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Comparison of ultrasound controlled aspiration puncture to clinical examination in detection of breast cancer recurrence

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ABSTRACT

Background: *Breast carcinoma recurrence appears in 5%–30% of cases, after the completion of breast cancer treatment. Recurrence appears on thoracic wall (chest wall), on the skin, on the breast tissue remaining after the surgery, equal sided axillary lymph nodes, supraclavicular lymph nodes or on the internal mammary lymph nodes. Recurrence often stays undetected by clinical examination, while it can be detected by ultrasound and punctured under ultrasound control. Cytological confirmation of malignant cells represents a signal to commence a specific recurrence treatment.*

Methods: *Aspiration puncture under ultrasound control has been performed within 128 patients. Only 38 patients, out of 128, did not have distant metastasis at the moment of recurrence detection, so the recurrence was surgically removed and was subjected to the histopathological analysis. The results of definite histopathological analysis were compared to the clinical results and cytological results, which had been obtained preoperatively.*

Results: *31 patients, out of above mentioned 38 patients, have had breast carcinoma recurrence, while 7 patients have had benign tumor lesion. Clinical diagnoses were correct in 47.4% of cases, and incorrect for 52.6%. False positive finding result happened in 7.89% cases and false negative finding result happened in 39.47% cases. Ultrasound diagnoses were correct for 86.84% of patients and incorrect for 13.16% of patients. Cytological analysis of material obtained by aspiration puncture under ultrasound control produced correct diagnoses for 86.84% of patients. 13.16% of patients had inconsistent cytological and histopathological findings result. Cytological analysis has detected malignant cells for 5.26%, but the recurrence was not histopathologically confirmed, which points that the results were falsely positive. Falsely negative results were confirmed for 7.89%.*

Conclusion: *Clinical examination was reliable for 52.6% of patients examined. Cytological analysis of material obtained by ultrasound-controlled puncture was reliable for 86.84% of patients examined. Aspiration puncture followed by cytological analysis gave falsely negative result for 7.89% of patients examined, while clinical examination gave falsely negative result for 39.47% of patients examined. Aspiration puncture gave falsely positive result for 5.26%, and clinical examination gave falsely positive result for 7.89%. Aspiration puncture is simple, easy to perform, without damaging effect for the patient or the medical personnel, it is not expensive and it is significantly more reliable than clinical examination itself for detection of breast carcinoma recurrence.*

Key words: *Breast Neoplasms; Neoplasm Recurrence, Local; Diagnosis; Biopsy, Needle; Ultrasonography; Cytodiagnosis; Sensitivity and Specificity*

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INTRODUCTION

The breast carcinoma is the most frequent malignant disease within female population, which, in spite of performed treatment, often appears as recurrence or metastasis (1). This is the reason why control examination on regular basis is recommended (2). This term refers to a tumor in thoracic wall (chest wall), skin of that area, on surgically spared breast, on equal sided axillary lymph nodes, on supraclavicular nodes or internal mammary nodes (3). Risk from recurrence manifestation depends on tumor penetration range on axillary group of lymph nodes, tumor size when first diagnosed, as well as it depends on receptive status, tumor grade, angioinvasion etc. Loco-regional recurrence manifestation rate varies from 5% to 30% (4). 60%-80% of recurrences appear within first two years after mastectomy. It rarely appears after 5 or more years (5). Clinically suspicious tumor lesion should be confirmed cytologically and/or histopathologically, whenever possible (2,6). Approximately 25% of patients will develop metastasis soon after appearance of recurrence. Such recurrence is not necessary a signal for upcoming systematic disease (7). Approximately 5% to 15% of patients treated with lumpectomy and radiation, will develop some type of recurrence during the control period (8). Mammography and clinical examina-

