European Journal of Cardio-Thoracic Surgery 60 (2021) 881–887
doi:10.1093/ejcts/ezab224 Advance Access publication 23 May 2021

ORIGINAL ARTICLE

Cite this article as: Guerrera F, Falcoz PE, Moser B, van Raemdonck D, Bille' A, Toker A *et al.* Thymomectomy plus total thymectomy versus simple thymomectomy for early-stage thymoma without myasthenia gravis: a European Society of Thoracic Surgeons Thymic Working Group Study. Eur J Cardiothorac Surg 2021;60:881–7.

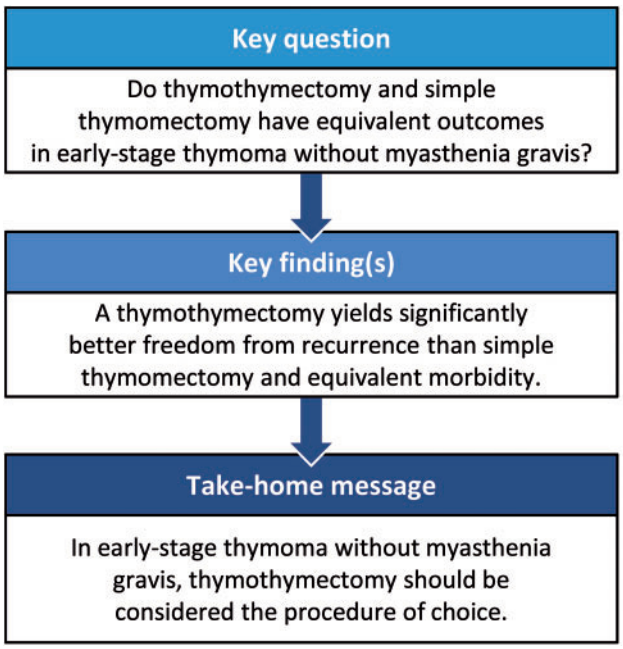
Thymomectomy plus total thymectomy versus simple thymomectomy for early-stage thymoma without myasthenia gravis: a European Society of Thoracic Surgeons Thymic Working Group Study

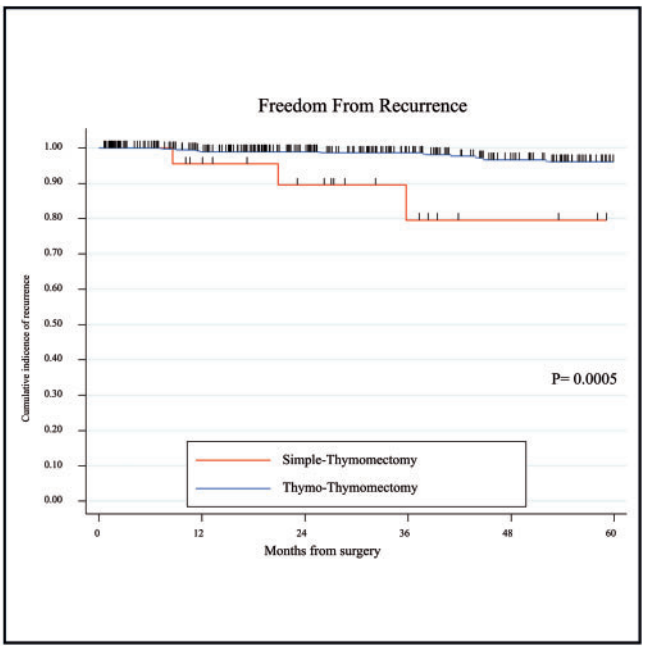
Francesco Guerrera [a,b,*], Pierre Emmanuel Falcoz[c], Bernhard Moser [d], Dirk van Raemdonck [e,f], Andrea Bille[g,h], Alper Toker[i], Lorenzo Spaggiari [j,k], Luca Ampollini [l], Claudia Filippini [b], Pascal Alexandre Thomas [m], Bram Verdonck[n], Paolo Mendogni[o], Clemens Aigner [p], Luca Voltolini[q], Nuria Novoa [r], Miriam Patella [s], Sara Mantovani [t], Ivan Gomes Bravio[u], Charalambos Zisis[v], Angela Guirao[w], Francesco Londero [x], Miguel Congregado[y], Gaetano Rocco [z], Bert Du Pont[e,f], Nicola Martucci[aa], Matthias Esch [bb], Alessandro Brunelli[cc], Frank C. Detterbeck[dd], Federico Venuta[t], Walter Weder[s] and Enrico Ruffini[b,c], on behalf of the European Society of Thoracic Surgeons (ESTS) Thymic Working Group Participating Centers Walter Klepetko[d], Anne Olland[c], Bert Du Pont[e,f], Daisuke Nonaka[dd,ee], Berker Ozkan[ff], Giorgio Lo Iacono[j], Cesare Braggio[l], Pier Luigi Filosso[b,c], Geoffrey Brioude[m], Paul van Schil[n], Mario Nosotti[o], Daniel Valdivia[p], Stefano Bongiolatti[q], Ilhan Inci[s], Rontogianni Dimitra[ff,gg], David Sànchez[w], William Grossi[x], Sergio Moreno-Merino[y] and Martin Teschner[v]

