META ANALYSIS OF THE VALUE OF ULTRASONOGRAPHY COMBINED WITH NANO CARBON IN THE DETECTION OF AXILLARY SENTINEL LYMPH NODES IN BREAST CANCER

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ABSTRACT

Objective: to systematically evaluate the feasibility of sentinel lymph node biopsy (SLN) in patients with lymph node positive breast cancer after neoadjuvant chemotherapy (NAC).

Methods: the full-text databases of PubMed, Cochrane Library, Springer, Elsevier, national technical, Wanfang and other journals were searched by computer. The literatures of sentinel lymph node biopsy in breast cancer patients after neoadjuvant chemotherapy were included. The retrieval time was from January 2000 to December 2013. The literatures that met the inclusion criteria were analyzed by meta analysis.

Results: totally 10 clinical studies were included and 1437 patients were included. The sensitivity of sentinel lymph node biopsy was 0.867 (95% confidence interval: 0.835-0.894), and the specificity was 1.000 (95% confidence interval: 0.988-1.000).

Conclusion: sentinel lymph node biopsy after neoadjuvant chemotherapy for breast cancer patients with positive axillary lymph nodes has high sensitivity, specificity, feasibility and accuracy.

Keywords: Sentinel lymph node biopsy, neoadjuvant chemotherapy, breast cancer, meta analysis.

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Introduction

Neoadjuvant chemotherapy (NAC) has become an indispensable part in the treatment of locally advanced and early breast cancer[1-5]. It can increase the probability of breast conserving, evaluate the sensitivity of tumor to chemotherapy, and make axillary lymph nodes descending[6-8]. Sentinel lymph node biopsy (SLNB) can correctly judge the axillary lymph node metastasis and classification. Compared with the axillary lymph node dissection (ALND), SLNB can greatly reduce the incidence of various acute and chronic complications[9-11]. In recent years, SLNB has replaced ALND as a standard model for the treatment of axillary lymph node negative early breast cancer, but it is still unclear when sentinel lymph node biopsy should be performed in the initial stage of axillary lymph node positive breast cancer around NAC, especially for the post NAC sentinel biopsy, which is controversial and lacks sufficient evidence-based[12-14]. In order to understand the feasibility and accuracy of SLNB for NAC in clinical work, we use meta analysis method to combine and analyze the existing data[15].

Objective and method

Research type and research object data source of clinical data

Computer searches PubMed, embasmedline, CNKI and Wanfang databases. The retrieval time is from the establishment of the database to March 2018. The combination of subject words and free words is used for data retrieval. See Table 1 for the

specific retrieval method. The type of study was limited to RCT, and the language was limited to Chinese or English. The subjects of the study were: breast cancer patients with axillary sentinel lymph nodes who were finally treated by surgery and confirmed by pathological biopsy; all sentinel lymph nodes were examined by contrast-enhanced ultrasound; all the studies were based on pathological diagnosis as the gold standard.

The basic contents of literature extraction include

The author's name publishing time, average age, ultrasound equipment, ultrasound contrast method, true positive rate (TP), false positive rate (FP), true negative rate (TN), false negative rate (FN), etc.

Literature quality evaluation

Newcastle Ottawa scale (NOS) was used to evaluate the cohort study.

The evaluation criteria included:

• Study population selection (4 items), inter group comparability (1 item) and outcome measurement (3 items).

A total of 9 points were evaluated by using octane risk bias assessment tool, It mainly includes:

• Selection bias: random sequence generation and assignment concealment;

• Implementation bias: blinding researchers and subjects;

• Measurement bias: blind evaluation of research results;

• Follow-up bias: integrity of data;

• Reporting bias: selective reporting of research results;

• Other bias: other sources of bias.

Results

Characterization of carbon nanoparticles

As shown in Figure 1, the nano carbon system is composed of a layer of cylindrical surface with graphite sheet structure around the tube axis.

The orientation of the graphite layer is parallel to the tube axis (known as "parallel type"), and the two kinds of nano carbon particles prepared on the same Ni catalyst have obvious differences in the orientation of the wall like graphite layer relative to the central axis of the tube.

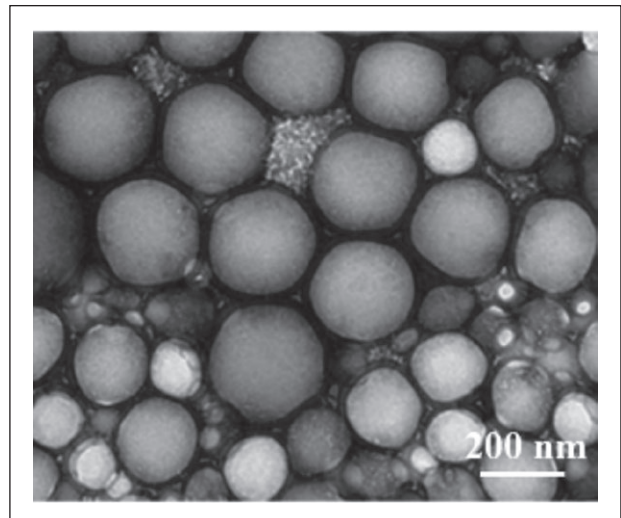The reason may be that the orientation of the two kinds of feed gas molecular catalysis.

