Resection of thymoma should include nodal sampling

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Objective: Thymoma is best treated by surgical resection; however, no clear guidelines have been created regarding lymph node sampling at the time of resection. Additionally, the prognostic implications of nodal metastases are unclear. The aim of this study was to analyze the prognostic implications of nodal metastases in thymoma.

Methods: The Surveillance, Epidemiology, and End Results database was queried for patients who underwent surgical resection of thymoma with documented pathologic examination of lymph nodes. The impact of nodal status on survival and thymoma staging was examined.

Results: We identified 442 patients who underwent thymoma resection with pathologic evaluation of 1 or more lymph nodes. A median of 2 nodes were sampled per patient. Fifty-nine patients (59 of 442, 13.3%) had $\geq$1 positive node. Patients with positive nodes were younger and had smaller tumors than node-negative patients. Median survival in the node-positive patients was 98 months, compared with 144 months in node-negative patients ($P = .013$). In multivariable analysis, the presence of positive nodes had a significant, independent, adverse impact on survival (hazard ratio 1.945, 95% confidence interval 1.296-2.919, $P = .001$). The presence of nodal metastases resulted in a change in classification to a higher stage in 80% of patients, the majority from Masaoka-Koga stage III to stage IV.

Conclusions: Nodal status seems to be an important prognostic factor in patients with thymoma. Until the prognostic significance of nodal metastases is better understood, surgical therapy for thymoma should include sampling of regional lymph nodes. (J Thorac Cardiovasc Surg 2015;149:737-42)

See related commentary on pages 743-4.

Thymoma is a rare tumor of the anterior mediastinum with an incidence of 0.15 per 100,000 person-years.[1] The most commonly accepted staging system for thymomas is the modification of the Masaoka classification by Koga and colleagues,[2] which classifies tumors according to invasion of adjacent organs. In this classification, thymoma with nodal metastases is classified as stage IVB. Kondo and Monden[3,4] compiled a database of 1320 patients with thymic epithelial tumors and found a 1.8% incidence of nodal metastases in patients with thymoma. Most metastases were to anterior mediastinal lymph nodes, and there was no significant difference in survival between patients with stage IVA thymoma (pleural/pericardial spread) and patients with stage IVB thymoma (nodal or hematogenous metastases). To our knowledge, Kondo and Monden's work is the only publication to date reporting on the incidence and prognostic relevance of nodal metastases in patients with thymoma. The goals of the present study were to identify the incidence and prognostic significance of nodal metastases in patients with thymoma in a large database of patients in the United States.

METHODS

The Surveillance, Epidemiology, and End Results (SEER) database is sponsored by the National Cancer Institute and has been used to track cancer incidence and patient survival since 1973. The SEER database currently covers approximately 28% of the US population and captures 98% of all cancer cases within the surveyed geographic areas. We used the SEER 18 Registry, including the Hurricane Katrina Impacted Louisiana Cases, for this analysis (SEER Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2010 Sub (1973-2007 varying) National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011, based on the November 2010 submission).

This SEER database was queried for all cases of thymoma from January 1, 1988 to December 31, 2009 using the International Classification of Diseases–03 codes for thymoma (8580, 8581, 8582, 8583, 8584, and 8585). Specific fields for number of lymph nodes examined and number of positive nodes were created in 1988. Patients with thymic carcinoma were not included in this analysis. We included only patients who had resection of the thymus and had at least 1 lymph node analyzed pathologically, and who survived for more than 30 days after resection. SEER*Stat software (seer.cancer.gov/seerstat) version 6.6.2 was used for data mining. Using available data, patients were staged according to the

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Disclosures: Authors have nothing to disclose with regard to commercial support.

Read at the 40th Annual Meeting of The Western Thoracic Surgical Association, Dana Point, California, June 25-28, 2014.

Received for publication June 23, 2014; revisions received Nov 16, 2014; accepted for publication Nov 19, 2014; available ahead of print Jan 13, 2015.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.11.054

Abbreviations and Acronyms

CI = confidence interval
ITMIG = International Thymic Malignancy Interest Group
SEER = Surveillance, Epidemiology, and End Results
TNM = tumor, node, metastases
WHO = World Health Organization

Masaoka-Koga classification. Stage I (no transcapsular invasion) and stage IIa (microscopic transcapsular invasion) thymomas could not be separated using the available data and were therefore analyzed together.

