

Axillary management after identify the sentinel lymph node in breast cancer. A literature review

Abstract

Histological status of axillary lymph nodes represents one of the most important prognostic factors for the long term outcome of patients with breast cancer. In order to achieve a good control of the disease, axillary lymph node dissection was for a long period of time the standard of care for treating the possible lymphatic metastases. However, this surgical procedure is usually associated with a high level of severe postoperative complications such as debilitating lymphedema of the upper limb. In the attempt to limit the postoperative morbidity, the concept of sentinel lymph node has brought a significant improvement in the outcome of these patients. Moreover, recent studies reported the possibility to treat conservatively via oncological treatment the sentinel lymph node, reducing even more the rate of unnecessary lymph node dissection. This is a literature review of the latest studies conducted on this theme.

Keywords: breast cancer, lymph node metastases, sentinel lymph node

Introduction

Breast cancer remains a common gynecologic malignancy which is characterized by a high propensity for lymphatic spread, the histopathological status of axillary lymph nodes remaining one of the most important prognostic factors for the long term outcomes of these patients⁽¹⁾. Moreover, a relationship between the number of the involved axillary lymph nodes and the long term outcome was established, patients presenting more than three metastatic nodes having a significantly poorer outcome⁽²⁾. Moreover, the adipose tissue were incriminated to have a role in this pathology, being the major location for the metabolization of sex steroid hormones⁽³⁾.

Once these aspects have been widely accepted worldwide, the surgeons' attention was focused on performing an adequate axillary lymph node dissection in order to achieve a good control of the disease. However, although in most cases the oncological results were satisfactory, a significant number of patients developed debilitating postoperative complications such as upper limb lymphedema, seroma or neuropathies.

However, the incidence of this complication decreased in the last decades, once the technique of sentinel lymph nodes has been widely introduced, becoming at this moment the standard of care⁽⁴⁾. It is estimated that the technique is associated with a success rate of in up to 90% of cases and is significantly influenced by the surgeon's experience⁽⁵⁾. It is widely accepted that in cases presenting negative sentinel lymph nodes no further surgery is needed while cases with positive sentinel lymph nodes are further submitted to axillary lymph node dissection⁽⁶⁾.

In the meantime, association of neoadjuvant oncologic treatment in order to limit the extent of the disease and to increase the chance of performing a conservative surgical approach has also proven to eradicate in certain cases the axillary micrometastases⁽⁷⁾. This is a literature review of the most relevant studies conducted on this theme.

Axillary lymph node management after neoadjuvant chemotherapy

Beginning from the hypothesis that after completing the neoadjuvant chemotherapeutic treatment significant number of patients does not necessitate axillary lymph node dissection, it can be stipulated that these patients do not require further axillar exploration. However, it has been showed that the false negative rates for sentinel lymph node biopsy after neoadjuvant chemotherapy ranges between 0-20%^(8,9). However, the decision of administration of systemic chemotherapy is significantly influenced by the tumor histological subtype too. For example in patients presenting triple negative tumors the aggressivity of the tumor itself is indeed the indication for systemic chemotherapy even in the presence of a single positive sentinel lymph node⁽¹⁰⁾. A more debate subject is the one regarding the administration of systemic therapy in patients with hormone positive breast cancer and positive sentinel lymph nodes. In these cases endocrine therapy is widely administrated with good results in terms of survival and systemic toxicity^(11,12). In these cases determination of Ki67 antigen levels and genetic tests play a crucial role in order to assess which cases can benefit more from the association of systemic chemotherapy. Recent studies evaluated that estimation of Oncotype DX (one of the first approved gene

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Received:
February 12, 2017
Revised:
February 20, 2017
Accepted:
March 25, 2017

expression tools) in association with the presence of one to three positive sentinel lymph nodes could become a positive indication for systemic chemotherapy administration⁽¹³⁾.

However, a study published in 2015 in Maastricht, evaluated the further management of the axilla after systemic chemotherapy and demonstrated that axillary lymph node dissection could not be systemically omitted in clinically node positive patients with negative sentinel node biopsy after administration of neoadjuvant systemic chemotherapy⁽¹⁴⁾.

Axillary radiotherapy protocol

In cases presenting one or two positive sentinel lymph nodes submitted to breast conserving surgery whole breast radiotherapy has been proposed in association with omission of axillary lymph node dissection. This therapeutic protocol decreases the rate of postoperative morbidity; however it does not offer any information about the tumoral burden of the axilla⁽¹⁵⁾. Three retrospective studies conducted on the subject of the axillary lymph node management after determining the positivity of one sentinel lymph node demonstrated that in the absence of completing the axillary lymph node dissection the overall survival rate was similar with the one reported by the cases submitted to complete axillary lymph node dissection⁽¹⁶⁻¹⁹⁾.

In order to determine in which cases the axillary lymph node dissection could be replaced with axillary radiotherapy, two trials have been conducted and published recently^(15,19). In AMAROS trial the authors demonstrated the non-inferiority of axillary radiotherapy when compared to axillary lymph node dissection in patients with clinical T1-2N0 breast tumors regardless the number of positive sentinel lymph nodes. In the meantime the rate of post-procedural complications at 5 year follow up was significantly lower among patients submitted to radiatiotherapy when compa-

red to those submitted to axillary lymph node dissection⁽¹⁶⁾. Moreover, in ACOSOG Z0011 trial which was published in 2013 the authors stated that omission of both axillary lymph node dissection and axillary radiotherapy can be taken in consideration with similar results, the very low rate of axillary progression of the disease being explained by the effectiveness of the administration of systemic therapy and high tangential field radiotherapy⁽¹⁵⁾.

Another trial which studied the optimal treatment of the axilla in positive sentinel lymph node biopsy for early stage breast cancer comes from Savolt and contributors⁽²⁰⁾. The study included 1054 patients randomized for axillary lymph node dissection and 1052 patients randomized for regional nodal irradiation between 2002 and 2009. The principal inclusion criterion was related to the stage of disease, all patients being diagnosed with stage I or II breast cancer. The primary endpoint of the study was to compare the axillary recurrence between the two groups while the secondary endpoints were to compare the disease-free and overall survival. The authors showed that the axillary recurrence rate was 2% in the axillary lymph node dissection group versus 1.7% in the radiotherapy group while the disease free survival and respectively overall survival at eight year follow up was 72.1% and 77.9% in the axillary dissection group versus 84.8% and 77.4% in the radiotherapy group. These results enabled the authors to conclude that axillary radiation therapy is not inferior to axillary lymph node dissection and could be an efficient therapeutic option in patients with early stage breast cancer⁽²⁰⁾.

Conclusions

All these data come to support the hypothesis that in selected patients a conservative axillary management can be performed with good early and long term outcomes. ■

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