each panel were resolved by consensus. Both readers were aware of the patient's past history of breast cancer and of no previous hepatic metastasis but were unaware of the results of other imaging examinations and final diagnosis. Two reviewers analyzed images obtained using four settings, individually at 2-week intervals: Abdominal US, NECT, NECT + US, and CECT scan. Largest diameter of each identified lesion was measured in millimeters and localized in the liver segment according to the Bismuth and Couinaud classification[10] on schematic liver charts. For each lesion, readers expressed diagnostic confidence according to a 5-grade scale (1, absolutely benign; 2, probably benign; 3, indeterminate; 4, probably metastasis; and 5, absolute metastasis).[11,12] The appendices show the diagnostic criteria employed for the diagnosis of metastatic [Appendix 2] and benign liver lesions [Appendix 3]. Changes in therapeutic regimens (radiofrequency ablation or surgical resection vs. palliative treatment) due to the detection of hepatic metastases by different imaging modalities in each patient were considered.

Reference standards

The study coordinators had 15 and 10 years of clinical experience, respectively, in abdominal radiology. Decisions regarding the presence or absence of metastasis were made in consensus based on CECT, US, MRI, positron emission tomography (PET)-CT, follow-up US, CT, and MRI and pathological findings of the excision/biopsy specimens. Confirmation of malignancy was based on pathology or imaging surveillance. A total of 556 metastatic lesions were identified in 362 patients based on the following criteria: (1) surgery (42 lesions in 30 patients), (2) needle biopsy (92 lesions in 90 patients), and (3) tumor growth observed on cross-sectional follow-up imaging (422 lesions in 242 patients). All patients who underwent surgery or biopsy were followed up with CECT for at least 6 months. In the absence of histopathological data, metastasis was confirmed when the lesion showed the typical findings of metastasis[13,14] on at least two imaging modalities and when the interval growth in the longest axial diameter was at least 20%, as shown by follow-up imaging. The mean follow-up interval was 13.2 ± 4.7 months (range: 6–13 months). In 1108 patients without metastasis, the absence of metastasis was confirmed by follow-up imaging studies performed at least 6 months after the initial CT.

Statistical analysis

First, liver metastases were detected analyzed on a patient-by-patient basis. Because the Shapiro-Wilk test failed to show a normal distribution of data, Wilcoxon's signed rank test was employed to compare paired data of abdominal US, NECT, NECT + US, and CECT. Second, a detailed lesion-by-lesion analysis was performed, and sensitivity and specificity (diagnostic performance) of abdominal US, NECT, NECT + US, and CECT were compared using the McNemar test. Third, alternative free-response receiver operating characteristic (ROC) analysis of all lesions was performed with each set of images, and the area under each ROC curve (AUC; diagnostic confidence) was calculated using the nonparametric Beck and Schultz method.[15] Data were analyzed using SPSS Statistics (version 18.0, SPSS Inc., Chicago, IL, USA), and statistical significance threshold was set at $P < 0.05$. Appendix 4 describes the details.

Results

Finally, we included 1470 patients 362 and 1108 patients with and without hepatic metastases (without focal lesions and benign focal lesions), respectively. According to reference standards, a total number of 556 metastases were diagnosed in 362 patients. Detailed characteristics of the included patients are listed in Table 1. The mean ± SD number of identified metastases/patient was significantly higher with CECT (1.82 ± 1.79) than with abdominal US (0.88 ± 0.61; $P < 0.01$) or NECT (0.78 ± 0.42; $P = 0.02$); there was no significant difference between CECT and NECT + US (1.98 ± 1.11; $P > 0.05$). The maximum size of the tumor was significant larger in the abdominal US (3.12 ± 2.39, $P = 0.031$) images and insignificantly smaller in NECT (1.90 ± 2.54) images than in CECT (2.23 ± 1.55) images.

Patient-by-patient analysis

Abdominal ultrasound versus contrast-enhanced computed tomography

The sensitivity of abdominal US (66.9%) was significantly lower than that of CECT (97.8%; $P = 0.03$). Abdominal US revealed higher number, same number, and lower number of metastases in 4/362 (1.2%), 158/362 (43.6%), and 200/362 (55.2%), patients, respectively, than did CECT. Additional lesions detected by CECT (diameter, 4–15 mm) were predominantly located in the caudate lobe or in the left hepatic dome [Figure 2]. In patients with heterogeneous liver parenchyma on gray-scale US ($n = 11$), even subcentimetric metastatic lesions were identified on CECT images.