tion are used for detection of recurrence in breasts after surgery (9). However, due to the development of improved ultrasound devices, this method has taken leading role in observation of such patients, together with puncture followed by cytological analysis (10,11). The techniques for performing ultrasound controlled aspiration puncture can vary from author to author and institution to institution.(12). Today ultrasound is the only acceptable method for evaluation and examination of thoracic wall after mastectomy. Approximately 80% of palpable lesions can be defined as benign or malignant in those cases, while simple palpation method can do the same in approximately 36% of cases (13). The ultrasound is useful to evaluate the depth of infiltration, the relation of lesion to surrounding structures, and it is especially useful when observing and controlling those patients, that were subjects to surgical intervention and radiation of remaining breast tissue (14). A simple way for obtaining recurrence confirmation is ultrasound controlled aspiration puncture (fine needle aspiration-FNA), that has 90% diagnostic accuracy, and 1% of falsely positive and 15% of falsely negative results (15). The sensitivity of fine-needle aspiration, according to the literature, goes up to 95.33%, and its specific rate goes up to 99.22% (16). Different results can be found in literature regarding fine-needle aspiration cytology. For example, sensitivity rates from 65.4% to 99%, while specific rate goes from 96% to 100% (17). If the material is examined macroscopically and microscopically by experienced pathologist, the accurate diagnosis can be expected for 98% of tumors. False negative result is always possible due to the limiting factors of diagnosing (18). Appropriate procedure for obtaining material, its dispatch to the laboratory, as well as way of material processing have great effect on interpretation, whether it will be correct or not. Impressive results are given by institutions, which have well trained radiologists and, above all, cytologists (19). Sometimes it is sufficient to determine existence of malignant disease (for example disease recurrence), if it is not possible to determinate histological form (20). Because of increased interest in cytology breast puncture it is necessary to uniform indication criteria (21). Also the matter of damaging factors of cytodiagnostic breast puncture is often addressed. By observing overall survival and disease recurrence with patients who have been subjected to puncture and with control group, there was neither found difference regarding 5 year survival, nor regarding recurrence appearance. This confirms statement that cytological puncture is not damaging (22).

Aims of the study were: to analyze and compare concordance of clinical examination results to the results of aspiration puncture followed by histopathological diagnoses (PHD) of breast carcinoma recurrence; to show that fine-needle aspiration is more accurate and reliable than clinical examination in recurrence detection, and to show that fine-needle aspiration followed by cytological analysis is irreplaceable diagnostic method in detection of breast carcinoma recurrence.

PATIENTS AND METHODS

Study period was from January 2002 to August 2004. In this period, 128 patients were diagnosed with loco-regional recurrence of malignant breast disease. Some of the tumor lesions were palpable and clinically visible, and the other could not be clinically observed, so they had to be verified by ultrasound, during routine ultrasound examinations of post-operative incision area and area of regional lymph nodes. The stated number of patients included 38 of those who were re-operated and had histopathologically (PHD) verified disease. The other 90 patients were treated by other modalities, chemotherapy (HT), and/or radiation, because at the moment of recurrence detection, they have already had distant metastasis.

The ultrasound device that was used for examination is equipped with linear sound of 5 and 7.5. The 3.5MHz sound was also used to confirm or exclude existence of distant metastasis (liver, etc).

If pathological tumor lesions were found clinically or by ultrasound examination, they were exposed to puncture under ultrasound control, to provide assurance that the needle was in this very lesion and that sample was taken from adequate localization.

Technique of performing aspiration breast biopsy under ultrasound control

This method can be performed by needle leader or by hand, without needle leader, as it was performed in our institution, as it is shown on scheme.

