Computed Tomography Assessment of Hepatic Metastases of Breast Cancer with Revised Response Evaluation Criteria in Solid Tumors (RECIST) Criteria (Version 1.1): Inter-Observer Agreement

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Summary

Background: To assess inter-observer agreement of revised RECIST criteria (version 1.1) for computed tomography assessment of hepatic metastases of breast cancer.

Material/Methods: A prospective study was conducted in 28 female patients with breast cancer and with at least one measurable metastatic lesion in the liver that was treated with 3 cycles of anthracycline-based chemotherapy. All patients underwent computed tomography of the abdomen with 64-row multidetector CT at baseline and after 3 cycles of chemotherapy for response assessment. Image analysis was performed by 2 observers, based on the RECIST criteria (version 1.1).

Results: Computed tomography revealed partial response of hepatic metastases in 7 patients (25%) by one observer and in 10 patients (35.7%) by the other observer, with good inter-observer agreement (k=0.75, percent agreement of 89.29%). Stable disease was detected in 19 patients (67.8%) by one observer and in 16 patients (57.1%) by the other observer, with good agreement (k=0.774, percent agreement of 89.29%). Progressive disease was detected in 2 patients (7.2%) by both observers, with perfect agreement (k=1, percent agreement of 100%). The overall inter-observer agreement in the CT-based response assessment of hepatic metastasis between the two observers was good (k=0.793, percent agreement of 89.29%).

Conclusions: We concluded that computed tomography is a reliable and reproducible imaging modality for response assessment of hepatic metastases of breast cancer according to the RECIST criteria (version 1.1).

MeSH Keywords: Liver • Multidetector Computed Tomography • Neoplasm Metastasis

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Background

Breast cancer is the most common cancer in women and is the leading cause of cancer death among women worldwide, accounting for 15% of cancer deaths among women [1–3]. Patients with newly diagnosed breast cancer have modestly improved survival over time. Twenty to thirty percent of patients with early breast cancer will eventually relapse with distant metastases [4]. The median survival of patients with metastatic breast cancer is approximately 24 months. Hepatic metastases occur in about 50% of patients with metastatic breast cancer. Early
identification of patients with metastatic breast cancer who do not respond to systemic treatment is important in order to avoid unnecessary drug-related toxicities [4,5].

Different imaging modalities are used for the assessment of hepatic metastases in patients with breast cancer [6–9]. Ultrasound is a simple imaging modality for initial diagnosis, but it is operator dependent [7,8]. Positron emission tomography and/or computed tomography are sensitive methods for detection of hepatic metastases, but they are associated with radiation exposure and are expensive [7–9]. Different pulse sequences of magnetic resonance imaging (MRI) are used for the assessment of hepatic metastases, such as diffusion-weighted MR imaging, but MRI is an expensive imaging technique for a serial follow up [10–12]. Currently, computed tomography is considered as an essential imaging modality for the assessment and measurement of lesions in patients who are selected for response assessment. The main advantages of computed tomography are its availability, accepted cost, short scanning time, and the possibility of post scanning processing [13–16].

The Response Evaluation Criteria in Solid Tumor guidelines (RECIST) were published in 2000. The RECIST criteria defined the minimum size of measurable lesions, specified the number of lesions and applicable imaging techniques, and described unidimensional measurements for the evaluation of tumor burden [17–19].

Aim of the work

To assess inter-observer agreement of the revised RECIST criteria (version 1.1) for CT-based assessment of hepatic metastases of breast cancer.

Material and Methods

Institutional review board approval was obtained, and an informed consent was obtained from all patients. This prospective study was carried among 32 female patients in the period between January 2012 and December 2016. All included patients had pathologically proven breast cancer and at least one measurable metastatic lesion in the liver that was treated with three cycles of anthracycline-based chemotherapy. Four patients were excluded due to previous exposure to anthracycline (one patient) and contraindications to anthracycline treatment (3 patients). In total, the study included 28 female patients (mean age of 48.39 years; age range: 22–72 years) who underwent CT of the abdomen before and after 3 cycles of anthracycline-based chemotherapy. The pathological subtypes of breast cancer were as follows, infiltrating duct carcinoma – 24 (85.7%), infiltrating lobular carcinoma – 3 (10.7%), and mucinous carcinoma – 1 (3.6%).