Noncontrast-enhanced computed tomography versus contrast-enhanced computed tomography

The sensitivity of NECT (80.9%) was significantly lower than that of CECT (97.8%; $P = 0.04$). NECT revealed higher number, same number, and lower number of metastases than did CECT in 12/362 (3.3%), 259/362 (71.6%), and 91/362 (25.1%) patients, respectively. Lesions that were missed by NECT (diameter, of 5–18 mm) were located in the fourth, seventh, and eighth segments of the liver [Figure 3].

Noncontrast-enhanced computed tomography plus ultrasound versus contrast-enhanced computed tomography

The sensitivity of NECT + US was slightly but insignificantly lower than that of CECT (90.9% and 97.8%, respectively, $P = 0.06$). NECT + US detected higher number, same number, and lower number of metastases in 11/362 (3.0%), 303/362 (83.7%), and 48/362 (13.3%) patients, respectively, than did CECT. Lesions that were missed by NECT + US were

Figure 2: A 60-year-old woman affected by breast cancer. The lesions missed with ultrasound (a) and detected with noncontrast-enhanced computed tomography (b), contrast-enhanced computed tomography (c) (white arrows, 6 mm) at S8 of liver

Table 1: Demographic and disease characteristics of included patients

Characteristic	With hepatic metastasis	Without hepatic metastasis	*P*
Number of patients (female/male)	362 (358/4)	1108 (1101/7)	
Histologic finding (%)			
Ductal carcinoma	260 (71.9)	811 (73.2)	0.65
Lobular carcinoma	91 (25.1)	259 (23.4)	
Unknown	11 (3.0)	38 (3.4)	
Type of surgery (%)			
Mastectomy	141 (39.0)	458 (41.3)	0.38
Partial mastectomy	121 (33.4)	376 (33.9)	
Partial mastectomy and lymphadenectomy	65 (18.0)	160 (14.5)	
Lymphadenectomy	7 (1.9)	22 (2.0)	
No surgery	16 (4.4)	50 (4.5)	
Unknown	12 (3.3)	42 (3.8)	
Metastatic site (%)			
Liver only	141 (39.0)		
Liver and bone	174 (48.1)		
Liver and lung	29 (8.0)		
Liver, bone, and lung	11 (3.0)		
Liver, bone, and pleura	7 (1.9)		
Previous treatment (%)			
Chemotherapy	119 (33.0)	365 (32.9)	0.47
Hormonal therapy	43 (11.9)	128 (11.6)	
Chemotherapy and radiation therapy	145 (40.1)	426 (38.4)	
Chemotherapy and hormonal therapy	30 (8.1)	110 (9.9)	
Chemotherapy, radiation therapy, and hormonal therapy	11 (3.0)	55 (5.0)	
None	10 (2.8)	14 (1.3)	
Unknown	4 (1.1)	10 (0.9)	

Data in parentheses are percentages

metastases (diameter, 4–8 mm) and were noted in patients with severe-degree uneven fatty liver disease [Figure 4].

Lesion-by-lesion analysis

Diagnosis of liver metastases

Table 2 shows the results of lesion-by-lesion analysis for abdominal US, NECT, NECT + US, and CECT. Abdominal US ($P < 0.01$) and NECT ($P = 0.01$) differed significantly and NECT + US differed insignificantly from CECT in terms of sensitivity ($P = 0.09$), specificity ($P = 0.5$), and AUC ($P = 0.43$). CECT showed more metastatic lesions (528/556 lesions; 95.0% sensitivity) than did abdominal US (298/556 lesions in 242/362 patients; 53.6% sensitivity) and NECT (406/556 lesions in 293/362 patients; 73.0% sensitivity). CECT and NECT + US revealed suspected malignant breast cancer metastases in 528 and 484 lesions, respectively, and the true positive rates (accuracy) were 89.0% (528/556) and 81.0% (484/556), respectively (Wilcoxon signed rank test: $P = 0.053$) [Table 2].

Fifty-two lesions were observed on CECT but not on NECT + US. Eight lesions were missed by both NECT + US and CECT but not by the reference standard techniques.