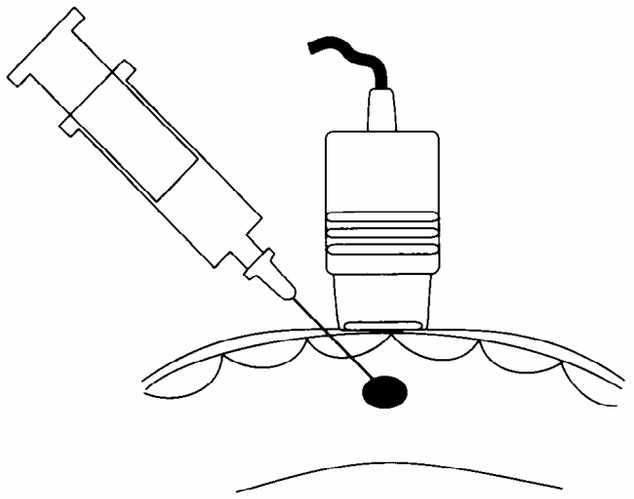

Figure 1. Ultrasound controlled puncture

Fine-needle aspiration biopsy is performed in sterile local field conditions, which requires skin cleansing in area where puncture is to be performed. Sound cleansing is required also. After this, targeted lesion is shown by ultrasound. Needles of 0.7 x 65 mm or 0.9 x 90 mm are used for puncture. These needles are fixed to the syringe of 10 ccm or 20 ccm. The greater volume is better because it has stronger suppress. The puncture is performed under ultrasound control, following and directing the needle into the lesion. When it is certain that needle is in the lesion (which is monitored) syringe clip is pulled and by moving needle with syringe many times (10 – 20) into the lesion, backward and forward, the cytological analysis material is obtained. Cytological analysis is done in Institute for Pathology of Clinical Centre Banja Luka by a pathologist-cytologist. Staining is done according to Giemsa, the material is analyzed, and results are brought in.

The results of cytological analysis are compared with definite histopathological results of material obtained after the surgical removal of tumor lesion. This determines the percentage of accuracy of the method in practical use and its usage justification. Of course, being that it is analysis of the cytological material, the presence of malignant cells would be valid confirmation. The absence of malignant cells does not exclude the possibility of existence of malignant disease. The repetition of punctures is approved.

Data processing and presentation of results

Results were processed as follows:

1. It was marked whether the lesion was diagnosed clinically and/or by ultrasound
2. Ultrasound characteristics were marked as benign or malignant lesions
3. All lesions are punctured under ultrasound control
4. Obtained material was stained by May – Grűnwald – Giemsa method
5. Cytological analysis was marked with “present” or “absent” malignant cells
6. The results of cytological analysis of material obtained preoperatively were compared to histopathological finding, obtained after surgical removal of lesion.

Obtained data were imported into PC database and processed. The results were presented by diagrams, tables, and photos. As only absolute frequencies were given (number of patients), the only possible method to be used is χ^2 test. Thus, Fisher method of exact probability of null hypothesis was used, that allows existence of null and frequencies lss valued than 5 in specific table cells.

RESULTS

Distribution of clinical examination and PHD concordance

Out of total number of 38 patients, 19 had tumor lesion that were detected during the clinical examination by palpation. These lesions were found in thoracic wall, axilla or in the breast tissue that remained after surgery. The disease clinical diagnosis was set (positive clinical examination or finding). No palpable lesions were detected for other 19 patients in stated regions, so the breast carcinoma recurrence was not suspected to exist (negative clinical examination).

Table 1. Distribution of concordance of clinical examination and PHD

	Number of clinical findings in relation to PHD				
Clinical examination	Positive/positive	Positive/ negative	Negative/ positive	Negative/ negative	Total
f	16	3	15	4	38
%	42.11	7.89	39.47	10.53	100.00

PHD-pathohistological diagnoses

Out of 19 palpable lesions, 16 were detected to be tumor recurrence indeed, which was confirmed histopathologically. For 3 patients, that were clinically suspected to have disease recurrence, recurrence was not confirmed, but benign lesions (Table 1). Out of 19 patients that did not have palpable recurrence, 15 had malignant disease confirmed, and 4 were confirmed not to have disease recurrence. In table 1, it is evident that in 42.11% cases the clinical diagnosis was correlated to definite PHD finding result. It is evident that the recurrence was confirmed by histopathological method after the surgical removal of tumor in 42.11% of cases.

