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Percutaneous core biopsy of palpable breast lesions: accuracy of frozen section histopathological exam in the diagnosis of breast cancer

Avaliação da acurácia do exame histopatológico por congelação em fragmentos de tecido obtidos por biópsia percutânea com agulha grossa no diagnóstico do câncer de mama em tumores palpáveis

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A B S T R A C T

Objective: to evaluate the accuracy of frozen section histopathology from fragments of tissue obtained by percutaneous core needle biopsy of palpable tumors in the diagnosis of breast cancer. **Methods**: a cohort study was performed on 57 patients with palpable tumors and suspected breast cancer undergoing percutaneous thick needle core biopsy. The fragments were analyzed by the same pathologist. **Results**: frozen section diagnosed 16 benign cases (28.6%) and 40 malignant (71.4%), whereas paraffin showed that 15 were benign (26.8%) and 41 malignant (73.2%). Histopathological examinations were concordant in 55 cases and there was one false-negative (6.2%). Statistics rates were: negative predictive value of 93.8%, positive predictive value of 100%, no false-positive (0%), one false negative (6.2%), specificity of 100%, sensitivity of 97 6%; observed agreement = 98.2%; expected agreement = 59.9%, Kappa = 0.955 [95% CI = 0.925-0.974, $p < 0.01$]. **Conclusions**: frozen section histopathological findings showed excellent correlation with the findings by the technique in paraffin in the fragments of palpable breast tumors obtained by thick needle percutaneous core biopsy (98.2% accuracy). Therefore, in these patients, it was possible to anticipate the diagnosis, staging and the breast cancer treatment planning.

Key words: Biopsy, Needle; Breast neoplasms; Freezing; Frozen sections; Diagnostic tests and procedures.

INTRODUCTION

Breast cancer is the second most common cancer in the world and the first of the female reproductive system. There are estimates that in Brazil, in the years 2012 and 2013, 52,680 new cases will have been diagnosed, with an estimated risk of 52 cases per 100,000 women (NCI 2012)[1]. The mortality rate of breast cancer remains high in Brazil and its prognosis is directly related to early diagnosis and treatment agility.

According to the literature, the delay in diagnosis of breast cancer is a major factor for worsening of prognosis[2-6].

Core Needle Biopsy (CNB) is performed in an outpatient setting and can replace the incisional biopsy performed in the operating room, being more practical and less costly. When combined with frozen section histopathology, it can anticipate the diagnosis and procedures for staging and appropriate therapy of breast cancer.

The social relevance of this study is the evaluation of the accuracy of the association of CNB with frozen section histopathology in breast tumors, the control being the paraffin histopathology.

In the public health care network the implementation of methods for the improvement of the diagnosis, staging and treatment of early breast cancer is essential.

Another important factor is the solvability by means of biopsy and rapid diagnostic confirmation of palpable lesions at the first specialized consultation and without the need for hospital admission. Thus, it would be possible to lower hospital costs and minimize health, family, economic and professional problems in these patients. These resources could be used for non-palpable lesions with invasive procedures guided by imaging methods.

By setting up a flow of reference and counter-reference for this disease, with demand control, it would be possible to speed up the first specialized consultation and anticipate diagnosis.

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This study was done to evaluate the accuracy of frozen section histopathology in fragments of tissue obtained by percutaneous core needle biopsy of palpable breast tumors for the diagnosis of breast cancer.

METHODS

We conducted a cohort study using frozen section histopathology of the specimens obtained from 57 suspected breast cancer patients with palpable tumors and treated at the mastology sector of the Department of Gynecology of the Piety Municipal Hospital (SGHMP). The fragments obtained by CNB were analyzed by the histopathological techniques of frozen section and paraffin. All patients were informed of the risks and benefits of the procedure and signed an informed consent form.

To obtain the specimens of the target tumor we used with an automatic pistol with 25mm advance and 14G gauge needle. We obtained at least three and no more than five fragments of good quality, measuring 12mm each. The number of punctures through the same skin site was limited to eight.