After an additional review of abdominal US, readers changed the diagnostic confidence score of 106 metastatic lesions diagnosed with NECT. In 78/556 metastases, abdominal US allowed readers to propose a correct diagnosis by shifting the diagnostic score from 1–3 to 4–5; in 15/556 metastases, readers were more confident about the correct characterization by shifting the diagnostic score from 4 to 5. In the remaining 13/556 metastases, readers degraded the diagnostic score from 4 or 5 to 1, 2, or 3, enabling a more accurate diagnosis.

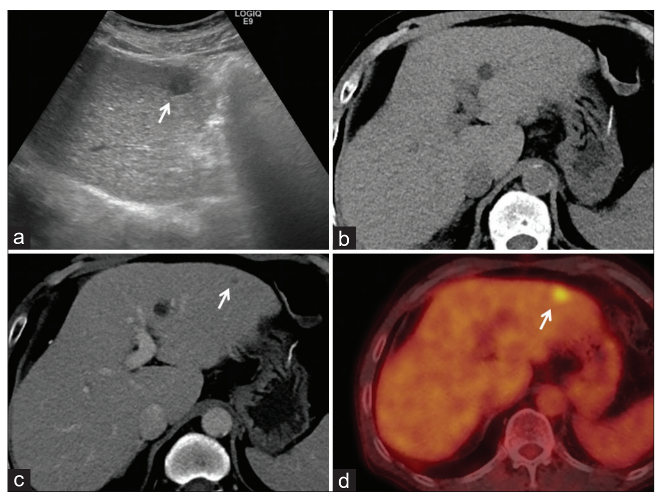

Figure 3: A 53-year-old woman affected by breast cancer. Detected with ultrasound (a), the lesions missed with noncontrast-enhanced computed tomography (b), contrast-enhanced computed tomography (c) (white arrows, 4 mm) at S3 of liver. The lesion showed fluorodeoxyglucose uptake on positron emission tomography-computed tomography scan (d)

Table 2: Lesion-by-lesion analysis

Modality	Sensitivity, %	Specificity, %	Accuracy, %	AUC
US	53.6 (49.3-57.8)	65.3 (62.1-67.8)	61.2 (58.8-63.5)	0.579
NECT	73.0 (69.1-76.7)	84.0 (81.7-86.1)	80.4 (78.4-82.2)	0.754
US + NECT	87.1 (84.0-89.7)	78.0 (75.4-80.4)	81.0 (79.0-82.9)	0.832
CECT	95.0 (92.8-96.6)	86.0 (83.8-88.0)	89.0 (87.4-90.5)	0.945
NECT + CECT	96.4 (93.1-98.2)	86.1 (81.4-89.2)	89.7 (86.9-94.2)	0.952

Diagnostic performance and confidence of the different imaging techniques in liver metastases detection. Percentages are presented in parentheses. CT: Computed tomography, NECT: Noncontrast-enhanced CT, CECT: Contrast-enhanced CT, AUC: Area under receiver operating characteristic curve, US: Ultrasound

Figure 4: A 58-year-old woman affected by breast cancer. The lesions missed with ultrasound (a), noncontrast-enhanced computed tomography (b) and detected with contrast-enhanced computed tomography (c) (white arrows, 4 mm) at S8 of liver. The lesion showed diffusion restriction on liver magnetic resonance imaging (d)

Interobserver agreement between the reviewers was good for abdominal US (κ =0.76; 95% confidence interval [CI]: 0.67–0.82) and NECT (κ =0.75; 95% CI: 0.59–0.79) and very good for NECT + US (κ =0.82; 95% CI: 0.69–0.89) and CECT (κ =0.85; 95% CI: 0.73–0.92).

Clinical impact of noncontrast-enhanced computed tomography plus ultrasound

Additional review of abdominal US results helped achieved a correct diagnosis in 91/1108 (8.2%) patients. This allowed a change in the therapeutic plan in 108 patients: changes in the therapeutic plan from surgery or palliative chemotherapy to observation and imaging follow-up due to benign lesions (*n* = 55), in the follow-up treatment plan from observation to palliative chemotherapy (*n* = 36), and in the initial treatment plan from surgery to palliative chemotherapy (*n* = 17) due to the detection of additional hepatic metastases.