Data are presented as median, and 25th and 75th percentile. Survival is presented in months and with a 95% confidence interval (CI). Continuous data variables were analyzed using Student *t* test. Nominal data were analyzed utilizing crosstabs and Pearson χ^2 statistic. Kaplan–Meier survival curves were constructed and compared using the log-rank test.

A Cox proportional hazard model was used to identify the relevant variables that affected overall survival. Only variables that significantly affected survival in univariable analysis were included in the Cox model. The proportionality of hazards was evaluated using the Cox regression analysis with time-dependent covariables. The assumption of proportionality of hazards was tested and was not broken in any of the Cox regression models. Statistical analysis was performed with SPSS statistical software package version 19.0 (SPSS, Inc, Chicago, Ill). Significance was set at $P < .05$. This study was approved by the University of Pittsburgh Institutional Review Board, and the requirement for informed consent was waived.

RESULTS

From 1988 to 2009, a total of 2227 patients with thymoma were entered into the SEER database. Of these, 442 patients (19.8%) had undergone thymoma resection, with pathologic analysis of the lymph nodes, and therefore qualified for the study. The majority of patients were white males, with a median age of 58 years. Most tumors were Masaoka-Koga stage III, and the median number of lymph nodes analyzed was 2. There were 59 (13.3%) patients with involved lymph nodes (node positive), and 383 patients whose nodes were not involved (node negative). Patients with positive nodes were younger (53 years vs 58 years) and had smaller tumors (37 mm vs 50 mm) than patients with node-negative thymoma (Table 1). The median number of positive nodes per patient was 1. Forty-seven patients had 1 positive lymph node, 8 had 2 positive nodes, 1 patient had 3 positive nodes, 1 patient had 4, and 2 patients had 5 positive lymph nodes.

Lymph Node Assessment and Thymoma Staging

Changes to thymoma staging as a result of the identification of involved nodes could be assessed in 56 of the 59 node-positive patients. The presence of nodal metastases led to the thymoma being classified as a higher stage in a significant number of patients. If the positive nodes were discounted, 4 of 56 (7.1%) would have been classified as Masaoka-Koga stage I/IIA, 9 of 56 (16.1%) as stage IIB, and 32 of 56 (57.1%) as stage III. The remaining patients (11 of 56, 19.6%) were already classified as stage IV, and therefore, the stage could not be increased. Effectively, the presence of positive nodes led to reclassification at a higher stage in 80% of patients who would not have been classified as having stage IV thymoma based on other morphological features of the tumor.

Survival

Overall median survival for the full cohort was 139 months. Five-year survival for the whole cohort was 77%, and 10-year survival was 29%. Node-negative patients had a median survival of 144 months, and a 5- and 10-year survival of 79% and 32%, respectively. In contrast, node-positive patients had a median survival of 98 months, and a 5- and 10-year survival of 66% and 16%, respectively, which differed significantly from that seen in patients with node-negative thymoma ($P = .013$; Figure 1). Over the 21-year study period, a total of 106 patients without nodal metastases died; 32 patients who had nodal metastases died. Node-negative patients had a mean disease-specific survival of 205 months (5-year: 94%; 10-year: 74%), compared with 152 months (5-year: 77%; 10-year: 48%) in node-positive patients ($P < .001$; Figure 2).

In univariable analysis (Table 2), older age at diagnosis ($P < .001$); Masaoka-Koga stage I/IIA versus IV ($P = .027$); Masaoka-Koga stage IIB versus IV ($P = .006$); and positive lymph nodes ($P = .019$) were significant variables affecting survival. Because of the strong correlation between nodal status and Masaoka-Koga classification (all patients with positive nodes are classified as Masaoka-Koga stage IV), we could use only one of these variables at a time in the Cox model used to calculate the hazard ratio. In a first model, being older than 58 years at diagnosis ($P < .001$); Masaoka-Koga stage I/IIA versus IV ($P = .016$); and Masoka-Koga stage IIB versus IV ($P = .004$) were significant factors affecting survival. In a second model, older age at diagnosis ($P < .001$) and positive lymph nodes ($P = .001$) were the only factors affecting survival (Table 3).

