

## Contralateral axillary disease management

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Contralateral axillary lymph node metastasis without distant organ involvement in breast cancer is relatively rare, with a reported prevalence ranging from 1% to 6%. This specific condition presents significant challenges due to insufficient data and a lack of clear treatment guidelines.

The most controversial issue regarding contralateral axillary lymph node metastasis is whether it is regarded as a distant metastasis or regional metastasis. In the American Joint Committee on Cancer (AJCC) staging system, only the ipsilateral axillary, subclavian, supraclavicular, and internal mammary lymph nodes have been defined as the regional lymph nodes for the breast. Contralateral axillary lymph node metastasis without distant organ involvement is usually classified as M1 (Stage IV). However, recent studies have provided conflicting evidence on the matter that the prognosis of patients with contralateral axillary lymph node metastasis was similar to that of patients with Stage III or locoregional recurrence and significantly better than that of patients with distant metastases. Nevertheless, all of these studies have inherent limitations of being retrospective studies with a small number of patients.

In addition, it is still questionable whether local treatment such as surgery or radiotherapy is beneficial for patients with contralateral axillary lymph node metastasis. Research on this topic has yielded contradictory findings, with some studies showing improved survival outcomes with axillary lymph node dissection or radiotherapy, whereas others report no significant benefits. Meanwhile, there is a consensus that contralateral mastectomy is unnecessary due to the extremely low incidence of contralateral breast cancer.

The development of contralateral axillary lymph node metastasis in breast cancer may be attributed to two possible mechanisms: hematogenous spread from the original primary tumor or abnormal regional lymphatic drainage to the contralateral axilla. Based on these mechanisms, some argue for considering the former as stage IV and the latter as a locoregional disease. Additionally, the timing of contralateral axillary lymph node metastasis occurrence is crucial. It can be categorized into two types: synchronous and metachronous. Synchronous contralateral axillary lymph node metastasis is defined as when it occurs simultaneously with the primary breast tumor, while metachronous contralateral axillary lymph node metastasis is defined as when it appears over 6 months or 1 year after the initial diagnosis. Most patients usually tend to experience metachronous disease rather than synchronous disease. Interestingly, the prognosis is generally more favorable in metachronous than synchronous disease. Given that primary surgery or radiotherapy may cause changes in the lymphatic drainage to the contralateral axillary lymph node, it is assumed that metachronous disease is more likely to be a locoregional disease. Accordingly, it is cautiously suggested that local therapy is more actively considered in the case of metachronous disease.

Despite the ongoing debate regarding whether contralateral axillary lymph node metastasis is considered a distant metastasis or regional metastasis, systemic therapy is still crucial in managing these patients. Recent advances in novel drugs offer multiple treatment options for patients with stage IV breast cancer. With the development of various novel drugs, we have many options for patients with Stage IV breast cancer. By leveraging these therapeutic options, significant improvements in survival outcomes can be expected with fewer adverse effects.

This presentation aims to review the available evidence concerning the characteristics and treatment options for patients with contralateral axillary lymph node metastasis in breast cancer. Ultimately, managing contralateral axillary lymph node metastasis in breast cancer requires a comprehensive and individualized approach. Also, I hope to explore the various perspectives on this controversial topic through the discussion during this session.