Figure 1: Characterization of carbon nanoparticles.

Results of literature search and basic characteristics of the accepted literature

A total of 1644 literatures were retrieved. Through the screening of inclusion and exclusion criteria (see Figure 1 for the specific process), a total of 10 literatures were finally included: 2 randomized controlled trials, 2 prospective cohort studies, 6 retrospective cohort studies.

The no score of cohort study showed that the quality of literature was reliable (the scores were greater than or equal to 6 points); the "Cochrane risk bias assessment tool" of randomized controlled trial showed that the risk of bias was low.

The total number of cases in this study was 5704, including 3822 cases of CLND and 1882 cases without CLND, mainly from the United States and Europe, with a median follow-up of 20-84 months. See Figure 2 for the basic characteristics of Naren literature and various studies.
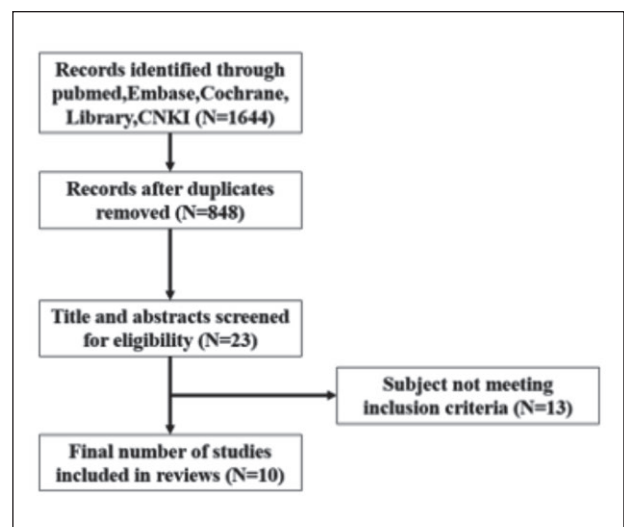

Figure 2: Document retrieval and screening process.

Meta analysis results

Ten articles reported tpfp, TN, FN measured by sentinel lymph node biopsy and axillary lymph node dissection after NAC,. These data were input into the metadisc1 software and the sensitivity heterogeneity test was 2 = 68.1% <75%.

There was heterogeneity, but it could be combined. The combined sensitivity was 0.867, and 95% confidence region was 0.835-0.894. The forest map was made as shown in Figure 1. P>0.05, P = 0%, good homogeneity. The total number of sentinel lymph nodes detected was 1268, with a combined detection rate of 88.2%. SLNB correctly judged the number of axillary lymph node staging 168, with a combined accuracy rate of 92.1%, indicating that patients with axillary lymph node positive breast cancer were more sensitive to SLNB after receiving NAC, which was feasible. See Figure 3.
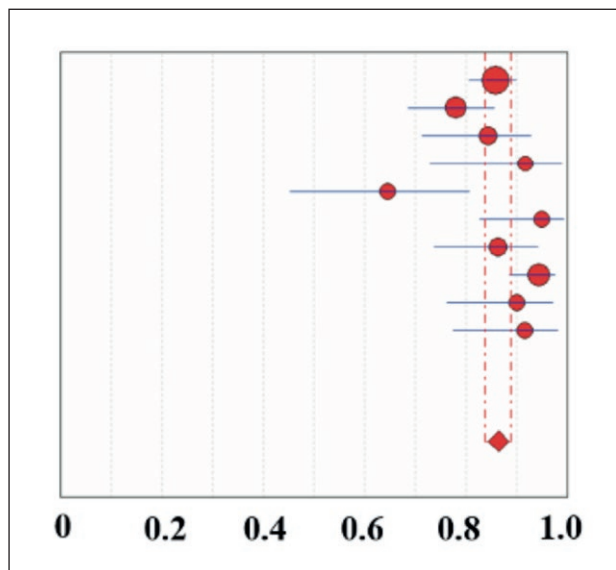

Figure 3: Sensitivity analysis forest map.

Ultrasonic image analysis of research object

Among the 83 cases of mass, 49 cases were less than 2.0 cm, 31 cases were 2.1-3.0 cm, and 3 cases were more than 5.0 cm.