In node-positive patients, data on adjuvant radiation therapy were available in 56 of 59 patients; 39 of 56 (69.6%) patients received adjuvant radiation therapy, and 17 of 56 (30.4%) did not. Survival in node-positive patients who received adjuvant radiation was 145 months, compared with 62 months in patients who did not receive adjuvant therapy, but this difference was not significant ($P = .317$).

DISCUSSION

In the present study, we used a large database to identify a cohort of patients with thymoma who had at least 1 lymph node analyzed pathologically. We found that among

TABLE 1. Patient demographics

Variable	Full cohort	Node negative	Node positive	*P* value
n (%)	442 (100)	383 (87.7)	59 (13.3)	
Sex				.578
Male, n (%)	231 (52.3)	198 (51.7)	33 (55.9)	
Female, n (%)	211 (47.7)	185 (48.3)	26 (44.1)	
Median age, y (25th, 75th percentile)	58 (46, 68)	58 (46, 69)	53 (39, 65)	.015
White, n (%)	303 (68.6)	266 (69.5)	37 (62.7)	.292
Tumor size, mm (25th, 75th percentile)	48 (7, 75)	50 (7.75, 75)	37 (5, 55)	.050
WHO classification, n (%)				.473
Type A	26 (5.9)	26 (6.8)	0 (0)	
Type AB	53 (12.0)	48 (12.5)	5 (8.5)	
Type B1	44 (9.9)	40 (10.4)	4 (6.8)	
Type B2	47 (10.6)	45 (11.7)	2 (3.9)	
Type B3	76 (17.2)	65 (17.0)	11 (18.6)	
NOS	196 (44.3)	159 (41.5)	37 (62.7)	
Masaoka-Koga Stage, n (%)				.001
Stage I/IIA	82 (18.6)	82 (21.4)	N/A	
Stage IIB	83 (18.8)	83 (21.7)	N/A	
Stage III	153 (34.6)	153 (39.9)	N/A	
Stage IV	90 (20.4)	31 (8.1)	59 (100)*	
Stage unknown	34 (7.7)	34 (8.9)		
Lymph nodes analyzed, median (25th, 75th percentile)	2 (1, 4)	2 (1, 4)	2 (1, 4)	.283

WHO, World Health Organization; *NOS*, not otherwise specified; *N/A*, not applicable.
*By definition, the presence of positive lymph nodes dictates classification as stage IV.

patients who had lymph nodes analyzed, the incidence of metastases was relatively high (13.3%). Age at diagnosis, Masaoka stage, and nodal metastases were important prognostic predictors. The presence of nodal metastases was an important adverse prognostic factor in patients with thymoma, doubling the risk of death compared with patients who were node negative. The results of our study suggest the need to sample lymph nodes during curative surgery for thymoma.

A significant proportion (80%) of patients who had positive lymph nodes would not have been classified as having stage IV thymoma if this indicator had not been examined. The majority of patients would have been classified as stage III (57.1%), but surprisingly, 23.2% would have been classified as stage I or II in the absence of data regarding lymph node metastases. The significant number of patients who were reclassified from stages I, II, and III to stage IV thymoma as a result of lymph node sampling highlights the need for nodal sampling even in patients with early-stage tumors, as the prognosis for a patient with stage IV thymoma would be significantly different.

Like many other investigators,[3,5-7] we demonstrated the prognostic relevance of the Masaoka staging system in patients with thymoma and demonstrated that patients with stage IV thymoma have twice the risk of dying compared with patients with stage I or stage II thymoma. In this study, thymoma stage, determined using the World Health Organization (WHO) histologic classification, was not found to be a significant factor affecting survival. Unfortunately, WHO classification was only available in 56% of patients in our cohort, which may decrease its usefulness as a prognostic factor. Nonetheless, WHO classification has not been uniformly found to be a prognostic indicator in thymoma,[7,8] and its reproducibility has been questioned.[9] In addition, significant disagreement may occur among pathologists about how to differentiate WHO B3 thymoma from thymic carcinoma.[10,11]

Patients with nodal metastases were younger and had slightly smaller tumors than patients without nodal metastases. Contradictory findings regarding the significance of both age and tumor size in patients with thymoma have been reported. Age has been a controversial prognostic factor in patients with thymoma, and no evidence indicates that younger patients fare worse or have more-aggressive tumors than older patients. We previously found increased age to be a significant prognostic variable in patients with stage III thymoma.[12] Wilkins and colleagues[13] reported a 40-year experience with 196 thymomas, and found that patients age >57 years had a 2.46 higher risk of death. This finding is very similar to the observation in our current study that patients age ≥58 years at the time of resection were twice as likely to die as those age <58 years. Okereke and colleagues[8] found that age was the only significant factor predictive of survival. However, other investigators did not find age to be an important prognostic factor in thymoma.[7,14,15]