[a] Department of Thoracic Surgery, Azienda Ospedaliera Universitaria Città della Salute e Della Scienza di Torino, Torino, Italy
[b] Department of Surgical Sciences, University of Torino, Torino, Italy
[c] Department of Surgical Sciences, Strasbourg University Hospital, Strasbourg, France
[d] Department of Thoracic Surgery, Vienna University Hospital, Vienna, Austria
[e] Department of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium
[f] Department of Chronic Diseases and Metabolism, Katholieke Universiteit Leuven, Leuven, Belgium
[g] Department of Thoracic Surgery, Guy's Hospital London, London, UK
[h] Division of Cancer Studies, King's College London, Guy's Hospital London, London, UK
[i] Department of Cardiovascular and Thoracic Surgery, West Virginia University Heart and Vascular Institute, Morgantown, WV, USA
[j] Division of Thoracic Surgery, European Institute of Oncology, IRCCS, Milano, Italy
[k] Department of Oncology and Hemato-oncology, University of Milan, Milano, Italy
[l] Thoracic Surgery, Department of Medicine and Surgery, University Hospital of Parma, Milano, Italy
[m] Department of Thoracic Surgery, North Hospital Aix-Marseille University, Marseille, France
[n] Department of Thoracic and Vascular Surgery, Antwerp University Hospital and Antwerp University, Antwerp, Belgium
[o] Department of Thoracic Surgery, Foundation IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy
[p] Department of Thoracic Surgery, Essen University Hospital - Ruhrlandklinik, Essen, Germany
[q] Department of Thoracic Surgery, Careggi University Hospital, Firenze, Italy
[r] Thoracic Surgery Service, Salamanca University Hospital and School of Medicine, Salamanca, Spain
[s] Department of Thoracic Surgery, Zurich University Hospital, Zurich, Switzerland
[t] Division of Thoracic Surgery and Lung Transplant, Sapienza University of Rome and AOU Policlinico Umberto I, Roma, Italy
[u] Department of Thoracic Surgery, Francisco Gentil Portuguese Institute of Oncology CUF Infante Santo Hospital, Lisboa, Portugal
[v] Department of Thoracic Surgery, Athens Evangelismos Hospital, Athens, Greece
[w] Department of Thoracic Surgery, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain
[x] Thoracic Surgery Unit—Cardiothoracic Department, Azienda Sanitaria Universitaria Integrata S Maria della Misericordia, Udine, Italy
[y] General Thoracic Surgery Department, Virgen Macarena University Hospital and University of Seville, Seville, Spain
[z] Thoracic Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[aa] Division of Thoracic Surgery, Department of Thoracic Surgery and Oncology, Istituto Nazionale Tumori - IRCCS - Fondazione "G. Pascale", Naples, Italy
[bb] Department of Thoracic Surgery, Josef Hospital Delmenhorst, Delmenhorst, Germany
[cc] St. James's University Hospital, Leeds, UK
[dd] Section of Thoracic Surgery, Department of Surgery, Yale Thoracic Oncology Program, Yale University School of Medicine, New Haven, CT, USA
[ee] Department of Pathology, Guy's Hospital London, London, UK
[ff] Department of Thoracic Surgery, Istanbul Medical School, Turkey
[gg] Department of Pathology, Athens Evangelismos Hospital, Greece

* Corresponding author. Department of Surgical Sciences, University of Torino, Corso Dogliotti 14, 10126 Torino, Italy. Tel: +39 342 993 7761; fax: +39-011-6336635; e-mail: francesco.guerrera@unito.it (F. Guerrera).

Received 3 November 2020; received in revised form 17 March 2021; accepted 19 March 2021





Abstract

OBJECTIVES: Resection of thymic tumours including the removal of both the tumour and the thymus gland (thymothymectomy; TT) is the procedure of choice and is recommended in most relevant articles in the literature. Nevertheless, in recent years, some authors have suggested that resection of the tumour (simple thymomectomy; ST) may suffice from an oncological standpoint in patients with early-stage thymoma who do not have myasthenia gravis (MG) (non-MG). The goal of our study was to compare the short- and long-term outcomes of ST versus TT in non-MG early-stage thymomas using the European Society of Thoracic Surgeons thymic database.

METHODS: A total of 498 non-MG patients with pathological stage I thymoma were included in the study. TT was performed in 466 (93.6%) of 498 patients who had surgery with curative intent; ST was done in 32 (6.4%). The completeness of resection, the rate of complications, the 30-day mortality, the overall recurrence and the freedom from recurrence were compared. We performed crude and propensity score-adjusted comparisons by surgical approach (ST vs TT).

RESULTS: TT showed the same rate of postoperative complications, 30-day mortality and postoperative length of stay as ST. The 5-year overall survival rate was 89% in the TT group and 55% in the ST group. The 5-year freedom from recurrence was 96% in the TT group and 79% in the ST group.

CONCLUSION: Patients with early-stage thymoma without MG who have a TT show significantly better freedom from recurrence than those who have an ST, without an increase in postoperative morbidity rate.

Keywords: Thymoma • Thymectomy • Thymomectomy • Extended thymectomy • Thymothymomectomy • Recurrence • Survival

ABBREVIATIONS

CIs	Confidence intervals
ESTS	European Society of Thoracic Surgeons
FFR	Freedom from recurrence
HRs	Hazard ratios
IQR	Interquartile range
JART	Japanese Association for Research on the Thymus
MG	Myasthenia gravis
OS	Overall survival
PS	Propensity score
ST	Simple thymomectomy
TT	Thymothymectomy
WHO	World Health Organization

INTRODUCTION

Despite its rarity, thymoma is the most common neoplasm of the anterior mediastinum in adults [1]. Surgery still represents the mainstay of treatment for resectable thymomas [2]. Resection of thymic tumours including the removal of both the tumour and the thymus gland (thymothymectomy; TT) is the procedure of choice and is recommended in most articles in the literature [3–7]. Indeed, the results of TT for early-stage thymoma in terms of 5-year overall survival (OS) rates range from 96% to 100%, whereas 5-year disease-free survival rates range from 92% to 97% [8].

