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Perspectives / Perspectivas

Indications for Bone Scintigraphy Use in Breast Cancer

Indicações para Utilização da Cintigrafia Óssea no Cancro da Mama

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Abstract

Bone scintigraphy is a useful imaging modality in breast cancer, by assessing the presence of metastasis with osteoblastic activity. Nevertheless, information on its appropriate use is sparse and the evidence supporting it is limited. The purpose of this article is to review and synthesize the current recommendations for ordering bone scintigraphy in the staging and surveillance of patients with breast cancer, as well as in monitoring metastatic disease. It aims to provide a convenient tool for clinical practice, so that bone scintigraphy use results in benefits for the patient, simultaneously with a rational consumption of health-care resources.

Keywords

Scintigraphy; Breast cancer; Tumor staging; Follow-up care; metastasis.

Resumo

A cintigrafia óssea é um exame de imagem útil no cancro da mama por permitir a deteção de metástases com atividade osteoblástica. No entanto, a informação sobre as situações em que o seu uso está indicado encontra-se dispersa e a evidência que a suporta é limitada. O presente artigo procura rever e sintetizar as recomendações atuais para a requisição da cintigrafia óssea no estadiamento e seguimento de doentes com cancro da mama, bem como na monitorização da doença metastática, podendo constituir uma ferramenta útil na prática clínica, para que a aplicação deste exame se traduza em benefícios para o doente, simultaneamente com uma utilização racional de recursos de saúde.

Palavras-chave

Cintigrafia; Cancro da Mama; Estadiamento tumor; Seguimento; Metástases.

Introduction

Bone is one of the most common sites of metastasis in breast cancer and may be the only site of disease in 28%-44% of patients.[1] Bone scintigraphy (BS) is one of the imaging examinations required in patients with breast cancer, as it allows the detection of bone metastases with osteoblastic activity.[2] Its accessibility, the ability to assess the entire body at a lower cost than other imaging methods and its high sensitivity for detecting active metastatic disease[1,2] contribute to its frequent use in clinical practice.

Despite the widespread use of BS, there is a lack of randomized controlled clinical trials to support the indication for its application in breast cancer.[2] Currently, there is an excessive use of imaging exams in patients with breast cancer: in the initial diagnosis, in the follow-up of cases of non-metastatic breast cancer and among patients with metastatic disease.[3] The inappropriate use of imaging examinations raises problems for patients and healthcare systems, namely: possible false positive or indeterminate findings, with the consequent need for additional imaging examinations and potential delays in starting treatment; unnecessary patient exposure to radiation and inappropriate consumption of resources.[3]

This article aims to systematize the current recommendations for the request of BS in the staging and follow-up of patients with breast cancer and in monitoring metastatic disease, reviewing the guidelines issued by the main international societies of Oncology and Nuclear Medicine.

Non-Metastatic Breast Cancer

Staging

The staging of early breast cancer (clinical stages 0, I or II) is aimed at locoregional disease, since asymptomatic distant metastases are rare in these patients:[4] the probability of

metastatic disease is 0.2% in stage I and 1.2% at stage II.[5] False positives outnumber true positives and can delay the start of treatment.[6] Thus, BS is not routinely necessary in the staging of asymptomatic patients,[3,4] being recommended only in the presence of factors considered to be of greater risk, namely: clinically positive axillary nodes; bulky tumors (e.g., ≥5cm); aggressive biology (such as the triple negative subtype[6]); clinical (signs or symptoms) or laboratory values (namely a high level of alkaline phosphatase[2]) suggestive of the presence of metastases.[4] Patients with symptoms related to the bone should be investigated, using BS or other means, since these symptoms are related to a higher prevalence of metastatic disease.[2]

In locally advanced (stage III) breast cancer, BS is indicated in the staging of all patients, as the probability of identifying metastatic disease increases with tumor size and lymph node involvement.[2,3]

Follow-up

The follow-up of patients treated with curative intention generally consists of regular consultations and annual mammography,[4] where one of the objectives is to detect early locoregional recurrence or a new contralateral primary breast cancer.[3] The aim of surveillance in these patients is not to detect asymptomatic metastatic disease, as there is no evidence that early detection of metastases in patients without symptoms improves clinical outcomes, such as overall survival or quality of life.[3]

Thus, in patients treated for stage 0-III breast cancer and who are asymptomatic, examinations for the detection of distant recurrence are not recommended, so that BS is not routinely indicated in the follow-up.[2,3] In patients with symptoms or changes during physical examination, exams directed to the problem in question should be performed.[4,6]