Size of the tumor is a controversial prognostic factor in thymoma. Blumberg and colleagues[14] found that patients with tumors >11 cm had a worse prognosis, and Wright and colleagues[7] found that patients with tumors >8 cm had a worse prognosis than patients with smaller tumors. Others have not found tumor size to be a significant prognostic factor.[8,12] In the latest staging proposal by the International Thymic Malignancy Interest Group (ITMIG),[16] tumor size was not found to be a relevant prognostic factor in patients undergoing a complete resection and was not included in the final tumor, node, metastases (TNM) classification proposal.

Our knowledge of nodal metastases in thymoma is limited to the study by Kondo and Monden.[4] In that study, the investigators sent a questionnaire to 185 Japanese centers and were able to compile a database of 1320 patients with thymic tumors; 1093 of those were thymomas. Nodal metastases were present in 19 patients (1.8%), the majority (14 patients) were metastases to the anterior mediastinal

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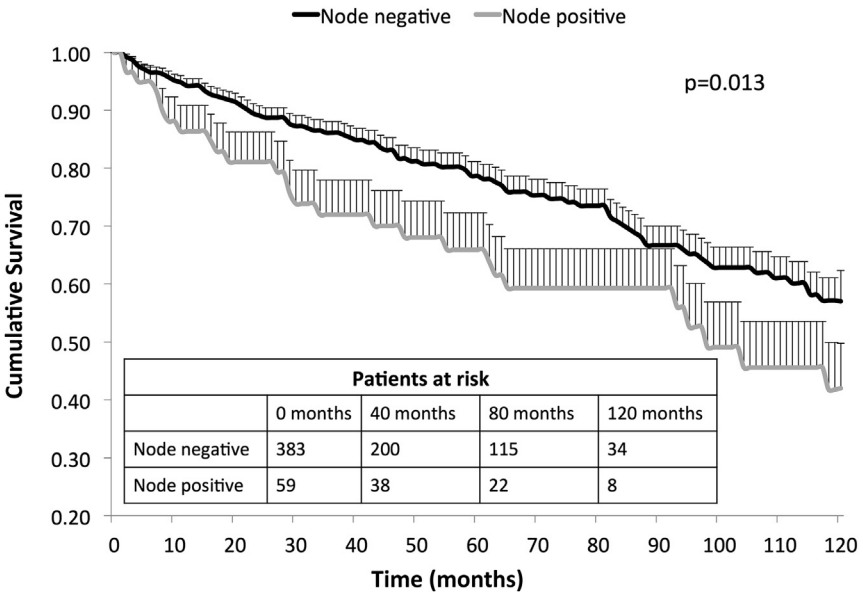

FIGURE 1. Kaplan-Meier survival curves in node-negative and node-positive patients.

nodes; 5 patients had other intrathoracic nodes involved as well. There were no instances of involvement of extrathoracic lymph nodes. In addition, the 5-year survival rate in patients with thymoma without nodal involvement was 95.6%, and 5-year survival was 61.5% in patients with nodal involvement.

These findings are quite similar to our observation of an estimated 66% survival at 5 years in patients with nodal metastases. It is unclear why the prevalence of nodal metastases in our work is higher than that in Kondo and Monden's[4] (13.3% vs 1.8%). Because we included only patients whose lymph nodes were examined in the specimen, it is possible that our cohort had a higher median Masaoka-Koga stage than the cohort assembled by Kondo and Monden. There were differences in the Masaoka stage between the 2 studies: 55% of our patients had stage III or IV thymoma compared with only 28.9% in Kondo and Monden's series,[3] and nodal metastases are likely more common in more-advanced tumor stages. Another possibility is that our study overestimated the incidence of nodal metastases and that the true incidence is between 1.8% and 13.3%.