Nevertheless, in recent years, some authors questioned the need to remove the thymus gland from patients without

myasthenia gravis (non-MG) with early-stage thymoma, suggesting that resection of the tumour [simple thymomectomy (ST)] may suffice from an oncological standpoint [8].

Moreover, improvements in minimally invasive thoracic surgery (video- or robotic-assisted) have stimulated thoracic surgeons to treat smaller thymomas by performing an ST, without consensually resecting the entire thymus [9–11].

In the last decade, several studies described the equivalence between TT and ST in terms of oncological outcomes [12–14]. However, all these studies were affected by several biases because most of them analysed small and single-institution cohorts [8]. Furthermore, the outcomes of ST compared to TT published in 2016 from 3 studies based on large national thymic databases [the Korean Association for Research on the Thymus database; the Chinese Alliance for Research in Thymoma database; and the Japanese Association for Research on the Thymus (JART) database] produced conflicting results [10, 15, 16].

The objective of our study was to compare the short- and long-term outcomes of ST versus TT in patients with non-MG early-stage thymomas using the European Society of Thoracic Surgeons (ESTS) thymic database [17, 18].

METHODS

In the 2000–2017 period, out of a total of 1435 patients with thymic epithelial tumours contributed by 23 centres, 498 non-MG patients with pathological stage I thymoma (cT1a-bN0M0, according to the eighth edition of the Union for International Cancer Control/American Joint Committee on Cancer tumour/node/metastasis stage classification) were included in the study (Supplementary Material, Table S1). Participation in the ESTS thymic database was approved by the institutional review board of each participating centre.

Statistical analyses

Baseline patient characteristics are summarized descriptively by their median and interquartile range (IQR) or by number and percentages. Between-group differences were evaluated by the *t*-test for continuous variables and the χ^2 test or the Fisher's exact test for categorical variables. OS and freedom from recurrence (FFR) were estimated by the Kaplan–Meier method. The observation period in the OS was defined as the time from the date of surgery to the date of death by any cause (failure) or until the last follow-up visit (censoring). A Cox proportional hazard model was used to estimate the crude hazard ratios (HRs) with 95% confidence intervals (CIs) and to assess the influence of ST and TT on survival. FFR was also estimated: The observation period started on the day of surgery until death without recurrence or the date of recurrence diagnosis (failures), whichever occurred first, or until the last follow-up visit (censoring) (according to the International Thymic Malignancy Interest Group standard outcome measures for thymic malignancies) [19]. FFR was assessed in R0 patients only [*N* = 471 (94.6%)], and deaths were considered as a competing event using the method of Gooley. We estimated sub-distributional Sub-distributional Hazard Ratio (SHR) in a semiparametric model according to Fine and Gray. Differences in outcomes between the 2 surgical approaches were also assessed using a propensity score (PS)-matched analysis: Based on the PS, patients undergoing ST versus TT were matched with the nearest neighbour method without replacement.

PS was estimated using a priori selected variables that have been associated with the likelihood of TT: age, gender, cardiac comorbidity, other comorbidities, thymoma size, surgical approach, World Health Organization (WHO) histological analysis and pathological tumour/node/metastasis (TNM). After matching, outcomes were evaluated with the same methods described previously.

All statistical tests were two-sided, and *P*-values of 0.05 or less were considered statistically significant. Statistical analyses were conducted using Stata software version 15.1 (Stata Corp, College Station, TX, USA), R software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org/) and SAS software package version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Whereas TT was performed in 466 (93.6%) of 498 patients who underwent surgery with curative intent for pT1a-b thymoma, ST was done in 32 (6.4%). Most patients were men [*N* = 254 (51.0%)], and the median age at the time of surgery was 63 years (IQR 53–72). A minimally invasive approach (video-assisted or robotic-assisted thoracoscopic surgery) was used in 141 patients (28.3%). According to the WHO histological analysis, the AB type occurred with the greatest frequency [*N* = 221 (42.4%)], followed by type A [*N* = 94; (19%)], B2 [*N* = 78 (16%)], B1 [*N* = 75 (15%)] and B3 [5 cases (1%)] (Table 1). The perioperative outcomes of the TT

Table 1: Baseline characteristics in the overall population

Factors	All (*n* = 498)
Surgical resection, *n* (%)	
Thymothymomectomy	466 (93.6)
Simple thymomectomy	32 (6.4)
Age (years), mean (SD)	61.5 (12.9)
Gender (male), *n* (%)	254 (51.0)
Cardiac comorbidity, *n* (%)	164 (32.9)
Other comorbidities, *n* (%)	109 (21.9)
Surgical approach, *n* (%)	
Open	357 (71.7)
VATS/RATS	141 (28.3)
Thymoma size, *n* (%)	
<3 cm	52 (10.4)
3–5 cm	139 (27.9)
>5 cm	284 (57.0)
Missing	23 (4.6)
pTNM, *n* (%)	
T1a	440 (88.4)
T1b	58 (11.6)
WHO histological diagnosis, *n* (%)	
A	94 (18.9)
AB	211 (42.4)
B1	75 (15.1)
B2	78 (15.7)
B3	35 (7.0)
Missing	5 (1.0)
Pathological resection status, *n* (%)	
R0	471 (94.6)
R1	27 (5.4)
Postoperative chemotherapy, *n* (%)	5 (1.0)
Postoperative radiotherapy, *n* (%)	66 (13.3)

pTNM: pathological tumour/node/metastasis; RATS: robotic-assisted thoracoscopic surgery; SD: standard deviation; VATS: video-assisted thorcacoscopic surgery; WHO: World Health Organization.