In table 1, it is evident that correlation and concordance of clinical examination with PHD finding results for exclusion of tumor recurrence, was in 10.53% of cases.

Once these results are put together, we get that clinical examination in detection of tumor recurrence was reliable in 52.64% of cases. It is evident that in 7.89% of cases that were suspected to have disease recurrence after the clinical examination, the recurrence was not confirmed by PHD. It can be said that clinical examination had false positive results in 7.89% of cases.

In table 1 it is evident that in 39.47% of cases that were not suspected to have disease recurrence after the clinical examination, the recurrence was confirmed by PHD after the extirpation, meaning that 39.47% of cases had false negative clinical results.

Distribution of FNAC and PHD concordance

In order to achieve higher accuracy of lesions etiology evaluation that were clinically detected and those confirmed by ultrasound, one step further is being taken and lesions are punctured under ultrasound control, after which the cytological analyses of material is done (FNAC-fine-needle aspiration citology). If in the obtained material malignant breast carcinoma cells are detected, the results are declared positive, meaning that it is local breast carcinoma recurrence. If the malignant cells are not detected, the results are declared negative.

Out of 38 patients that had been put through fine needle aspiration and cytological analysis of material (FNAC), 30 patients had malignant cells detected, which had confirmed breast carcinoma recurrence.

Analyzing concordance of positive cytological result for 30 patients, with definite histopathological results, we have found that for 28 patients, or 73.68%, the results were in concordance with each other. For 2 patients, or 5.26%, the cytological result was not in concordance with histopathological result, thus those were the cases of false positive results (Table 2).

Table 2. Distribution of concordance of Ultrasound – FNA finding and PHD

	Number of ultrasound – FNAC finding in relation to PHD				
Ultrasound - FNAC	Positive/positive	Positive/ negative	Negative/ positive	Negative/ negative	Total
f	28	2	3	5	38
%	73.68	5.26	7.89	13.16	100.00

FNAC- **fine-needle aspiration citology**
PHD-pathohistological diagnoses

In table 2 it is evident that for 8 patients, or 21.05%, there were no malignant cells detected by cytological analysis. However, in definite histopathological material for 5 patients (13.16%) there was no disease recurrence found, indeed. While for 3 patients, (7.89%) the recurrence was confirmed. Those were the cases of false negative FNAC (Table 1).

Concordance of results of FNAC and PHD, the method accuracy rates for recurrence confirmation (73.68%), as well as for recurrence exclusion (13.16%) in total of 86.84%.

DISCUSSION

According to the literature data, local disease recurrence most commonly appears within first two years after mastectomy, and appearance rate varies from 5% to 30% (5,6). European Oncologists' Association recommends regular control in order to detect tumor recurrence as early as possible, and it also requires cytological and/or histopathological confirmation of recurrence whenever possible (2). Those were the reasons why our Institution has developed regular usage of fine-needle aspiration of suspected lesions, followed by cytological analysis of material.

The fact itself that 52.6% patients have had clinically detected recurrence, requires further clinical testing in order to detect recurrence at early stage. It is possible to define the detected lesion as malignant or benign by palpation in 36% cases. The ultrasound, is exceptionally useful, not only in lesion detection, but also in evaluation of infiltration depth, relation of lesion to the surrounding structures, as well as in observation and control of those patients that have already been treated by surgery and radiation (14).