All patients were examined with a 64-MDCT scanner (Brilliance 64, Philips Medical Systems, Cleveland, OH, USA). Non-ionic contrast was injected intravenously through a power injector (1.5 ml/kg) at a rate of 3–5 ml/sec. The CT examination of the abdomen was performed in the supine position. Scanning started 30-60 seconds after contrast injection. A collimation of 64×0.6 mm, with 0.5 second rotation time, and a pitch factor of 1.4 were used. The tube voltage was 120 kV, 100-200 mAs. Images were reconstructed with an overlapping technique in the axial plane with an effective slice thickness of 1–1.5 mm and a reconstruction increment of 0.7–0.8 mm.

The analysis of computed tomography images was performed by one radiologist (AA) and one oncologist (F) who were blinded to the clinical presentation and data of the patients. Response assessment was performed according to the revised RECIST guideline (version 1.1) [17]. Disappearance of all target lesions was regarded as complete response (CR), a decrease of at least 30% in the sum of diameters of target lesions was regarded as partial response (PR), an increase of at least 20% in the sum of diameters of the target lesions or appearance of new lesions was regarded as progressive disease (PD), and no change in size was regarded as stable disease (SD).

Statistical analysis of data was performed with the Statistical Package for Social Science (SPSS) software, version 16. The inter-observer agreement was expressed with the kappa (κ) statistic with 95% confidence intervals (CI). P value <0.05 was considered to indicate statistical significance. The κ statistic is the amount of observed agreement. A κ value of 0.81 to 1.0 is an excellent agreement, 0.61 to 0.80 is good agreement, 0.41 to 0.60 is moderate agreement, 0.21 to 0.40 is fair agreement, and 0.0 to 0.20 represents slight agreement, and a κ value of 1.0 represents perfect agreement.

Results

Partial response (Figure 1) was detected in 7 patients (25%) by one observer and in 10 patients (35.7%) by the other observer, with good agreement (κ=0.750, percent agreement of 89.29%). Stable disease (Figure 2) was detected in 19 patients (67.8%) by one observer and in 16 patients (57.1%) by the other observer, with good agreement (κ=0.774, percent agreement of 89.29%). Progressive disease (Figure 3) was detected in 2 patients (7.2%) by both observers, with perfect agreement (κ=1, percent agreement of 100%) (Table 1). The overall inter-observer agreement in response assessment between both observers was good (κ=0.793, percent agreement of 89.29%).

Discussion

The main finding of the study is good overall inter-observer agreement in response assessment of hepatic metastasis in patients with breast cancer (κ=0.793, percent agreement=89.29%). In practice, post treatment imaging of hepatic metastases varies widely by center and remains variable despite the consensus guidelines.

In this study, there was good inter-observer agreement with respect to the CT-based assessment of hepatic metastases of breast cancer. Few available studies discuss the inter-observer agreement of computed tomography assessment in hepatic and other malignancies [20–23]. One study reported that evaluation of 80 lymph nodes, 120 pulmonary lesions, and 120 hepatic lesions by 17 radiologists with variable levels of experience was characterized by excellent inter-observer agreement with respect to hepatic...
lesions. Those authors added that larger lesion size and greater reader experience resulted in a higher consistency of measurements [20]. Abdel Razek et al. added that the overall inter-observer agreement in staging and response assessment of lymphoma after a complete course of treatment, that was carried out with whole-body computed

Figure 1. Partial response: (A) Baseline axial CT of the abdomen shows multiple hepatic metastatic focal lesions in a patient with breast cancer before chemotherapy. (B) Follow-up axial contrast CT shows regression of hepatic focal lesions after chemotherapy.

Figure 2. Stable disease: (A) Baseline axial contrast CT scan of the abdomen shows hepatic metastatic lesions before chemotherapy. (B) Follow-up axial contrast CT scan after chemotherapy shows stable appearance of the hepatic focal lesions.