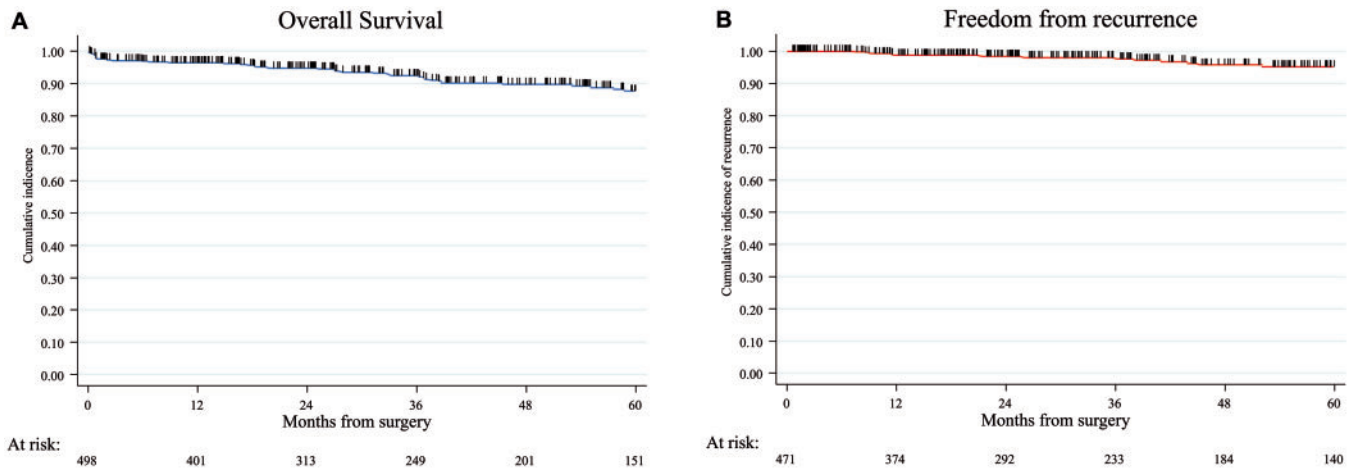


Figure 1: Overall population: overall survival (**A**) and freedom from recurrence (based on competing risk analysis) (**B**).

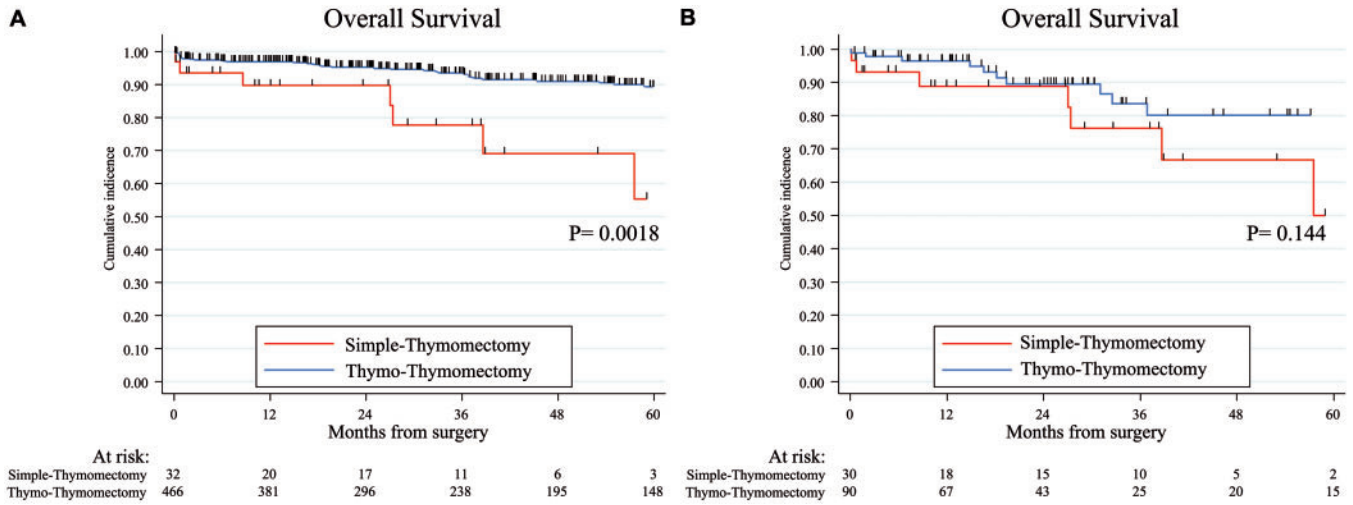


Figure 2: Thymothymomectomy versus simple thymomectomy: overall survival before (**A**) and after (**B**) propensity score matching.

group did not differ significantly from those of the ST group with regard to incomplete resection (R1) rate [$N = 25$ (5.4%) vs $N = 2$ (6.3%); $P = 0.83$], complication rate [$N = 62$ (13.3%) vs $N = 4$ (12.5%); $P = 0.79$] and 30-day mortality rate [$N = 12$ (2.6%) vs $N = 2$ (6.3%); $P = 0.23$].

At a median follow-up of 37 months (IQR 17–72), a total of 69 (13.9%) deaths of any cause and a total of 15 (3.0%) recurrences were recorded (Fig. 1). Eight patients (53.3%) developed a local relapse, whereas 5 patients (33.3%) experienced distant metastases to the lung or the pleura, and 2 (13.4%) patients had both local and distant relapses.

