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Computed Tomography / Tomodensitométrie

Contrast-Enhanced Computed Tomography Evaluation of Hepatic Metastases in Breast Cancer Patients Before and After Cytotoxic Chemotherapy or Targeted Therapy

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Abstract

Purpose: To evaluate change in size vs computed tomography (CT) density of hepatic metastases in breast cancer patients before and after cytotoxic chemotherapy or targeted therapy.
Methods: A database search in a single institution identified 48 breast cancer patients who had hepatic metastases treated with either cytotoxic chemotherapy alone or targeted therapy alone, and who had contrast-enhanced CT (CECT) scans of the abdomen at baseline and within 4 months of initiation of therapy in the past 10 years. Two radiologists retrospectively evaluated CT scans and identified up to 2 index lesions in each patient. The size (centimeters) of each lesion was measured according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria, and CT density (Hounsfield units) was measured by drawing a region of interest around the margin of the entire lesion. The percent change in sum of lesion size and mean CT density on pre- and post-treatment scans was computed for each patient; results were compared within each treatment group.
Results: Thirty-nine patients with 68 lesions received cytotoxic chemotherapy only; 9 patients with 15 lesions received targeted therapy only. The mean percent changes in sum of lesion size and mean CT density were statistically significant within the cytotoxic chemotherapy group before and after treatment, but not significant in the targeted therapy group. The patients in the targeted therapy group tend to have better 2-year survival. The patients who survived at 2 years tend to have more decrease in tumour size in the cytotoxic chemotherapy group.
Conclusion: Cytotoxic chemotherapy produced significant mean percent decrease in tumour size and mean CT density of hepatic metastases from breast cancer before and after treatment, whereas targeted therapy did not. Nonetheless, there is a trend that the patients in the targeted therapy group had better 2-year survival rate. This suggests that RECIST is potentially inadequate in evaluating tumour response in breast cancer liver metastases treated with targeted therapy alone, calling for an alternative marker for response evaluation in this subset of patients.

Résumé

Objectif : Évaluer la variation de la taille des métastases au foie par rapport à la densité en tomodensitométrie (TDM) chez les patients atteints d'un cancer du sein avant et après une chimiothérapie cytotoxique ou un traitement ciblé.
Méthodes : Une recherche dans la base de données d'un établissement a permis d'identifier 48 patients atteints d'un cancer du sein qui ont été soumis à une chimiothérapie cytotoxique seulement ou à un traitement ciblé seulement en raison de la présence de métastases hépatiques, et qui ont subi une TDM avec injection de produit de contraste de l'abdomen comme examen de référence et dans les quatre mois suivant le début du traitement au cours des 10 dernières années. Deux radiologistes ont examiné de façon rétrospective les résultats des TDM et cerné jusqu'à deux lésions chez chaque patient. La taille (en centimètres) de chaque lésion a été mesurée selon les critères RECIST (Response Evaluation Criteria in Solid Tumors), et la densité en TDM (unités Hounsfield) a été mesurée en traçant une région d'intérêt autour de la lésion. La variation en pourcentage de la somme de la taille des lésions et de la densité moyenne en TDM sur les examens avant et après le traitement a été calculée pour chaque patient. Les résultats ont ensuite fait l'objet de comparaisons pour chaque type de traitement.

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Résultats : Trente-neuf patients totalisant 68 lésions ont été soumis à une chimiothérapie cytotoxique uniquement, et 9 patients totalisant 15 lésions ont été soumis à un traitement ciblé uniquement. La variation moyenne en pourcentage de la somme de la taille des lésions et de la densité moyenne en TDM était statistiquement significative dans le groupe soumis à une chimiothérapie cytotoxique, mais ne l'était pas dans celui soumis à un traitement ciblé. Les patients du groupe de thérapie ciblée affichent généralement un meilleur taux de survie à deux ans. Au sein du groupe soumis à une chimiothérapie cytotoxique, les patients toujours vivants après deux ans affichent généralement une plus grande diminution de la taille des tumeurs.
Conclusion : La chimiothérapie cytotoxique entraîne une diminution moyenne en pourcentage significative sur le plan statistique, avant et après le traitement, de la taille des lésions et de la densité moyenne en TDM chez les patients atteints d'un cancer du sein et qui présentent des métastases hépatiques, ce qui n'est pas le cas chez les patients soumis à un traitement ciblé. Néanmoins, les patients du groupe de thérapie ciblée affichent généralement un meilleur taux de survie à deux ans. Ces résultats suggèrent que les critères RECIST ne sont peut-être pas appropriés pour évaluer la réponse de la tumeur au traitement chez les patients souffrant d'un cancer du sein et de métastases du foie traitées par traitement ciblé uniquement. L'utilisation d'un autre marqueur serait souhaitable pour évaluer la réponse au traitement dans ce sous-ensemble de patients.