Figure 3. Progressive disease: (A) Baseline axial CT scan of the abdomen shows small metastatic focal lesions in the liver before chemotherapy. (B) Follow-up axial CT scan after chemotherapy shows progression of hepatic focal lesions.
Table 1. Inter-observer agreement with 95% CI and percent agreement of response assessment of hepatic metastases in patients with breast cancer.

| Category  | 1st reader | 2nd reader | K       | 95% CI          | Percent agreement | P value |
|-----------|------------|------------|---------|-----------------|-------------------|---------|
| PR        | 7 (25%)    | 10 (35.7%) | 0.75    | 0.491–1.0       | 89.29             | 0.001   |
| SD        | 19 (67.8%) | 16 (57.1%) | 0.774   | 0.539–1.0       | 89.29             | 0.001   |
| PD        | 2 (7.2%)   | 2 (7.2%)   | 1.00    | 1.00–1.0        | 100.0             | 0.001   |
| Overall   | 28 (100%)  | 28 (100%)  | 0.793   | 0.573–1.0       | 89.29             | 0.001   |

There were a few limitations of this study. First, the sample size was small and therefore further studies with larger numbers of patients that will analyze pulmonary, nodal, and hepatic metastases are recommended. Second, this study was performed with a 64-row CT scanner, which was associated with radiation exposure. Further studies with the application of advanced computed tomography techniques, such as whole-body computed tomography [24], CT perfusion [25–27], dual energy computed tomography [28], and advanced magnetic resonance sequences, like diffusion-weighted MR imaging [29–31], diffusion tensor MR imaging [32], dynamic contrast enhanced MR imaging [33], dynamic susceptibility contrast-enhanced MR imaging [34,35], will improve outcomes, as they can detect small hepatic focal lesions, thereby improving prognosis and survival.

Conclusions

We concluded that computed tomography is a reliable and reproducible imaging modality for response assessment of liver metastases in patients with breast cancer.

References:

1. Torre LA, Bray F, Siegel RL et al: Global cancer statistics, 2012. Cancer J Clin, 2015; 65: 67–108
2. Canadian Cancer Society/National Cancer Institute of Canada. Canadian Cancer Statistics 2015. Toronto, Canada, 2015
3. Davood S, Broglio K, Gonzalez-Angulo AM et al: Trends in survival over the past two decades among white and black patients with newly diagnosed stage IV breast cancer. J Clin Oncol, 2008; 26: 4891–98
4. Kennecke H, Yerushalmi R, Woods R et al: Metastatic behavior of breast cancer subtypes. J Clin Oncol, 2010; 28: 3271–77
5. Bonotto M, Germantana L, Poletto E et al: Measures of outcome in metastatic breast cancer: Insights from a real-world scenario. Oncologist, 2014; 19: 608–15
6. Matos AF, Altun E, Ramalho M et al: An overview of imaging techniques for liver metastases management. Expert Rev Gastroenterol Hepatol, 2015; 9: 1561–76
7. Tirmumi SH, Kim KW, Nishino M et al: Update on the role of imaging in management of metastatic colorectal cancer. Radiographics, 2014; 34: 1908–28
8. Kaneswari M, Konde H, Goshima S et al: Imaging liver metastases: Review and update. Eur J Radiol, 2006; 58: 217–28
9. Namavisayam S, Martin DR, Saini S: Imaging of liver metastases: MRI. Cancer Imaging, 2007; 7: 2–9
10. Bruegel M, Rummeny EJ: Hepatic metastases: Use of diffusion-weighted echo-planar imaging. Abdom Imaging, 2010; 35: 454–61
11. Razek AA, Latif MA, Denewer A et al: Assessment of axillary lymph nodes in patients with breast cancer with diffusion-weighted MR imaging in combination with routine and dynamic contrast MR imaging. Breast Cancer, 2016; 23: 525–32
12. Abdel Razek AA, Gahalla G, Denewer A et al: Diffusion weighted MR imaging of the breast. Acad Radiol, 2010; 17: 382–86
13. Razek AA, Ghonim MR, Ashraf B: Computed tomography staging of middle ear cholesteatoma. Pol J Radiol, 2015; 80: 328–33
14. Razeek AA, Huang BY: Lesions of the petrous apex: Classification and findings at CT and MR imaging. Radiographics, 2012; 32: 151–73
15. Razeek AA, Castillo M: Imaging appearance of granulomatous lesions of head and neck. Eur J Radiol, 2010; 76: 52–60
16. Abdel Razek AA, Abu Zeid MM, Bilal M et al: Virtual CT colonoscopy versus conventional colonoscopy: A prospective study. Hepatogastroenterology, 2005; 52: 1698–702
17. Eisenhauser EA, Therasse P, Bogaerts J et al: New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). Eur J Cancer, 2009; 45: 228–47
18. Minocha J, Lewandowski RJ: Assessing imaging response to therapy. Radiol Clin North Amer, 2015; 53: 1077–86
19. Gonzalez-Gualdani E, Botelho M, Harmath C et al: Assessment of liver tumor response to therapy: Role of quantitative imaging. Radiographics, 2013; 33: 1781–800
20. McErlane A, Panicek DM, Zahor EC et al: Intra – and interobserver variability in CT measurements in oncology. Radiology, 2013; 269: 451–59
21. Abdel Razek A, Shamaa S, Abdel Lattif M et al: Inter-observer agreement of whole body computed tomography in staging and response assessment of lymphoma: The Lugano classification. Pol J Radiol, 2017 [in press]