The 5-year OS was 55% for the ST group and 89% for the TT group ($P = 0.002$) (Fig. 2). The 5-year FFR was 79% for the ST group and 96% for the TT group ($P < 0.001$) (Fig. 3). The crude Cox regression models demonstrated that ST was associated with an inferior OS compared to TT (Fig. 4) (HR 3.31, 95% CI 1.49–7.35; $P = 0.003$). The crude Fine–Gray models showed that ST was correlated with a worse FFR than TT (Fig. 4) (HR 6.04, 95% CI 1.71–21.4; $P = 0.005$).

Propensity score-matched analysis

PS matching was used to create a cohort of 120 patients (3:1 ratio), each of whom had a complete resection (R0) either through ST or TT. The 2 groups were well matched with regard to demographic and clinicopathological characteristics (Table 2).

Before matching, the patients in the ST group were older (mean age 65.9 vs 60.9 years; $P = 0.041$), had a higher incidence of cardiac comorbidity [$N = 15$ (50%) vs $N = 141$ (32%); $P = 0.042$] as well as of other comorbidities [$N = 13$ (43%) vs $N = 93$ (21%); $P = 0.005$]. Moreover, compared to the TT group, the ST patients were less likely to present with larger tumours [>5 cm, $N = 21$ (70%) vs $N = 255$ (58%); $P = 0.032$] and more frequently had minimally invasive surgery [$N = 11$ (37%) vs $N = 112$ (25.4%); $P < 0.001$].

After matching, no significant differences were observed between the ST and TT groups with regard to age, gender, cardiac comorbidity, other comorbidities, thymoma size, surgical approach, WHO histology and pathological TNM (Table 2).

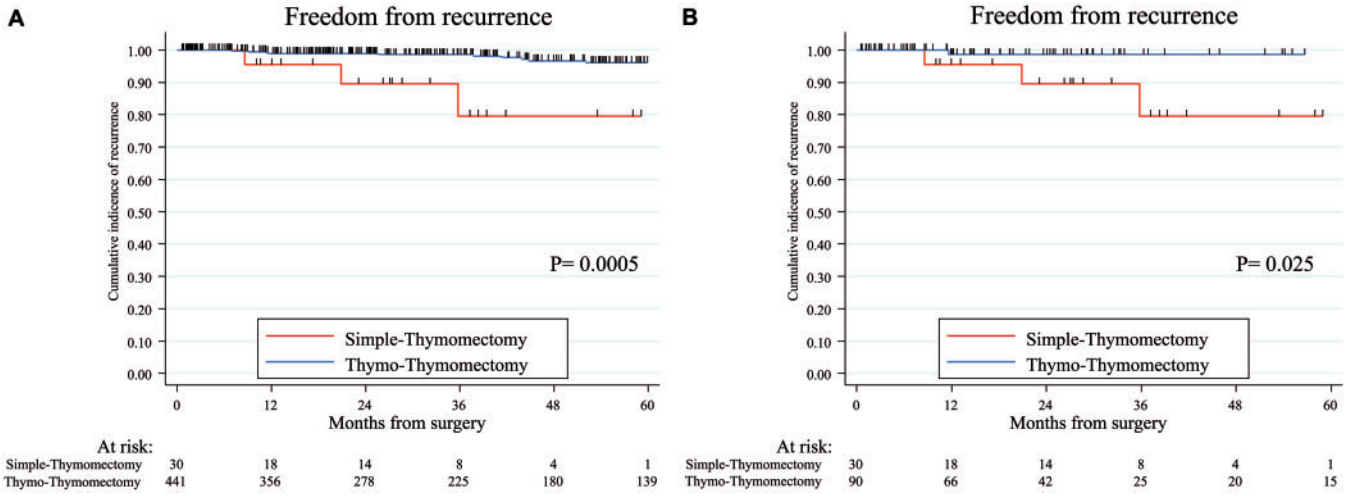


Figure 3: Thymothymomectomy versus simple thymomectomy: freedom from recurrence (based on competing risk analysis) before (**A**) and after (**B**) propensity score matching.

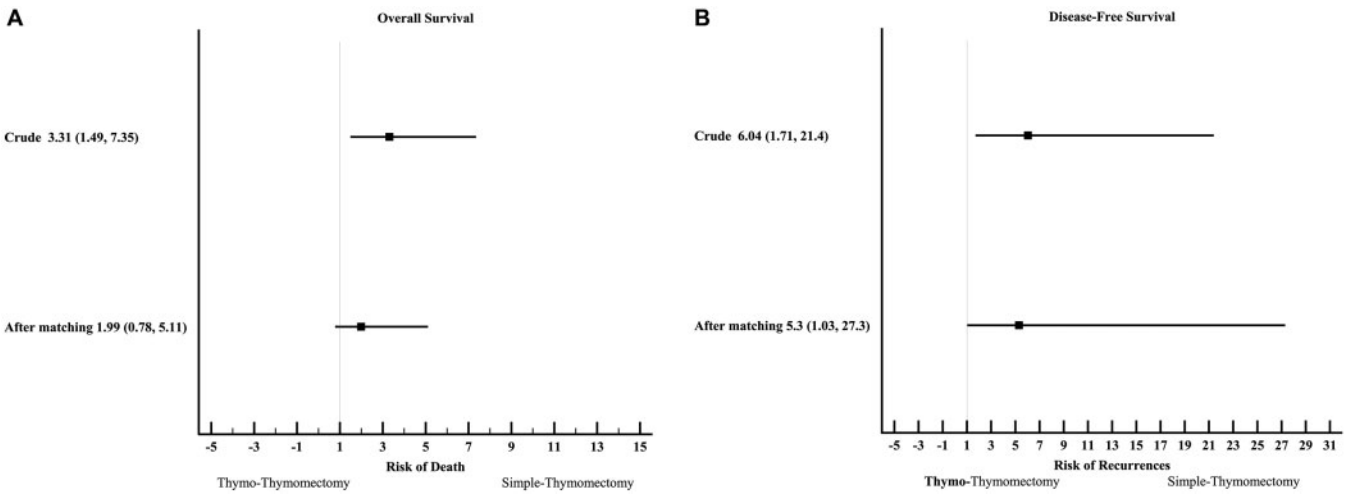


Figure 4: Thymothymomectomy versus simple thymomectomy: univariate, multivariable-adjusted and propensity score-matched analysis for overall survival (**A**) and freedom from recurrence (based on a competing risk analysis) (**B**).