Key Words: Computed tomography evaluation; Hepatic metastases; Breast cancer; Targeted therapy

The liver is one of the most common sites for metastasis in breast cancer patients. The treatment of choice for breast cancer metastases is systemic therapy with cytotoxic chemotherapy and/or targeted therapy (hormone and growth factor targeted) [1,2]. Accurate objective early assessment of tumour response is crucial for delivering the optimal regimen and for changing treatment. Currently, the most commonly used system to quantify tumour response is Response Evaluation Criteria in Solid Tumors (RECIST), which is based on 1-dimensional size measurement of the target lesions [3]. However, RECIST may underestimate tumour response in the setting of targeted therapies, as these therapies tend to cause disease stabilization and result in improved patient survival rather than substantial tumour regression. These effects have been demonstrated in metastatic renal cell carcinoma, gastrointestinal stromal tumour, and colorectal cancer with liver metastasis treated with targeted therapies [4–9].

Hormonal or growth factor-targeted agents have been widely used in the treatment of breast cancer, either alone or in conjunction with cytotoxic chemotherapy. For example, tamoxifen or other aromatase inhibitors have been used to treat breast cancers overexpressing human estrogen receptor (ER) [10–12]. Trastuzumab (Herceptin, Genentech/Roche, San Francisco, CA) has been used to treat breast cancer overexpressing human epidermal growth factor receptor 2 (HER-2) [13]. As more and more agents are being developed that target specific receptors on tumour cells in breast cancer, there is a growing need for surrogate markers for the early assessment of tumour response. In recent years, functional imaging modalities such as positron emission tomography computed tomography (PET-CT) and dynamic-enhanced or diffusion-weighted magnetic resonance imaging have shown promise for monitoring of tumour response [14–17]. However, these modalities are costly and not readily available in general practice.

Serial contrast-enhanced CTs (CECT), on the other hand, are routinely performed in clinical practice to monitor tumour response. Both size and enhancement characteristics, as measured by CT density of the metastatic lesions, can be readily evaluated on CECTs. Choi et al [5] demonstrated that tumour CT density provides a reliable quantitative means of monitoring tumour response for patients with gastrointestinal stromal tumours receiving targeted therapy. Smith et al [6] showed that measuring changes in both tumour size and CT attenuation markedly improved response assessment in metastatic renal cell carcinoma receiving targeted therapy.

To the best of our knowledge, the adequacy of RECIST criteria response assessment in the setting of targeted therapy for metastatic breast cancer has not been investigated. Also, CT density as a potential parameter to assess tumour response has not been evaluated in metastatic breast cancer. Thus, the purpose of our study was to evaluate size change vs CT density change in hepatic metastases before and after cytotoxic chemotherapy or targeted therapy in breast cancer patients.

Material and Methods

Subjects

Approval was obtained from the institutional review board; informed consent was waived. We retrospectively searched the breast medical oncology database at our institution to identify breast cancer patients who had hepatic metastases treated with systemic therapy in the past 10 years; 158 patients were identified. The initial systemic therapy agents used at our institution, the dates administered and the dates these patients had serial CECTs during the course of the systemic therapy were recorded from the institutional database. The patients who received both cytotoxic chemotherapy and targeted therapy simultaneously were excluded. The patients who had no baseline CECT or no CECT within 4 months after initiation of systemic therapy were also excluded. Four months was chosen as the endpoint because most of the restaging CECTs were performed around 3-4 months after initiation of the systemic therapy at our institution. Forty-eight patients were included in the study.