Thymoma is an indolent disease, and many patients who have it die of other causes. In the series by Okereke and

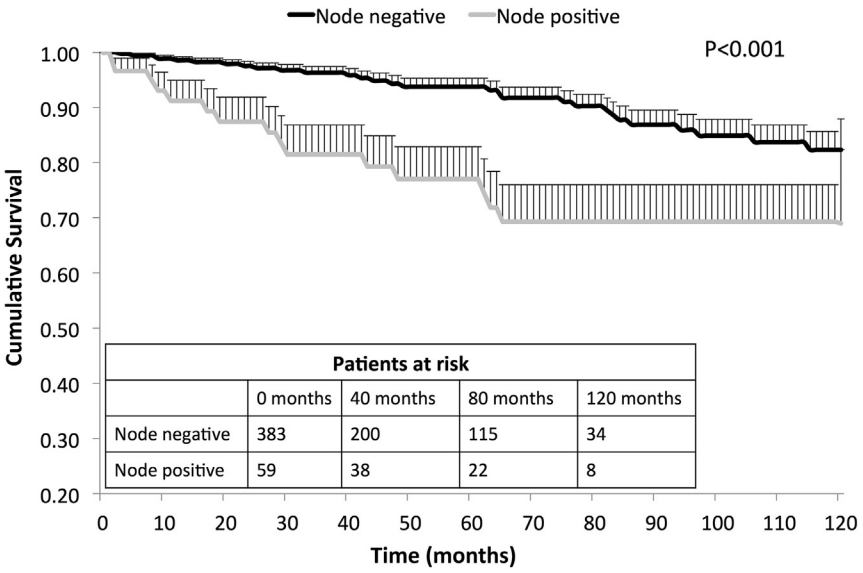

FIGURE 2. Kaplan-Meier disease-specific survival curves in node-negative and node-positive patients.

TABLE 2. Univariable analysis of variables affecting survival

Variable	HR (95% CI)	*P* value
Sex (male vs female)	0.875 (0.622-1.231)	.445
Age at diagnosis	1.030 (1.017-1.043)	<.001
Race (white vs others)	1.165 (0.941-1.444)	.171
Tumor size	1.000 (0.996-1.004)	.897
Number of lymph nodes examined (≤2 vs ≥3)	1.322 (0.923-1.894)	.128
WHO classification (B vs A/AB)	1.102 (0.581-2.092)	.764
Masaoka-Koga stage		
I/IIA vs IV	0.515 (0.286-0.928)	.027
IIB vs IV	0.454 (0.259-0.796)	.006
III vs IV	0.822 (0.550-1.229)	.340
Positive lymph nodes (yes vs no)	1.647 (1.107-2.451)	.019
Postoperative radiation therapy (yes vs no)	1.178 (0.811-1.711)	.385

HR, Hazard ratio; *CI*, confidence interval; *WHO*, World Health Organization.

colleagues,[8] only 4.3% of patients died of thymoma. Even in patients with advanced-stage thymoma, most died of causes other than thymoma. In patients with stage III disease, fewer than 25% of patients died of thymoma 10 years after diagnosis.[12] In the present study, only 8.4% of node-negative patients died of thymoma within 10 years of resection, as compared with 27% of node-positive patients. These findings underscore the potential importance of identifying nodal metastases in thymoma.

One important question is whether the identification of nodal metastases should change the postoperative care of patients with thymoma. No studies have been done to specifically address postoperative adjuvant therapy in patients with stage IVB thymoma with nodal metastases. In our study, adjuvant radiation therapy did not significantly improve survival, but the number of patients that did not receive radiation was small. In a recent study on patients with thymoma and pleural dissemination, Okuda and colleagues[17] found that 18 of 136 (13.2%) patients with thymoma had stage IVB disease, and all underwent extrapleural pneumonectomy. The majority of patients (17 of 18, 94.4%) underwent adjuvant chemotherapy, but it did not significantly affect survival. The only factor affecting survival in that study was WHO classification. Currently, no guidelines are available on the treatment of patients found to have nodal metastases after resection of thymoma. Until further data are available, chemotherapy and radiation therapy to the mediastinum seem to be a prudent approach.