At first it is important to palpate the lesion as small dimension as possible. When the region that has already been radiated is in question (and it is known that those cases can develop tumor recurrence in 10% of cases (2), it is rather difficult to palpate the lesion of few millimeters to 1 cm in range, if there is a lot of fibrous tissue. In case that there is lymph node in between ribs, next to sternum, it is necessary that it has greater diameter in order to come out of rib line, so that it would be possible to palpate it. In order to palpate node located highly in the axilla, or under frontal axillar crease, between two pectoral muscles, or in subclavian region in space between clavicle and ribs, it is necessary that it has larger dimensions. Approximately 70% of all breast tumors are clinically palpable, and tumors smaller than 0.6cm to 1 cm are palpable in approximately 50% of cases (23). They also state that success depends on many conditions such as age, breast size, whether the radiation has been previously undertaken or not, depth of recurrence location, etc. On the other side, node of granuloma type often deceives medical experts and they can suspect it to be a recurrence. The same situation was in our case of 7.89% of false positive results, while 39.47% were false negative results (15). It has already been mentioned that many literature sources state the rate of 36% of cases in which it is possible to define clinical lesion as malignant or benign (13).

If the lesion is removed because it was suspected to be a recurrence, and this has not been confirmed histopathologically, further treatment in terms of radiation or systemic chemotherapy will not be required. The problem would occur if systemic treatment was started prior to confirmation of histopathological or cytological finding of recurrence.

Analysis of concordance of aspiration puncture and cytological analysis to PHD

Correlation between cytological and histopathological results is obtained in 86.84% cases. The rate of false positive results was 5.26%, and false negative results 7.89%. Literature sources state the rate of 0.1% to 2.5% for false positive, and 0% to35% for false negative results (15,16). Literature sources states that 90% accuracy of FNAC has 1% of false positive and 15% of false negative results (18). Specific rate goes even up to 99.22% (16). Even different results can be observed through literature for the accuracy of fine-needle aspiration cytology. For example, sensitivity rates from 53% to 99%, and specific rate goes from 96 to 100% (17).

Proper way of material obtaining, material laboratory dispatch, and the way of material is being processed has great influence on correct interpretation (18). Once all of this is overviewed, it is possible to explain why recurrence was finally confirmed after negative cytological finding for 3 patients. Material obtain is first in question. When it was analyzed which of the patients had negative finding, it was observed that those were the patients that had puncture done at the beginning of practice of this technique at the Institution, and at that time experience of performer was not as good as it is now. In time, the method of deposit, drying and transport of obtained material was agreed with Institute of Pathology. The experience of cytopathologist in malignant cells diagnoses has important role. If neoplasm is macroscopically and microscopically examined by pathologist that is experienced in this area, the accurate diagnoses can be expected in 98% of tumors. False negative result is always possible due to the limiting factors of diagnosing (18). Solving the problem of existence of malignancy is the basis of cytodiagnostics of breast carcinoma recurrence, since we already have histopathologically diagnosed disease (20). This is done in order to commence the treatment if necessary, as soon as possible. Good cooperation with surgeon, who extirpates the cytologically verified recurrence, also is very important.

In one case (out of 3 false negative cases) the surgeon has removed the lesion that was not punctured, meaning that the wrong lesion was extirpated, and the lesion that was recurrence in certain remained in patient's body. This patient was directed to surgery again, when the correct lesion was extirpated and confirmed by histopathological finding. This result was filed within positive results when specific method calculation was done. In other cases it is most probable that disintegrated, degenerative cells deceived cytopathologist who marked them malignant even though they were not malignant. Impressive results are given by institutions that have well trained radiologists, and above all well trained cytologists (11,24).

CONCLUSION

- Clinical examination has shown accuracy for 52.64%, and FNAC for 86.84%.
- Ultrasound controlled aspiration puncture with cytological sample analysis of palpable and impalpable lesion, showed to be efficient in early detection of repeated appearance of disease after breast carcinoma surgery.
- It is quick and minimally invasive diagnostic method. It is simple, easily performed, requiring minimum of staff and training, it is not damaging for staff or patient, it is efficient and not expensive method.
- FNAC is very valuable and exact method, but there is still work to be done until the results can correlate to those in literature.
- Significance of fine-needle aspiration, its cytological analysis and aspiration of obtained material, is in early detection of recurrence and commencement of adequate treatment.

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