The specimens were immediately sent to the Pathology Service without being immersed in formalin. Histopathological frozen section and paraffin examinations of all cases were performed by the same pathologist, responsible for choosing the fragment for the frozen section examination.

Tissue sections obtained by the frozen technique were 5ìm thick and were stained with 1% toluidine blue, whilst the ones embedded in paraffin by were 3ìm and were stained with hematoxylin and eosin. The slides were analyzed by light microscopy.

Histopathological paraffin examination established diagnosis and served as a reference for the assessment of frozen section. For statistical analysis we used the Kappa coefficient (Cohen's kappa).

RESULTS

Tumor size ranged from 1.5 to 10cm in its greatest diameter and the most prevalent histological type was invasive ductal carcinoma (IDC), with 36 occurrences in both histopathology techniques, corresponding to 90% of cases in frozen section and 87.8% in paraffin.

Frozen section agreed with paraffin in 55 cases – 98.2% accuracy. It presented one false negative (6.2%), when considering a benign injury diagnosed by paraffin as intraductal carcinoma of intermediate grade. It diagnosed 16 benign cases (28.6%) and 40 malignant (71.4%), while the paraffin technique revealed that 15 cases were benign (26.8%) and there were 41 malignant (73.2%). No false positive case.

The Kappa coefficient determined the following statistics rates when compared the two techniques: observed agreement of 98.2%, expected agreement 59.9%, kappa = 0.955 (95% CI=0.925 to 0.974, $p<0.01$), negative predictive value (NPV) of 93.8%, positive predictive value (PPV) of 100%, specificity of 100% and sensitivity of 97.6%. No false positive (0%) and there was one false negative (6.2%).

DISCUSSION

This study was conducted in patients from the Unified Health System (SUS) seen in the mastology sector of SGHMP, a municipal unit of Rio de Janeiro. The precarious administrative status of Brazilian public hospitals is notorious, which generates low- solving capacity of the problems presented by users.

Worsening of the disease is common in patients with breast cancer, with worse prognosis, while waiting in queues for specialized care.

In the SGHMP mastology sector, in order to obtain specimens from palpable breast tumor, CNB has replaced surgical biopsy, being a minimally invasive procedure.

CNB was carried out under local anesthesia already in first specialized consultation, without complications nor hospitalization, and patients were satisfied with aesthetic result. It hence proved to be effective and have low hospital cost[7-11]. The result of the frozen section diagnosis was made available quickly and not being merely "negative for malignancy" or "positive for malignancy". The report brought other information on the lesion, such as type and, in cases of cancer, differentiation and invasion[12].

The choice of histopathology by frozen section technique in our study was due to the possibility of such additional information. The cytological imprint of tissue fragments, on its turn, is limited to information as to whether positive or negative for malignancy[2-6,13-15], and the core wash cytology has high rates of unsatisfactory specimens[16].

In the analysis of fragments of palpable breast tumors obtained by CNB, frozen section histopathology showed a good correlation with the final diagnosis determined by histopathology in paraffin, with an accuracy of 98.2% in our survey. There was one discordant result between the two histopathological techniques where frozen section considered one intraductal carcinoma of intermediate grade as without malignancy. According to the literature, the false-negative results are common in carcinoma in situ[17].

Since we approached only palpable breast tumors, we believe this must have contributed to the low false negative index (6.2%).

In our study, paraffin histopathological examination confirmed all positive results for malignancy diagnosed by frozen section, which is

consistent with the literature[18-20]. As for statistical analysis, the rates found are also consistent with the reviewed literature.

Early studies with frozen section after "Tru-cut" breast biopsy of palpable tumors did not show a good performance[21]. Nonetheless, studies that followed showed good correlation, as mentioned below.

A prospective cohort study employed percutaneous breast core needle biopsy in 151 patients with palpable tumors and suspected breast cancer and the results showed an accuracy of 80%, sensitivity 77%, specificity 86.4%, PPV 100% and NPV 71.8%. The authors believed that the accuracy was not as high due to the lack of standardization of specimen collection at the beginning of the study and to the 36% rate of tumors smaller than 2cm in the sample[22].

