

Determinants of Complete Resection of Thymoma by Minimally Invasive and Open Thymectomy: Analysis of an International Registry

Bryan M. Burt, MD,^{a,*} Xiaopan Yao, MD,^b Joseph Shrager, MD,^c Alberto Antonicelli,^b Sukhmani Padda, MD,^c Jonathan Reiss, MD,^d Heather Wakelee, MD,^c Stacey Su, MD,^e James Huang, MD,^f Walter Scott, MD^e

^aBaylor College of Medicine, Houston, Texas

^bYale University, New Haven, Connecticut

^cStanford University School of Medicine, Stanford, California

^dUniversity of California Davis Medical Center, Sacramento, California

^eFox Chase Cancer Center, Philadelphia, Pennsylvania

^fMemorial Sloan-Kettering Cancer Center, New York, New York

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ABSTRACT

Introduction: Minimally invasive thymectomy (MIT) is a surgical approach to thymectomy that has more favorable short-term outcomes for myasthenia gravis than open thymectomy (OT). The oncologic outcomes of MIT performed for thymoma have not been rigorously evaluated. We analyzed determinants of complete (R0) resection among patients undergoing MIT and OT in a large international database.

Methods: The retrospective database of the International Thymic Malignancy Interest Group was queried. Chi-square and Wilcoxon rank sum tests, multivariate logistic regression models, and propensity matching were performed.

Results: A total of 2514 patients underwent thymectomy for thymoma between 1997 and 2012; 2053 of them (82%) underwent OT and 461 (18%) underwent MIT, with the use of MIT increasing significantly in recent years. The rate of R0 resection among patients undergoing OT was 86%, and among those undergoing MIT it was 94% ($p < 0.0001$). In propensity-matched MIT and OT groups ($n = 266$ in each group); however, the rate of R0 resection did not differ significantly (96% in both the MIT and OT groups, $p = 0.7$). Multivariate analyses were performed to identify determinants of R0 resection. Factors independently associated with R0 resection were geographical region, later time period, less advanced Masaoka stage, total thymectomy, and the absence of radiotherapy. Surgical approach, whether minimally invasive or open, was not associated with completeness of resection.

Conclusions: The use of MIT for resection of thymoma has been increasing substantially over time, and MIT can

achieve rates of R0 resection for thymoma similar to those achieved with OT.

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Keywords: Thymoma; Thymectomy; Minimally invasive; Complete resection; R0

Introduction

Minimally invasive surgical approaches for thymectomy have gained popularity for patients with non-thymomatous myasthenia gravis (MG), and a variety of single-institution studies suggest that that minimally invasive thymectomy (MIT) has improved short-term outcomes when compared with open thymectomy (OT). For example, when compared with OT, MIT has been associated with shorter hospital stays,¹⁻⁷ shorter length of stay in the intensive care unit,¹ lower operative blood loss,^{1,7,8} improved postoperative pulmonary function,⁹

*Corresponding author.

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Address for correspondence: Bryan M. Burt, MD, One Baylor Place, BCM390, Baylor College of Medicine, Houston, Texas. E-mail: bryan.burt@bcm.edu

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decreased postoperative pain,¹⁰ and similar operating room times.¹

Currently, there are few published oncologic outcomes data that support the adoption of MIT for patients with thymic malignancies. For resection of thymoma, MIT and OT could vary with respect to rates of R0 resection, extent of thymectomy, and risk of violation of the tumor capsule. It is well known that R0 resection is the most important long-term prognostic indicator in thymoma, and resection status at the time of thymectomy closely correlates with recurrence outcomes.^{11–15} Using the large international database of the International Thymic Malignancies Interest Group (ITMIG), we therefore set out to (1) determine whether MIT was associated with rates of incomplete resection equivalent to those with OT for thymoma and (2) identify factors that were independently associated with completeness of resection.

Materials and Methods

The ITMIG database is a multi-institutional retrospective database with contributions from 43 institutions on four continents.¹⁶ All data were deidentified and considered exempt from institutional review board review. This database was queried to define a cohort of patients who underwent OT or MIT for thymoma from the date of the first MIT entry in January 1997 up until the date of last entry in December 2012. This study was conducted on the basis of the data available in the ITMIG database at the time of data harvest. For this project, OT was defined as either sternotomy or thoracotomy, and MIT was defined as either a video-assisted thoracoscopic surgery (VATS)- or robotic-assisted thoracoscopic surgery (RATS)-based approach. The thoracosternotomy and clamshell approaches, cervical thymectomy, and mediastinotomy approaches were intentionally excluded as they represented a minority of resection types, as well as to balance the OT and MIT comparison groups. Variables examined in our analyses are listed in [Table 1](#) and each contained less than 5% missing data. The clinical stage variable was intentionally excluded because of 28% missing data. A total thymectomy was defined in the database as resection of the thymoma and the entire thymus gland, whereas a partial thymectomy was defined as resection of the thymoma with a margin of normal thymic tissue. The R0, R1, and R2 variables were defined in the database as being identified from surgical pathology reports. Conversion from MIT to OT data was not available from the retrospective ITMIG database.

All statistical analyses were performed with SAS 9.3 software (SAS Institute, Inc., Cary, NC). Patient characteristics were compared between the MIT and OT groups

using the chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Propensity matching was performed by the nearest available pair matching method, with utilization of all the variables in this study with the exception of completeness of resection. The patients undergoing MIT were ordered and sequentially matched to the nearest unmatched patients undergoing OT. If multiple patients in the OT group had propensity scores equally close to that of the patient in the MIT group, one of those patients in the OT group was selected at random. A *p* value less than 0.05 was used to determine significance. Univariate logistic regression analyses were used to investigate the relationship between resection status and clinical and patient characteristic variables, including age, sex, paraneoplastic syndrome, time period, WHO histologic type, pathologic Masaoka stage, tumor size, extent of thymectomy, surgical approach, and use of chemotherapy and radiotherapy. A multivariate logistic regression model was built to test the association between resection status and surgical approach (MIT versus OT), including other clinical factors and patient characteristic variables as covariates.

Results

A total of 2514 patients underwent thymectomy for thymoma between January 1997 and December 2012. Of those patients, 2053 (82%) underwent OT (1751 [85%] by sternotomy and 302 [15%] by thoracotomy) and 461 (18%) underwent MIT (315 [68%] by VATS and 146 [32%] by RATS). The numbers of MIT and OT cases performed from 1997 to 2012 are shown graphically in [Figure 1](#). The frequency of MIT cases was seen to increase from 2008 to 2012, at which time its frequency approached that of the of OT cases.

The demographic, clinical, and pathologic characteristics of these cases are shown in [Table 1](#). Most of the MIT cases were contributed from Asian institutions. Patients undergoing MIT were 2.1 years younger than those undergoing OT, and patients in the MIT group were more likely to be female (55%) than were those in the OT group (45%). Patients undergoing MIT had a more favorable World Health Organization (WHO) histologic type and less advanced pathologic Masaoka stage than patients undergoing OT. In the MIT group, the mean tumor size was 4.0 cm (range 0.4–15.5 cm) compared with 6.0 cm (range 0.1–28.0 cm) in the OT group. The rate of partial thymectomy was found to be higher in the MIT group (27%) than in the OT group (9%). Patients undergoing MIT were less likely to have received chemotherapy (3%) or radiotherapy (31%) than were those undergoing OT (16% and 37%, respectively), and most chemotherapy and radiotherapy was administered in the adjuvant setting.

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