The 5-year OS rate was 80% in the TT group and 49% in the ST group ($P = 0.144$) (Fig. 2). The 5-year FFR rate was 98% in the TT group and 79% in the ST group ($P = 0.025$) (Fig. 3). According to the Fine–Gray model, ST was associated with a worse FFR (HR 5.30, 95% CI 1.03–27.3; $P = 0.046$) (Fig. 4).

DISCUSSION

Conventionally, resection of the tumour and the entire thymus gland is considered the standard procedure for the treatment of thymoma, with or without MG [20]. Nevertheless, in the last decades, the desire to increase safety and to decrease operative time and surgical trauma was the motivation behind the advances in surgical oncology. In particular, it has been hypothesized that a tissue-sparing procedure like ST could be as effective as a radical oncological treatment for thymoma such as TT [10, 11].

The results of our study suggest that, in the cohort from the ESTS thymic database, TT showed the same rate of postoperative complications, 30-day mortality and postoperative length of stay as ST. However, compared to TT, ST was associated with decreased OS and FFR in patients affected by stage I thymoma.

Thymoma is generally considered to be an indolent disease, even though it can present a more aggressive behaviour including adjacent organ invasion or distant metastases [2, 20, 21]. Surgical resection remains the mainstay of treatment for most thymomas, and traditionally resection of the tumour is associated with resection of the entire thymus gland [2, 20]. However, an increasing number of authors raised the question about the possibility of performing, in early-stage non-MG thymomas, a more conservative and tissue-sparing approach, i.e. resecting the thymoma only. As a matter of fact, a simple thymectomy should provide the same oncological outcome as the thymothymomectomy and in order to be accepted as a valid alternative to the surgical treatment of early-stage thymoma.

In this context, the current literature, recently analysed by Fiorelli *et al.* [8], presented conflicting results. The majority of available papers indicated a similar recurrence rate for ST and TT,

Table 2: Thymothymomectomy versus simple thymomectomy: baseline characteristics before and after propensity score matching

	Before match (n = 471)				After match (n = 120)			
	Thymothymomectomy (N = 441)	Simple thymomectomy (N = 30)	P-value	SMD[a]	Thymothymomectomy (N = 90)	Simple thymomectomy (N = 30)	P-value	SMD[a]
Age (years), mean (SD)	60.9 (13.0)	65.9 (10.8)	0.041[b]	0.30	65.0 (11.3)	65.9 (10.8)	0.69[b]	0.08
Gender (male), n (%)	224 (50.8)	16 (53)	0.79[c]	0.30	47 (52)	16 (53)	0.92[c]	0.02
Cardiac comorbidity, n (%)	141 (32.0)	15 (50)	0.042[c]	0.15	45 (50)	15 (50)	1.00[c]	0.02
Other comorbidities, n (%)	93 (21.1)	13 (43)	0.005[c]	0.15	35 (39)	13 (43)	0.67[c]	0.09
Surgical approach, n (%)				0.34				0.02
Open	329 (74.6)	9 (30)	<0.001[c]		26 (29)	9 (30)	0.91[c]	
VATS/RATS	112 (25.4)	21 (70)			64 (71)	21 (70)		
Thymoma size, n (%)				0.56				0.02
<3 cm	44 (10.0)	6 (20)	0.032[c]		25 (28)	6 (20)	0.55[c]	
3–5 cm	121 (27.4)	13 (43)			37 (41)	13 (43)		
>5 cm	255 (57.8)	11 (37)			24 (27)	11 (37)		
Missing	21 (4.8)	0 (0)			4 (4)	0 (0)		
pTNM, n (%)				0.15				0.02
T1a	388 (88.0)	26 (87)	0.77[c]		79 (88)	26 (87)	1.00[c]	
T1b	53 (12.0)	4 (13)			11 (12)	4 (13)		
WHO histological analysis, n (%)				0.50				0.02
A	81 (18.4)	7 (23)	0.20[c]		14 (16)	7 (23)	0.52[c]	
AB	196 (44.4)	8 (27)			37 (41)	8 (27)		
B1	64 (14.5)	7 (23)			16 (18)	7 (23)		
B2	69 (15.6)	4 (13)			15 (17)	4 (13)		
B3	26 (5.9)	4 (13)			8 (9)	4 (13)		
Missing	5 (1.1)	0 (0)			0 (0)	0 (0)		

[a]Standardized mean difference.
[b]t-Test.
[c]χ^2 test or the Fisher's exact test.
pTNM: pathological tumour/node/metastasis; RATS: robotic-assisted thoracoscopic surgery; SD: standard deviation; SMD: standardized mean difference; VATS: video-assisted thoracoscopic surgery; WHO: World Health Organization.

corroborating the hypothesis of similar oncological outcomes. In particular, Narm *et al.* [10], using the Korean Association for Research on the Thymus register, did not document a difference in thymoma recurrence in patients undergoing ST and TT. On the other hand, analyses of the Chinese Alliance for Research in Thymoma and the JART databases reported a higher incidence of recurrence in the ST group [15, 16]. Moreover, the JART study reported a greater rate of R1 resection. Our study conducted on patients operated on in 23 centres from 11 countries showed that patients who had ST had worse 5-year OS (55% vs 89%) and 5-year FFR (79% vs 96%) than patients who had TT.