TABLE 3. Multivariable analysis of significant factors affecting survival

Variable	HR (95% CI)	*P* value
Model 1*		
Age at diagnosis	1.032 (1.018-1.045)	<.001
Masaoka-Koga stage I/IIA vs IV	0.504 (0.280-0.908)	.023
Masaoka-Koga stage IIB vs IV	0.421 (0.240-0.740)	.003
Masaoka-Koga stage III vs IV	0.742 (0.494-1.115)	.151
Model 2*		
Age at diagnosis	1.033 (1.020-1.046)	<.001
Positive lymph nodes (yes vs no)	1.945 (1.296-2.919)	.001

HR, Hazard ratio; *CI*, confidence interval. *Two models were used: Model 1 included Masaoka-Koga stage; Model 2 included nodal status.

Recently, the ITMIG and the International Association for the Study of Lung Cancer proposed a lymph-node map for thymic malignancies that supports a new TNM classification for thymic tumors.[16,18-21] The proposed nodal map includes 2 nodal compartments: an anterior compartment and a deep compartment. The anterior compartment encompasses the space anterior to the pericardium, ie, the space encompassing the thymus, and bordered by the pleura and the hyoid bone. The presence of positive lymph nodes in the anterior space is defined as N1 disease. The deep compartment is posterior to the anterior compartment, anterior to the esophagus, and between the pulmonary hila. The deep compartment includes the paratracheal nodes and the aorto-pulmonary window lymph nodes. The presence of positive lymph nodes in the deep compartment is defined as N2 disease.

In the new proposed TNM classification, patients with N1 disease and without other metastases are classified as stage IVA, and those with N2 disease are classified as stage IVB. We believe that, at the very least, anterior mediastinal nodes (perithymic, phrenic, lower neck) should be sampled during curative resection for thymoma. Available data are insufficient to suggest a recommendation on the number of nodes to be removed. All surgeons operating on patients with thymoma should be encouraged to join ITMIG and participate in the ITMIG prospective database, so that more data can be compiled on this rare disease.

The present study has limitations and is constrained by its retrospective nature and the limitations of the SEER database. Although broad in its reach, the SEER database is subjected to limited data points and potential reporting inaccuracies. The pathology data are obtained from multiple centers, without standardization among the pathologists, and each pathologist may have a different method of analyzing and identifying lymph nodes in the specimen. In addition, differences between thymic carcinoma and WHO B3 thymomas can be subtle and may be missed.[10,11] Only 11 patients had type B3 thymoma in our study, but the WHO classification was available in <40% of patients. Some patients with nodal metastases could have been misdiagnosed with thymic carcinoma, but the survival of our node-positive patients was very similar to that seen by Kondo and Monden,[3,4] so we do not believe that misdiagnosis of thymic carcinoma significantly affected our findings.

Another important limitation of the study is the lack of information on chemotherapy in the SEER database.

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Some patients may have had either preoperative or postoperative chemotherapy, and how this affects our findings is unclear. Additionally, the reporting of complete resection is somewhat subjective in the SEER database, and the reporting of complete thymic excision is not the same as an R0 resection in all cases. It is unclear how the fact that some patients may have had an incomplete resection might affect the results of our study. Other important limitations of the SEER database include lack of information on imaging, lack of information on the surgical approach for resection (minimally invasive vs traditional surgery), and lack of information on the anatomic location of the nodes sampled. Information is available in the SEER database on distant nodal metastases (outside the chest), and these patients were not included in our analysis because of this metastatic disease.

In summary, nodal metastases in patients with thymoma may occur more frequently than is currently recognized. Patients with lymph node metastases fare significantly worse than patients without nodal metastases, suggesting that sampling of anterior mediastinal nodes by the surgeon, and analysis by the pathologist of lymph nodes in the surgical specimen, should become routine in the treatment of thymoma. The role of adjuvant therapy in patients with positive nodal metastases from thymoma is currently unclear. Collaborative studies on the prognostic relevance of nodal metastases and treatment of patients with node-positive thymoma are warranted. Participation in the prospective thymoma database that is being compiled by the ITMIG will help advance clinical investigation of this rare disease.