The current follow-up strategy raises some questions: on the one hand, there is a lack of randomized data that support a defined protocol for surveillance; on the other hand, recommendations for follow-up are based on studies carried out at a time when diagnostic procedures were less sophisticated and treatment of advanced disease was less effective, which alerts to the need of new trials to reassess the surveillance strategy.[4]

Metastatic Breast Cancer

BS is part of the initial staging of metastatic breast cancer.[2,3,7] If, at staging, a Positron Emission Tomography with Computed Tomography (PET/CT) with 18F-fluorodeoxyglucose (FDG) is performed revealing bone metastases, it is not necessary to perform BS.[2,8] If there are bone lesions on other imaging scans, without avidity for ^{18}F-FDG on PET/CT, BS can be considered to evaluate the patient.[2]

After starting treatment, the objective of imaging exams is to guide the therapeutic intervention, in order to maximize the duration and quality of life.[3] As the clinical evolution of patients with metastatic breast cancer is variable, there is lack of data regarding which imaging technique to use in the follow-up of these patients and how often it should be performed.[3] BS is the exam of choice in the evaluation of patients who have only bone metastases.[7,9]

The NCCN (National Comprehensive Cancer Network®) guidelines recommend monitoring metastatic disease through Computed Tomography and BS, with a frequency range depending on the type of therapy performed (hormonal therapy or chemotherapy).[3] Therefore, they consider it indicated to perform BS at the following times: before starting a new therapy, as a baseline exam; every 4 to 6 cycles of chemotherapy; every 2 to 6 months, in patients on hormone therapy; in re-staging, in case of suspicion of disease progression, regardless of the time interval in relation to previous studies.[8] The monitoring frequency must be adapted to the individual case of each patient, and may be reduced in patients with long-term stable disease.[8]

It is important to mention that BS can pose problems in the assessment of early response to treatment, due to the potential transient increase in activity (flare effect) as a response after starting a new therapy[7,8] which, if incorrectly interpreted as disease progression, can lead to an inappropriate change in therapy.[3] An interval of 3 to 6 months from the beginning of the treatment is considered so that a correct evaluation of the response through BS[1] is possible.

Final Considerations

The indications for the use of BS in breast cancer, according to the current evidence, are summarized in Table 1. It should be noted that these indications constitute a guideline and must be adapted to the particular case of each patient, according to the clinical reasoning.

The use of BS should also be considered in patients with a pathological fracture, allowing the investigation of other areas of potential fracture and clarifying the extent of the disease.[2] In case of new bone pain or increase of alkaline phosphatase, BS should be performed for restaging of the disease.[2]

Despite its widespread use, it is recognized that BS has limitations in diagnostic specificity and in sensitivity and specificity in monitoring the response to treatment.[1] The use of hybrid SPECT (Single Photon Emission Computed Tomography) imaging with CT component (SPECT/CT) can increase sensitivity and, above all, specificity, reducing false positive diagnoses of metastases.[1] PET/CT with ^{18}F-FDG may allow an earlier assessment in the monitoring of bone-predominant metastatic disease,[7] possibly 2 or 3 months after starting treatment1; however, prospective trials are needed

Table 1 – Indications for Bone Scintigraphy (BS) Use in Breast Cancer

Breast Cancer		Staging	Follow-up
Non-Metastatic	Early (clinical stages 0, I or II)	Not indicated by routine. Only recommended if: •clinically positive axillary nodes; •bulky tumors (eg: ≥5cm); •aggressive biology (eg: triple negative, HER-2 positive); •clinical or laboratory values suggesting the presence of metastases (eg: high level of alkaline phosphatase, symptoms related to the bone).	Directed examination if signs/symptoms
	Locally advanced (stage III)	All patients	
Metastatic		All patients	•*Baseline* (before a new therapy); • If chemotherapy: each 4-6 cycles; • If Hormone therapy: each 2-6 months; •If suspicion of progression.

Notes:
* Consider requesting BS for evaluation after pathological fracture.
† If at staging the patient has performed a PET/CT with 18F-FDG that reveals bone metastases, it is not necessary to perform a BS.
‡ While assessing the response, consider the possible flare effect during the first 6 months after starting a new therapy.

to determine its impact on therapeutic decisions and overall survival.[7]

Finally, it should be noted that BS, as well as other imaging techniques, should only be performed if they have an impact on clinical decisions, that is, if they change the course of treatment in order to improve survival and/or the quality of the patient's life.[3] Thus, it is intended that the guidelines provided in this article constitute a useful tool in clinical practice, so that the use of BS translates into benefits for the patient and, simultaneously, into a rational use of health resources.

Ethical disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare.

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Confidencialidade dos dados: Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

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