All of them were hypoechoic, 14 cases had clear boundary, 69 cases had unclear boundary and irregular shape, showing "crab foot like" (see as Figure 4A) or "burr like "(see as Figure 4B). In 20 cases, there were multiple nodule foci, and in 9 cases, there was strong echo of gravel like spots. The results of color Doppler ultrasound showed that blood flow was seen in 56 cases of lesions, 45 cases with hyperplasia of mammary gland see from Figure 5A, 65 cases with enlargement of axillary lymph nodes, 39 cases with abnormal lymph nodes in bilateral axilla see from Figure 5B.
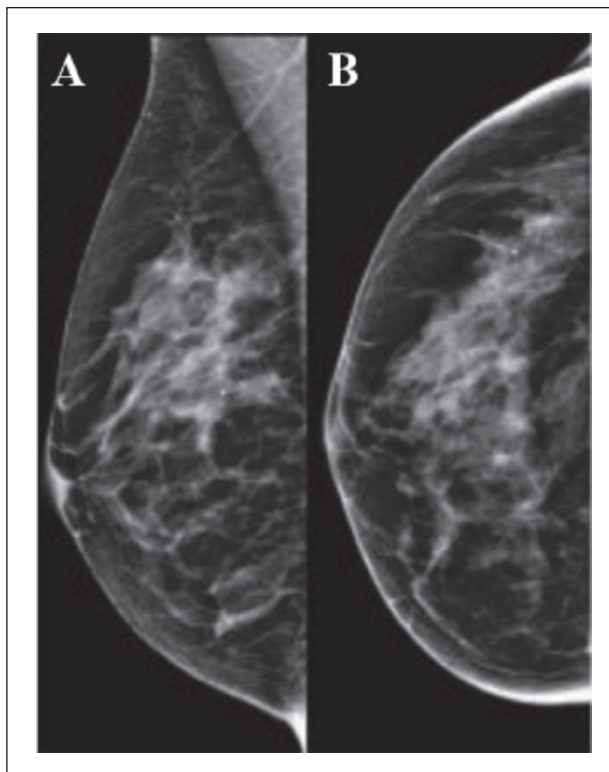

Figure 4: Ultrasonic image of infiltrating duct (A) burr sign on the edge of tumor, (B) obvious hyperechoic halo around.
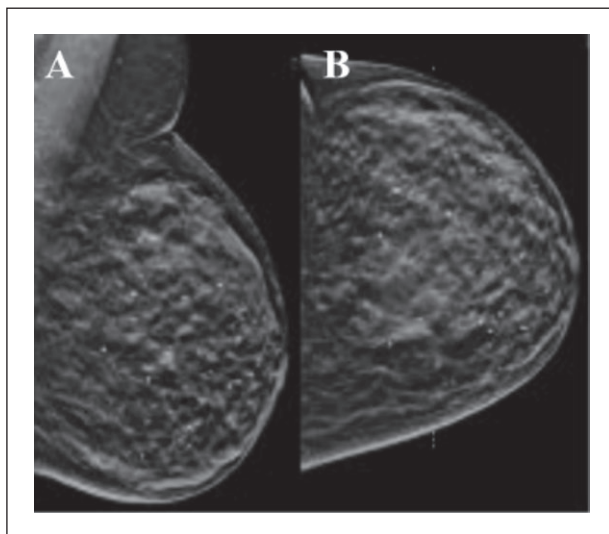

Figure 5: Sonography of invasive ductal carcinoma (A) multiple anechoic areas in the mass; and (b) positive PR expression in the pathological section.

Discussion

At present, lymph node labeling and sentinel lymph node biopsy have become the standard procedures for the treatment of axillary lymph node negative early breast cancer, but for axillary lymph node positive progression and early breast cancer after NAC, SLNB has not been conclusive, lack of high

evidence-based guidance, clinicians are still confused[16-18]. In 2005, the American Society of Clinical Oncology (ASCO) did not recommend slnbi after NAC[19-21]. At the 2009 St. Gallen meeting, experts basically reached a consensus that SLNB after NAC is safe, accurate and reliable. A meta-analysis of 449 patients was included in 10 articles. The combined IR was 94.3% and the sensitivity was 95%. 21 articles collected by people[22-24].

According to the meta-analysis of 1273 patients, the detection rate of SLNB was 90% and the sensitivity was 88%[25]. Both of them think that SLNB is accurate and feasible for breast cancer with negative lymph node after NAC. In this study, a total of 1437 patients were included in 10 literatures, including 6 retrospective studies (S10) and 4 prospective studies[2]. The sensitivity, specificity and 95% confidence interval were calculated and summarized by meta analysis[26-30]. The combined sensitivity and specificity were higher, consistent with the analysis results of the included studies, suggesting that SLNB diagnostic test has certain reliability, It can be used as a diagnostic method to evaluate axillary stage after NAC in locally advanced and early breast cancer[31-34]. This study also has its own limitations: the selection bias of search literature is only included in English literature published after 2007, and the publication bias of search literature.

Most of the results that can be retrieved from the database are positive, and the negative results are difficult to publish and not included. Lack of detailed data, SLNB detection rate is affected by tumor stage, doctor's experience, lymph staining method and so on. Therefore, the application of SLNB needs to be improved under the above limitations. The next research should be how to analyze and solve the factors that increase the false negative rate of SLNB in clinical practice.

Conclusion

To sum up, sentinel lymph node biopsy for breast cancer patients with axillary lymph node positive after NAC has high sensitivity, specificity, feasibility and accuracy.

SLNB technology is safe and reliable to evaluate axillary lymph node stage and avoid ALND. It can reduce various postoperative acute and chronic complications and greatly improve the quality of life of patients. Of course, in the future, a large sample and multi center clinical study is needed to expand the feasibility of SLNB in NAC stage.

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