Minimally invasive and tissue-sparing procedures generate great interest in the surgical oncology community due to the possibility of reducing surgical trauma, blood loss, surgical time, hospital length of stay and postoperative complications. The literature presented a high grade of granularity on this subject. Several reports documented the advantage of ST in terms of shorter operative time and less blood loss [11, 22, 23]. Others reported an advantage in terms of postoperative length of stay [22, 24]. Additionally, a minority of studies documented a higher rate of postoperative complications in patients having TT [16]. Although the cause of possible advantages in terms of intraoperative outcomes is reasonable, the clinical rationale of a reduction of postoperative morbidity is more difficult to justify. Indeed, the low morbidity and mortality associated with TT are well established in the literature, especially in patients with early-stage thymoma [9, 10, 24, 25]. Consequently, several of these differences reported could be related to the non-homogeneity of the cohorts in the analysis, such as different follow-up times, different ages and different thymoma dimensions. In this context, our results, derived from the matched analysis of 498 cases, suggested that TT yields the same rate of postoperative complications, 30-day mortality and postoperative length of stay as ST.

Our study presents several limitations, mainly those related to a large multi-institutional data set and the retrospective nature of the analysis. In particular, individual details about intraoperative techniques and variations (e.g. specific method for assessment of intraoperative surgical margins) could not be determined from the data set. Moreover, case-volume is understandably not homogeneous among participating institutions, and the ST group presents a relatively small number of cases. These limits may also clarify why the 30-day mortality is relatively high in our series, particularly in the ST group. However, this rate could be emphasized by the relatively low number of patients in the ST group. Nevertheless, in the modern era, 30-day mortality after resection for thymoma has been reported to be <1% [25]. Furthermore, errors in measurements and classifications (i.e. information bias), as well as selection bias, could not be completely prevented. Indeed, precise selection criteria for either procedure could not be determined, but ST patients were generally older with higher comorbidities. Consequently, we have adopted the PS-matched analysis that was used to minimize patient selection bias. Furthermore, the use of the ESTS thymic database, which represents one of the largest thymic databases in the world dedicated to such rare disease, warrants good data reliability and therefore supports our conclusions.

CONCLUSION

In conclusion, our study indicates that patients with early-stage thymoma without MG who have TT have significantly better FFR and OS compared to those who have ST, without an increase in the perioperative morbidity rate. Therefore, especially due to the indolent behaviour of an early-stage thymoma, we suggest that in patients with non-MG early-stage (stage I) thymomas, the resection of the thymoma and the thymus gland (TT) should be considered the procedure of choice.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

Author contributions

Francesco Guerrera: Conceptualization; Methodology; Project administration; Writing—original draft. **Pierre Emmanuel Falcoz:** Conceptualization; Data curation; Supervision; Writing—review & editing. **Bernhard Moser:** Conceptualization; Data curation; Supervision; Writing—review & editing. **Dirk van Raemdonck:** Data curation; Methodology; Supervision; Writing—review & editing. **Andrea Bille':** Data curation; Supervision; Writing—review & editing. **Alper Toker:** Conceptualization; Data curation; Validation; Writing—review & editing. **Lorenzo Spaggiari:** Data curation; Supervision; Writing—review & editing. **Luca Ampollini:** Data curation; Supervision; Writing—review & editing. **Claudia Filippini:** Data curation; Formal analysis; Methodology; Validation; Writing—original draft. **Pascal Alexandre Thomas:** Data curation; Supervision; Writing—review & editing. **Bram Verdonck:** Data curation; Writing—review & editing. **Paolo Mendogni:** Data curation; Writing—review & editing. **Clemens Aigner:** Data curation; Supervision; Writing—review & editing. **Luca Voltolini:** Data curation; Supervision; Writing—review & editing. **Nuria Novoa:** Data curation; Supervision; Writing—review & editing. **Miriam Patella:** Data curation; Writing—review & editing. **Sara Mantovani:** Data curation; Writing—review & editing. **Ivan Gomes Bravio:** Data curation; Supervision; Writing—review & editing. **Charalambos Zisis:** Data curation; Supervision; Writing—review & editing. **Angela Guirao:** Data curation; Writing—review & editing. **Francesco Londero:** Data curation; Visualization; Writing—review & editing. **Miguel Congregado:** Data curation; Methodology; Supervision; Visualization; Writing—review & editing. **Gaetano Rocco:** Data curation; Methodology; Supervision; Visualization; Writing—review & editing. **Bert Du Pont:** Data curation; Visualization; Writing—review & editing. **Nicola Martucci:** Data curation; Visualization; Writing—review & editing. **Matthias Esch:** Data curation; Writing—review & editing. **Alessandro Brunelli:** Supervision; Visualization; Writing—review & editing. **Frank C. Detterbeck:** Validation; Visualization; Writing—review & editing. **Federico Venuta:** Data curation; Supervision; Visualization; Writing—review & editing. **Walter Weder:** Supervision; Visualization; Writing—review & editing. **Enrico Ruffini:** Conceptualization; Supervision; Visualization; Writing—original draft.

Reviewer information

European Journal of Cardio-Thoracic Surgery thanks Servet Bölükbas, Hiroshi Date, Yui Watanabe and the other, anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

[1] Travis WD, Brambilla E, Mueller-Hermelink HK, Harris CC. WHO Classification of Tumors. Pathology and Genetics of Tumors of the Lung, Pleura, Thymus and Heart. Lyon, France: IARC Press, 2004.