Discussion

In the present study, the sensitivity and specificity of abdominal US (53.6%, 65.3%) and NECT (73.0%, 84.0%) were significantly lower than those of CECT (95.0%, 86.0%), but those of NECT + US (87.1%, 78.0%) were not significantly different from those of CECT. Already several studies have shown that the diagnostic performance of NECT or abdominal US is lower than that of CECT for detection of breast cancer metastasis.[16,17] Especially, NECT helped diagnose metastasis in the bone, the most common metastatic site in the abdominopelvis but had the disadvantage of low diagnostic performance in the diagnosis of hepatic metastasis. In the present study, we focused on the detection of hepatic metastases during the follow-up of patients with breast cancer without any evidence of liver metastasis. An increase in sensitivity from 73.0% to 87.1% for the detection of liver metastases was observed by the addition of abdominal US to NECT. In particular, the diagnostic capabilities of abdominal US were found to be higher in this study than in other studies conducted on gastrointestinal tract cancer[18] or liver cirrhosis.[19] It is already known that hormonal treatment often leads to fatty liver, which is thought to be a better detection of hypoechoic nodules[20,21] on increased echogenicity of hepatic parenchyma, in patients with breast cancer.

In our series, NECT + US was able to detect high number of metastases when NECT findings were inconclusive, thus leading to a dramatic change in patient management strategy, from observation to palliative chemotherapy. In addition, 25 metastases missed by CECT were found to be accurate. The lesions did not show low attenuation or peripheral enhancement due to uneven fat infiltration; in particular, the lesion of the left hepatic dome was difficult to detect due to cardiac motion on CECT, but the lesions could be detected, because of low body mass index, using abdominal US. The subcapsular lesion was misdiagnosed as an arterioportal shunt on CECT, but detection of subcapsular lesions was easier using abdominal US, predominantly at the anterior section of the right hemiliver because abdominal US is very sensitive to superficial tissue. Moreover, 12 lesions that were missed by CECT but detected NECT (diameter, of 11–21 mm) were misdiagnosed as AP shunt because of subcapsular location or hemangioma due to bright enhancement or missed due to cardiac motion on CECT of left hepatic dome lesion.

However, eight hepatic metastases were missed by NECT + US and CECT because the lesions were located in the fatty area of the liver and were isoechoic both on NECT + US and on CECT images, thus appearing indistinguishable from the adjacent liver parenchyma.

Although CECT performed slightly better than NECT + US in the detection of liver lesions, no statistically significant difference was found, thus confirming the importance of NECT + US in this particular clinical setting. Interestingly, in our series, CECT was associated with the misdiagnosis of geographic fatty changes mainly involving liver segments II, III, and IVa as liver metastases due to mild hypoattenuation. The wedge shape, subcapsular location, lack of mass effect, and undisturbed vessels traversing through the lesion could have suggested the correct diagnosis using NECT and US with Doppler image.

Fifty-two lesions that were missed by NECT + US but detected CECT were significantly smaller than lesions detected in both NECT + US and CECT (mean size: 4 mm vs. 13 mm, respectively, $P = 0.02$). And also, small deep located metastases were misdiagnosed as focal fat infiltration on NECT + US.

The size of metastasis measured using CECT was significantly smaller than that using abdominal US and insignificantly larger than that using NECT. Similar results were noted in previous studies. This is presumed to be because measurements are multidirectional, including in oblique direction, in gray-scale images unlike in CT, which obtains only true axial or coronal images.[22]

Based on the results of this study, an examination protocol for the diagnosis of liver metastasis was proposed. NECT + US should be performed in patients with poor renal function or allergy to CMs during the postoperative follow-up. Of course, considering the low frequency of hepatic metastasis, it does not mean that both modalities should be used in all patients with no suspicious lesions in a single imaging test. It is recommended that one test is performed first, followed by the other additional test, proceeding if an indeterminate lesion is detected. It is well known that abdominal US is not recommended as an alternative test in all patients with contraindication for CMs. CECT should be employed if abdominal US is unsuitable due to the large body habitus or interposed bowel gas or clinically suspected liver metastases in patients (e.g., increase in serum levels of tumor markers).

