



# Lymph node dissection in thymic malignancies

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Lymph node metastasis is not uncommon and an important clinical parameter in thymic malignancies. It is consistently reported that lymph node metastasis is a poor prognostic factor in thymic malignancies (1-4). Original Masaoka stage classification system and latest International Association for the Study of Lung Cancer (IASLC)/International Thymic Malignancy Interest Group (ITMIG) stage classification system for thymic malignancies classify lymph node metastasis as stage IV (5,6). Understandings, however, about the details of lymph node metastasis in thymic malignancies such as incidence, lymphatic pathway, method of lymph node dissection (LND), and the benefit of diagnosis of lymph node metastasis are extremely limited until now.

The ChART study about lymph node metastases in thymic malignancies by Gu *et al.* is the latest and largest series about this subject which evaluated 1,617 surgical cases (3). All lymph node metastases in this study were diagnosed pathologically with surgical specimens. In ChART study, incidence of lymph node metastasis had significant relation with World Health Organization (WHO) histologic subtype and T stage. There was no lymph node metastasis in type A/AB/B1. Lymph node metastasis rate were 1.3% in type B2/B3, 7.9% in type C, and 16.7% in neuroendocrine thymic tumors. Lymph node metastasis rate were 0.2% in T1, 6.9% in T2, 8.5% in T3, and 7.4% in T4. Nodal metastasis was independent prognostic factor in thymic carcinoma but was only marginally significant in thymoma (3). The results of ChART study are consistent with previous studies. Japanese multi-institutional study, Korean single institutional study and SEER data analyses from USA also showed WHO histologic subtype and tumor invasiveness (T stage) are factors for lymph node metastasis and lymph node metastasis is a poor prognostic factor (1,2,4). The ChART study, however, has limitations as

like other studies. Limitations are small number of subgroup due to rarity of thymic malignancies, heterogeneity between histologic subtypes, lack of standardized LND strategy, no detailed data about LND and inconsistent adjuvant treatment in patients with lymph node metastasis. The most crucial limitation is that no standardized protocol of LND ever has been applied in thymic malignancies. The IASLC/ITMIG staging project for thymic malignancies also failed to performed meaningful analysis about nodal metastasis because of paucity of available detailed data (6). Thus, accumulation of data under standardized LND protocol is the only realizable and exigent task at present. Without organized large scale data, this issue will be remain controversial forever. LND is recommended in other thoracic malignancies to achieve more accurate pathologic stage which enables precise prediction of prognosis and affords chance to perform possibly beneficial adjuvant treatment (7,8). Furthermore, removal of lymph node with metastasis can improve loco-regional disease control.

The first step to building an organized data for lymph node metastasis is using a universal and systematic lymph node map. Yamakawa had proposed a nodal classification system for thymic malignancies (9). But, the definition of that system was not minute. Recently, ITMIG proposed a systematic lymph node map for thymic malignancies with precise explanation (10). In ITMIG lymph node map, anterior regional nodal group including low anterior cervical and anterior mediastinal nodes are classified as N1 station. Deep regional nodes including deep cervical, internal mammary and middle mediastinal nodes are classified as N2 station. One of unique changes in ITMIG lymph node map is classifying paraaortic node group (IASLC lung cancer lymph node map station #6) as N1 station. N3 station does not exist and all other node metastases are classified as M1

**Table 1** Modified recommendation for lymph node dissection in thymic malignancies (4)

Lymph nodes	Recommendations
Anterior regional nodes (N1)	
Peri-thymic nodes	Routine <i>en-bloc</i> dissection
Prevascular nodes	
Supradiaphragmatic nodes	
Low anterior cervical nodes	Sampling in stage I, dissection in stage $\geq$ II
Paraaortic nodes	
Deep regional node (N2)	
Right paratracheal nodes	Sampling in stage I, dissection in stage $\geq$ II
Other nodes	Sampling in stage $\geq$ II thymic carcinoma
All suspicious nodes should be dissected.	

stage in ITMIG lymph node map (10). The ITMIG lymph node map should be used as a standard lymph node map for clinical practice and research of thymic malignancies because using common language is the starting point for the communication and collaboration among world-wide researchers studying this rare disease.

Another issue is ensuring quality of LND. The extent of LND and the number of dissected lymph node are generally used quality measures of LND in other thoracic malignancies. The extent and the number of dissected node would affect the accuracy of pathologic staging in thymic malignancies as proved in lung cancer and esophageal cancer (7,8). The ChART study and other large scale studies contain no detailed data about the extent of LND and the number of dissected lymph node. In SEER database studies, only median number of evaluated lymph nodes were reported and further meaningful analyses were impossible (2). Our group reported two studies about the extent of LND and the number of dissected lymph nodes in thymic malignancy patients who underwent intentional LND. We divided pathologic N0 thymic carcinoma into pN0a (dissected lymph nodes  $\leq$ 10) and pN0b (dissected lymph nodes  $>$ 10), then compared prognoses of two groups with Nx (no LND) and pN1 groups. Prognoses of pNx and pN0a groups were similar, and the prognoses of both groups were intermediate between the pN0b and pN1 groups. This finding suggests more than 10 nodes should be evaluated to predict prognosis accurately in thymic carcinoma (11). As like in ChART study, our study also showed WHO

histologic subtype and tumor invasiveness were factors for the lymph node metastasis in thymic malignancies. Rate of lymph node metastasis in T2/3 stage was 37.5% whereas only 1% of T1 stage had lymph node metastasis. Nodal metastasis rate was 5.1% in thymoma and 25% in thymic carcinoma. There was no nodal metastasis in 101 WHO type A/AB/B1. An important finding of our study is frequent metastasis to the right paratracheal lymph nodes group regardless of tumor location. Six out of 7 pN2 patients had metastases at right paratracheal lymph nodes (4). This phenomenon closely accord with the findings of anatomical study by Murakami *et al.*(12) The right paratracheal lymph node group plays important role in the lymphatic pathway of thymic malignancies and should be dissected in high grade histology or locally advanced thymic malignancies. ITMIG already proposed recommendation about LND strategy for thymic malignancies in 2011. ITMIG recommended removal of any suspicious nodes, removal of adjacent nodes and anterior mediastinal nodes in stage I and II thymomas, systematic anterior mediastinal node dissection and systematic sampling of appropriate intrathoracic nodes in stage III thymomas and at least a systematic sampling of anterior mediastinal, intrathoracic, supraclavicular, and lower cervical nodes for thymic carcinomas (if the diagnosis is suspected or known) (13). This recommendation was devised based on Yamakawa-Masaoka nodal staging system and available data at that time. In the meantime, new lymph node map and new stage classification system have replaced the former standards and more information about pattern of nodal metastasis have been accumulate. Thus, modification of ITMIG recommendation considering recent changes is necessary to improve quality LND for the future studies. We have proposed a modified recommendation based on ITMIG lymph node map and IASLC/ITMIG stage classification system for thymic malignancies and put emphasis on the dissection of right paratracheal lymph node group (Table 1) (4).

Lymph node metastasis is an important parameter in thymic malignancies. But current understandings about lymph node metastasis in thymic malignancies is substantial. LND is the only realizable method to achieve deep knowledge of lymph node metastasis in thymic malignancies and should be performed on the basis of new standards.

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