The following letter was written by Dr. Masaoka in response to the above article:
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Well-differentiated thymic carcinoma: Is it thymic carcinoma or not?

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To the Editor:

We read the article titled “Thymic Carcinoma: Current Staging Does Not Predict Prognosis” by Blumberg and associates of Sloan-Kettering Cancer Center (J Thorac Cardiovasc Surg 1998;115:303-9). Thymic carcinomas in this article consisted of type II malignant thymoma[1] and well-differentiated thymic carcinoma.[2] Our Nagoya City University series of thymic carcinoma consisted of 19 patients treated in 1980 through 1995. Inasmuch as there were 62 thymomas and 3 thymic carcinoids in the same period, the incidence of thymic carcinoma was 22.6% in thymic epithelial tumors. Because thymic carcinoma coincides with type II malignant thymoma according to our criteria, well-differentiated thymic carcinomas are excluded from our series. Histologic subtypes of our thymic carcinomas were as follows: squamous cell carcinoma, 11 cases; undifferentiated carcinoma, 3 cases; small cell carcinoma, 2 cases; lymphoepithelioma-like carcinoma, 1 case; papillary adenocarcinoma, 1 case; and unclassified carcinoma, 1 case. Associated diseases were observed in 2 patients: hypergammaglobulinemia in 1 patient and Cushing syndrome with hypogammaglobulinemia in another. Myasthenia gravis was not present. Applying the classification of thymoma to our thymic carcinomas yields the following stages: stage I, 1 case; stage II, 0 cases; stage III, 9 cases; stage IVa, 4 cases; and IVb, 5 cases. Follow-up results revealed a 42.7% 5-year survival and a 21.4% 10-year survival. The most important factor influencing survival was histologic subtype. Five-year survival was 65.6% in squamous cell carcinoma and 14.3% in the other types of carcinoma.On comparing our results with those of the Sloan-Kettering series, we observed some differences. First, survivals in our series were inferior to those of Sloan-Kettering. Second, advanced stages of disease (stages III and IV) were prevalent in our series, as in that of Hsu and associates,[3] which consisted exclusively of type II malignant thymoma. Accordingly, it is impossible to compare survivals of the patients with early and advanced stages of disease in our series. Third, none of our patients had associated myasthenia gravis. The explanation for these differences seems to be that our series excludes well-differentiated thymic carcinoma.

We think that well-differentiated thymic carcinoma is distinct from type II malignant thymoma (proper thymic carcinoma) because of differences of some markers (cytokeratins,[4] bcl-2, and Fas antigen[5]) and associated diseases. Well-differentiated thymic carcinoma has been considered to be epithelium-rich thymoma by most pathologists. It is related to cortical thymoma (Müller-Hermelink) or polygonal cell thymoma (Rosai) and frequently is associated with myasthenia gravis. Designation of well-differentiated thymic carcinoma has caused striking confusion, because it overlaps with well-differentiated squamous cell carcinoma.[6] The latter belongs to the category “proper thymic carcinoma” and constitutes a low-grade category of thymic carcinoma, together with well-differentiated mucoepidermoid carcinoma and basaloid carcinoma. We agree with Suster and Moran's proposal[7] to designate well-differentiated thymic carcinoma as “atypical thymoma.” Clinical results of “atypical thymoma,” well-differentiated squamous cell carcinoma (low-grade), and other types of thymic carcinoma (high-grade) should be evaluated separately. Although the article by Blumberg and associates revealed no significant difference between survivals of patients with well-differentiated thymic carcinoma and type II malignant thymoma, we expect that an increase in the number of patients and longer observation times may reveal a difference.Patients with proper thymic carcinoma usually have an advanced stage of the disease. Accordingly, it seems almost meaningless to compare results of each stage in patients with proper thymic carcinoma. We think that the TNM classification may be useful in thymic

carcinomas. Table I shows the TNM classification system of thymic epithelial tumors, which is revised minimally from the one described in our previous article.[8]

T factors mimic the stages. N factors are arranged according to the lymph node stations along the lymphatic route from the thymus. TNM numbers of 5 cases of stage IVb in our series were as follows: T2 N1 M0, T3 N1 M0, T3 N0 M1, T3 N3 M1, and T4 N0 M1. Three cases were N-positive and 3 cases were M-positive. However, evaluation of the N factor was not always complete, especially in the patients from the early period of our study. Therefore N-positive cases might be more frequent than our results indicate. As cases accumulate, this TNM classification system may become more useful.

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4. Fukai I, Masaoka A, Hashimoto T, Yamakawa Y, Mizuno T, Tanamura O, et al. Cytokeratins in normal thymus and thymic epithelial tumors. Cancer 1993;71:99-105.

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