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References

1. Engels EA, Pfeiffer RM. Malignant thymoma in the United States: demographic patterns in incidence and associations with subsequent malignancies. *Int J Cancer*. 2003;105:546-51.
2. Koga K, Matsuno Y, Noguchi M, Mukai K, Asamura H, Goya T, et al. A review of 79 thymomas: modification of staging system and reappraisal of conventional division into invasive and non-invasive thymoma. *Pathol Int*. 1994;44:359-67.
3. Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. *Ann Thorac Surg*. 2003;76:878-84; discussion 84-5.
4. Kondo K, Monden Y. Lymphogenous and hematogenous metastasis of thymic epithelial tumors. *Ann Thorac Surg*. 2003;76:1859-64.
5. Blumberg D, Burt ME, Bains MS, Downey RJ, Martini N, Rusch V, et al. Thymic carcinoma: current staging does not predict prognosis. *J Thorac Cardiovasc Surg*. 1998;115:303-8; discussion 8-9.
6. Ruffini E, Filosso PL, Mossetti C, Bruna MC, Novero D, Lista P, et al. Thymoma: inter-relationships among World Health Organization histology, Masaoka staging and myasthenia gravis and their independent prognostic significance: a single-centre experience. *Eur J Cardiothorac Surg*. 2011;40:146-53.
7. Wright CD, Wain JC, Wong DR, Donahue DM, Gaissert HA, Grillo HC, et al. Predictors of recurrence in thymic tumors: importance of invasion, World Health Organization histology, and size. *J Thorac Cardiovasc Surg*. 2005;130:1413-21.
8. Okereke IC, Kesler KA, Morad MH, Mi D, Rieger KM, Birdas TJ, et al. Prognostic indicators after surgery for thymoma. *Ann Thorac Surg*. 2010;89:1071-7; discussion 7-9.
9. Zucali PA, Di Tommaso L, Petrini I, Battista S, Lee HS, Merino M, et al. Reproducibility of the WHO classification of thymomas: practical implications. *Lung Cancer*. 2013;79:236-41.
10. Roden AC, Yi ES, Cassivi SD, Jenkins SM, Garces YI, Aubry MC. Clinicopathological features of thymic carcinomas and the impact of histopathological agreement on prognostical studies. *Eur J Cardiothorac Surg*. 2013;43:1131-9.
11. Verghese ET, den Bakker MA, Campbell A, Hussein A, Nicholson AG, Rice A, et al. Interobserver variation in the classification of thymic tumours—a multicentre study using the WHO classification system. *Histopathology*. 2008;53:218-23.
12. Weksler B, Shende M, Nason KS, Gallagher A, Ferson PF, Pennathur A. The role of adjuvant radiation therapy for resected stage III thymoma: a population-based study. *Ann Thorac Surg*. 2012;93:1822-8; discussion 8-9.
13. Wilkins KB, Sheikh E, Green R, Patel M, George S, Takano M, et al. Clinical and pathologic predictors of survival in patients with thymoma. *Ann Surg*. 1999;230:562-72; discussion 72-4.
14. Blumberg D, Port JL, Weksler B, Delgado R, Rosai J, Bains MS, et al. Thymoma: a multivariate analysis of factors predicting survival. *Ann Thorac Surg*. 1995;60:908-13; discussion 14.
15. Mariano C, Ionescu DN, Cheung WY, Ali RH, Laskin J, Evans K, et al. Thymoma: a population-based study of the management and outcomes for the province of British Columbia. *J Thorac Oncol*. 2013;8:109-17.
16. Nicholson AG, Detterbeck FC, Marino M, Kim J, Stratton K, Giroux D, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposals for the T component for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9:S73-80.
17. Okuda K, Yano M, Yoshino I, Okumura M, Higashiyama M, Suzuki K, et al. Thymoma patients with pleural dissemination: nationwide retrospective study of 136 cases in Japan. *Ann Thorac Surg*. 2014;97:1743-8.
18. Detterbeck FC, Asamura H, Crowley J, Falkson C, Giaccone G, Giroux D, et al. The IASLC/ITMIG Thymic Malignancies Staging Project: development of a stage classification for thymic malignancies. *J Thorac Oncol*. 2013;8:1467-73.
19. Bhora FY, Chen DJ, Detterbeck FC, Asamura H, Falkson C, Filosso P, et al. The ITMIG/IASLC Thymic Epithelial Tumors Staging Project: a proposed lymph node map for thymic epithelial tumors in the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9:S88-96.
20. Detterbeck FC, Stratton K, Giroux D, Asamura H, Crowley J, Falkson C, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposal for an evidence-based stage classification system for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9:S65-72.
21. Kondo K, Schil P, Detterbeck FC, Okumura M, Stratton K, Giroux D, et al. The IASLC/ITMIG Thymic Epithelieal Tumors Staging Project: proposal for the N and M components for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9:S81-7.