Conclusion

In this study, three principal limitations are present. The main limitation of this study is that the final diagnosis was established in the majority of cases without pathological evaluation. However, all the lesions were well characterized on the basis of typical contrast enhancement patterns that are considered as established diagnostic criteria for MRI, PET-CT, or follow-up images. Second, multiple exclusion criteria were employed that could overestimate the capabilities of abdominal US and NECT for the detection of hepatic metastases detection. We included only those who had not only abdominal US but also CECT data including non-contrast data. In conclusion, abdominal US improved the diagnostic performance of NECT for the detection of hepatic metastases; in patients with contraindication for CM, NECT + US can be considered as alterative diagnostic method of hepatic metastasis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Appendices

Appendix 1: Four experienced radiologists (>10 years of experience in liver ultrasound [US]), who were aware of the patients' clinical histories, performed gray-scale US scanning using either an EPIQ or iU22 unit (Philips Ultrasound, Bothell, WA, USA), both provided with a multifrequency convex array probe (CA541 1-8 MHz and C 5-2 MHz). A US survey examination, including a color/power and pulsed Doppler analysis was performed

Computed tomography (CT) examinations were performed using one of the five different scanners available at our institution: SOMATOM Sensation 64, SOMATOM Definition, SOMATOM Force, SOMATOM AS-Edge, and SOMATOM Definition Flash (Siemens Healthcare, Forchheim, Germany). A noncontrast image was obtained before the administration of contrast media (CM). CM was injected using a power injector via the antecubital vein at a rate of 2 mL/kg over 30 s. Using the bolus tracking technique, the portal venous phase was obtained at 55 s after the Hounsfield unit (HU) value of the abdominal aorta had increased by 100 HU compared to the baseline value or at 30 s after the end of the late arterial phase

The CT parameters were as follows: (1) rotation time: 0.5 s; (2) kV: 120 kV; (3) reference mAs: 240 mAs with automated tube current modulation; (4) beam collimation: 0.6 mm; (5) beam pitch: 1; and (6) slice thickness: 5 mm

Appendix 2: Diagnostic criteria for liver metastases

Baseline ultrasonography

Variable echogenicity, sharp or smooth margins ± peripheral hypoechoic halo at baseline grey-scale ultrasound (US)

Peripheral and central arterial vessels at colour Doppler US

Contrast-enhanced computed tomography

Hypervascular appearance with diffuse enhancement or hypovascular appearance ± peripheral rim-like enhancement at arterial-dominant phase. Hypovascular appearance at portal-venous phase and/or at late equilibrium phase

Diagnostic criteria for liver metastases. Malignancies other than metastases were not identified since patients with liver cirrhosis or chronic liver disease were preliminarily excluded

Appendix 3: Diagnostic criteria for benign tumoral histotypes

Hemangioma

Sharp margins, hyperechoic homogeneous appearance, possible posterior acoustic enhancement at baseline ultrasound (US)

Nodular peripheral enhancement with centripetal fill-in at contrast-enhanced computed tomography (CT)

Histology, or no change in dimension and number at follow-up

Focal nodular hyperplasia

Central arterial vessels with a spoke-wheel-shaped appearance[a] at baseline color Doppler US

Evidence of delayed central scar enhancement at contrast-enhanced CT

Histology

Hepatocellular adenoma

Histology

Heterogeneous appearance with evidence of haemorrhagic component at nonenhanced CT

Focal fatty sparing

Hypoechoic and wedge-shaped appearance in a bright liver parenchyma at baseline US

No change in dimension and number at follow-up

Focal fatty change

Persistent isovascular appearance at CT

No change in dimension and number at follow-up

Cysts

Anechoic appearance with posterior acoustic enhancement at baseline US

Liquid density (−10 up to + 10 Hounsfield unit) at nonenhanced CT

No change in dimension and number at follow-up

US ultrasound, CT contrast-enhanced CT

[a]Spoke-wheel-shaped = central arterial vessels branching toward the periphery of the lesion

Appendix 4: Statistical analysis

For the calculation of sensitivity and specificity, each finding was considered as true positive (metastatic lesion correctly characterized, confidence levels 4 or 5), false negative (metastatic lesion not identified or incorrectly characterized as benign, confidence levels 1 or 2; or indeterminate, confidence level 3), true negative (benign lesion correctly characterized, confidence levels 1, 2), or false positive (benign lesion incorrectly characterized as metastasis, confidence levels 4 or 5; or indeterminate, confidence level 3). AUCs were compared using the Hanley-McNeil method for paired data.[16] Cohen's kappa was calculated to assess inter-operator agreement. Agreement was graded as poor (≤0.20), moderate (0.20–0.40), fair (0.40–0.60), good (0.60–0.80), or very good (0.80–1.00)

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