Another study used the biopsy cut frozen technique and avoided surgical biopsy in 81% of cases of patients with palpable tumors and suspected breast cancer, with high accuracy (96%). In that study, despite the 96% sensitivity, 100% specificity and PPV 100%, the NPV was only 67%. The authors attributed this fact to the number of unsatisfactory or inadequate specimens for evaluation. This variation was consistent with the experience of breast cancer specialist and pathologist involved in the exams[7].

A more recent study showed an increased accuracy and predictive values, results similar to the ones found in our study, as in the study of 2619 cases, where the histological results obtained with CNB frozen sections found high accuracy, sensitivity of 99.5%, specificity 85.9%, PPV 99.9% and NPV of 99.4%, being reliable tool for earlier diagnosis of breast cancer[23].

In another prospective cohort study, with a sample of 120 CNBs of palpable and impalpable tumors suspicious of breast cancer, the authors compared the frozen section technique with paraffin and suggested that frozen section showed good accuracy and enabled earlier diagnosis of breast cancer. The results were: sensitivity 95%, specificity 100%, PPV 100% and NPV 90%[24].

In the study carried out in the SGHMP mastology sector, when the pathology result was positive for malignancy, the required exams for staging and appropriate therapy were expedited. The risk of worsening prognosis consequent of the delay in diagnosis, as already described in the literature, was minimized[25].

Therefore, this study suggests that the application of core needle biopsy associated with frozen section histopathology can be applied safely in anticipation of the diagnosis of breast cancer. As it is performed on an outpatient basis, without the need for hospitalization, it further suggests the possibility of decreasing hospital costs and minimizing the clinical and social problems of the patient. Confirmation of these findings requires a larger number of cases and use of these resources in other mastology services.

When comparing the results, frozen section histopathology showed excellent correlation with histopathology in paraffin, with an accuracy of 98.2%. In all patients in this study it was possible to anticipate the diagnosis, staging and appropriate treatment planning for breast cancer through the technique of frozen section of fragments of palpable tumors obtained by percutaneous core needle biopsy. Paraffin histopathology is the gold standard for the diagnosis of cancer and cannot be replaced by any other method.

R E S U M O

Objetivo: *avaliar a acurácia do exame histopatológico por congelação em fragmentos de tecido obtidos por biópsia percutânea com agulha grossa no diagnóstico do câncer de mama em tumores palpáveis.* ***Métodos:*** *foi realizado estudo de coorte em 57 pacientes portadoras de tumores palpáveis e suspeitos de câncer de mama, submetidas à biópsia por punção percutânea com agulha grossa. Os fragmentos foram analisados pela mesma anatomopatologista.* ***Resultados:*** *a congelação diagnosticou 16 casos benignos (28,6%) e 40 malignos (71,4%), enquanto a parafina revelou que 15 eram benignos (26,8%) e 41 malignos (73,2%). Os exames histopatológicos foram concordantes em 55 casos e houve um falso-negativo (6,2%). As taxas estatísticas foram: valor preditivo negativo de 93,8%, valor preditivo positivo de 100%, nenhum falso-positivo (0%), um falso-negativo (6,2%), especificidade de 100%; sensibilidade de 97,6%; concordância observada = 98,2%; concordância esperada = 59,9%;* Kappa *= 0,955 [IC 95% = 0,925 a 0,974, p<0,01].* ***Conclusão:*** *Os achados histopatológicos por congelação apresentaram excelente correlação com os achados pela técnica em parafina nos fragmentos de tumores mamários palpáveis obtidos por punção percutânea com agulha grossa (acurácia de 98,2%). Logo, nestas pacientes, foi possível antecipar o diagnóstico, o estadiamento e a programação terapêutica do câncer de mama.*

Descritores: *Biopsia por punção; Câncer de mama; Congelamento; Secções congeladas; Testes de diagnósticos e procedimentos.*

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