22. Monzawa S, Ichikawa T, Nakajima H et al: Dynamic CT for detecting small hepatocellular carcinoma: Usefulness of delayed phase imaging. Am J Roentgenol, 2007; 188(1): 147–53

23. Rothe J, Grieser C, Lehmkuhl L et al: Size determination and response assessment of liver metastases with computed tomography — Comparison of RECIST and volumetric algorithms. Eur J Radiol, 2013; 82: 1831–39

24. Razek AA, Ezzat A, Azmy E et al: Role of whole-body 64-slice multidetector computed tomography in treatment planning for multiple myeloma. Radiol Med, 2013; 118: 799–805

25. Tawfik AM, Razek AA, Elhawary G et al: Effect of increasing the sampling interval to 2 seconds on the radiation dose and accuracy of CT perfusion of the head and neck. J Comput Assist Tomogr, 2014; 38: 469–73

26. ElMaadawy MM, Elsorougy LG, Abdel Razek AA et al: Perfusion CT: A biomarker for soft tissue tumors of extremities. Egyptian J Radiol Nuclear Medicine, 2013; 44: 805–15

27. Razek AA, Tawfik AM, Elsorogy LG et al: Perfusion CT of head and neck cancer. Eur J Radiol, 2014; 83: 537–44

28. Tawfik AM, Razek AA, Kerl JM et al: Comparison of dual-energy CT-derived iodine content and iodine overlay of normal, inflammatory and metastatic squamous cell carcinoma cervical lymph nodes. Eur Radiol, 2014; 24: 574–80

29. Razek AA, Khashaba M, Abdalla A et al: Apparent diffusion coefficient value of hepatic fibrosis and inflammation in children with chronic hepatitis. Radiol Med, 2014; 119: 903–9

30. Abdel Razek AA, Elkamary S, Elmosry AS et al: Characterization of mediastinal lymphadenopathy with diffusion-weighted imaging. Magn Reson Imaging, 2011; 29: 167–72

31. Abdel Razek AA, Samir S, El-Said A: Role of diffusion-weighted MR imaging in differentiation of Graves’ disease from painless thyroiditis. Pol J Radiol, 2017 [in press]

32. Razek AA, Al-Adlany MA, Alhadiy AM et al: Diffusion tensor imaging of the renal cortex in diabetic patients: Correlation with urinary and serum biomarkers. Abdom Radiol, 2017 [Epub ahead of print]

33. Abdel Razek AA, Mousa A, Farouk A et al: Assessment of semiquantitative parameters of dynamic contrast-enhanced perfusion MR imaging in differentiation of subtypes of renal cell carcinoma. Pol J Radiol, 2016; 81: 99–94

34. Razek AA, Elsorogy LG, Soliman NY et al: Dynamic susceptibility contrast perfusion MR imaging in distinguishing malignant from benign head and neck tumors: A Pilot study. Eur J Radiol, 2011; 77: 73–79

35. Abdel Razek AA, Gaballa G: Role of perfusion magnetic resonance imaging in cervical lymphadenopathy. J Comput Assist Tomogr, 2011; 35: 21–25