[2] Kondo K. Therapy for thymic epithelial tumors. Gen Thorac Cardiovasc Surg 2014;62:468–74.

[3] Koppitz H, Rockstroh JK, Schüller H, Standop J, Skowasch D, Müller-Hermelink HK *et al.* State-of-the-art classification and multimodality treatment of malignant thymoma. Cancer Treat Rev 2012;38:540–8.

[4] Falkson CB, Bezjak A, Darling G, Gregg R, Malthaner R, Maziak DE *et al.* The management of thymoma: a systematic review and practice guideline. J Thorac Oncol 2009;4:911–19.

[5] Maggi G, Casadio C, Cavallo A, Cianci R, Molinatti M, Ruffini E. Thymoma: results of 241 operated cases. Ann Thorac Surg 1991;51:152–6.

[6] Venuta F, Rendina EA, Anile M, de Giacomo T, Vitolo D, Coloni GF. Thymoma and thymic carcinoma. Gen Thorac Cardiovasc Surg 2012;60:1–12.

[7] Regnard JF, Magdeleinat P, Dromer C, Dulmet E, de Montpreville V, Levi JF *et al.* Prognostic factors and long-term results after thymoma resection: a series of 307 patients. J Thorac Cardiovasc Surg 1996;112:376–84.

[8] Fiorelli A, Natale G, Freda C, Santini M. Is thymomectomy equivalent to complete thymectomy in non-myasthenic patients with early-stage thymoma? Interact CardioVasc Thorac Surg 2019;28:399–403.

[9] Toker A, Sonett J, Zielinski M, Rea F, Tomulescu V, Detterbeck FC. Standard terms, definitions, and policies for minimally invasive resection of thymoma. J Thorac Oncol 2011;6:S1739–42.

[10] Narm KS, Lee CY, Do YW, Jung HS, Byun GE, Lee JG *et al.*; Korea Association for Research on the Thymus. Limited thymectomy as a potential alternative treatment option for early-stage thymoma: a multi-institutional propensity-matched study. Lung Cancer 2016;101:22–7.

[11] Odaka M, Akiba T, Yabe M, Hiramatsu M, Matsudaira H, Hirano J *et al.* Unilateral thoracoscopic subtotal thymectomy for the treatment of stage I and II thymoma. Eur J Cardiothorac Surg 2010;37:824–6.

[12] Onuki T, Ishikawa S, Iguchi K, Goto Y, Sakai M, Inagaki M *et al.* Limited thymectomy for stage I or II thymomas. Lung Cancer 2010;68:460–5.

[13] Tseng YC, Hsieh CC, Huang HY, Huang CS, Hsu WH, Huang BS *et al.* Is thymectomy necessary in nonmyasthenic patients with early thymoma? J Thorac Oncol 2013;8:952–8.

[14] Bae MK, Lee SK, Kim HY, Park SY, Park IK, Kim DJ *et al.* Recurrence after thymoma resection according to the extent of the resection. J Cardiothorac Surg 2014;9:51.

[15] Gu Z, Fu J, Shen Y, Wei Y, Tan L, Zhang P *et al.*; Members of the Chinese Alliance for Research in Thymomas. Thymectomy versus tumor resection for early-stage thymic malignancies: a Chinese Alliance for Research in Thymomas retrospective database analysis. J Thorac Dis 2016;8:680–6.

[16] Nakagawa K, Yokoi K, Nakajima J, Tanaka F, Maniwa Y, Suzuki M *et al.* Is thymomectomy alone appropriate for stage I (T1N0M0) thymoma? Results of a propensity-score analysis. Ann Thorac Surg 2016;101:520–6.

[17] Ruffini E, Guerrera F, Brunelli A, Passani S, Pellicano D, Thomas P *et al.* Report from the European Society of Thoracic Surgeons prospective thymic database 2017: a powerful resource for a collaborative global effort to manage thymic tumours. Eur J Cardiothorac Surg 2019;55:601–9.

[18] Ruffini E, Falcoz PE, Guerrera F, Filosso PL, Thomas P, Novoa N *et al.* The European Society of Thoracic Surgeons (ESTS) thymic database. J Thorac Dis 2018;10:S3516–20.

[19] Huang J, Detterbeck FC, Wang Z, Loehrer PJ Sr. Standard outcome measures for thymic malignancies. J Thorac Oncol 2011;6:S1691–7.

[20] NCCN Clinical Practice Guidelines in Oncology. Thymomas and Thymic Carcinomas. Version 2. 2019. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1469.

[21] 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.

[22] Rusidanmu A, Huang S, Lv X. Is thymomectomy sufficient for nonmyasthenic early stage thymoma patients? A retrospective, single center experience. Thorac Cancer 2018;9:88–93.

[23] Sakamaki Y, Kido T, Yasukawa M. Alternative choices of total and partial thymectomy in video-assisted resection of noninvasive thymomas. Surg Endosc 2008;22:1272–7.

[24] Pennathur A, Qureshi I, Schuchert MJ, Dhupar R, Ferson PF, Gooding WE *et al.* Comparison of surgical techniques for early-stage thymoma: feasibility of minimally invasive thymectomy and comparison with open resection. J Thorac Cardiovasc Surg 2011;141:694–701.

[25] Kamel MK, Villena-Vargas J, Rahouma M, Lee B, Harrison S, Stiles BM *et al.* National trends and perioperative outcomes of robotic resection of thymic tumours in the United States: a propensity matching comparison with open and video-assisted thoracoscopic approaches†. Eur J Cardiothorac Surg 2019;56:762–9.