

# Does surgical debulking for advanced stages of thymoma improve survival?

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## Abstract

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was 'Does surgical debulking for advanced stages of thymoma improve survival?' Altogether, only 17 papers were found using the reported search, of which only 10 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated; these studies have mainly reported the survival and recurrence rates after total vs subtotal resection of thymic tumours in patients receiving or not receiving adjuvant chemoradiotherapy. These studies confirmed that complete resection is the best prognostic factor in thymomas. With regard to subtotal tumour resection/debulking, we did not find any randomized controlled trials. The evidence on this topic is scarce and these 10 reported were retrospective reviews of the operative, histology and survival data of patients with thymoma who had subtotal vs partial resection for advanced stages of thymoma. Although debulking surgery for thymoma had positively affected survival, in six studies, the difference failed to reach statistical significance. Three of the studies, on the other hand, showed a higher survival rate in thymomas in which maximum debulking was performed and the treatment was followed by high-dose irradiation. None of these studies showed any benefit in debulking surgery for thymic carcinoma. Besides histology and tumour cell-type, other factors influencing survival included the tumour stage and the presence of symptoms such as myasthenia gravis as a warning sign at an early stage. Current evidence in the literature on the survival after debulking surgery for thymoma is contradictory, and most of the studies do not show any survival benefit after debulking for thymoma. However, debulking surgery minimizes the tumour size and area for irradiation post-operatively, hence it can result in less damage to the adjacent tissue during radiotherapy and may be considered for patients in advanced stages of thymoma in whom extensive radiotherapy will be required. In these cases, however, the risks of surgery followed by radiotherapy or radiotherapy alone should carefully be assessed prior to the initiation of treatment.

**Keywords:** Review • Thymoma • Debulking surgery

## INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the ICVTS [1].

## THREE-PART QUESTION

In [patients with stage III or IV thymoma] does treatment of [surgical debulking without complete resection] result in [increased survival].

## CLINICAL SCENARIO

Oncologists have referred you a 27-year old woman with two young children who has been diagnosed with a large thymoma. Her chest computed tomography scan reveals that the tumour is invading the pericardium and the wall of the oesophagus. Her referring oncologist has told the patient that surgery offers her

no benefits in terms of survival and has offered her chemoradiotherapy, but she wants to meet you to get a surgeon's view. You decide to check the literature yourself before the clinic.

## SEARCH STRATEGY

Medline 1950 to March 2011 using OVID interface [exp debulking/OR surgical debulking.mp] AND [exp thymoma/OR thymectomy.mp OR exp thymectomy/OR thymoma.mp].

## SEARCH OUTCOME

Seventeen papers were found using the reported search. Non-English papers, the ones that had analysed the role of surgery after induction chemo/radiotherapy and papers that analysed subtotal and partial resection/biopsy as one group and not with each other were excluded. Finally, only 10 retrospective

**Table 1:** Studies on debulking surgery for thymomas

Author, date and study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Ciernik <i>et al.</i> (1994) [2], J Clin Oncol	Thirty-one patients with stages III and IV; debulking or partial resection	Stage of the tumour influenced the survival	Both groups yielded similar results with respect to survival	No difference in the survival between IVa and IVb observed
Retrospective (level 3 evidence)				Radiation therapy for local tumour control is most effective treatment
Curran <i>et al.</i> (1988) [3], J Clin Oncol	A total of 103 patients with stages I, II ( $n = 61$ , total resection), III, IV ( $n = 38$ , debulking or partial resection/biopsy)	No difference between debulking and partial resection	Five-year survival 21%, 5-year local recurrence 49%	Advantage of aggressive debulking is the reduced size of the radiotherapy field that would expose less normal tissues to radiation
Retrospective (level 3 evidence)			No difference between debulking and partial resection/biopsy	
Cohen <i>et al.</i> (1984) [4], J Thorac Cardiovasc Surg	Twenty-three patients stages III and IV; debulking following irradiation vs biopsy following irradiation	No difference in survival with cell type	5.3-years mean follow-up showed 35% survival	There was no value in debulking
Retrospective (level 3 evidence)		No difference between irradiation following partial excision and irradiation following biopsy		Irradiation may be of value in local control of thymoma
Akoum <i>et al.</i> (2003) [5], Mol Immunol	Twenty-seven patients stages II, III, IV; full resection, debulking (70% resection), biopsy	Significantly better survival with complete resection but no main difference between debulking and biopsy	Five-year survival 44%	Respectability is the most important survival factor
Retrospective (level 3 evidence)			Ten-year survival 16% in debulking and biopsy group	Better survival if myasthenia gravis presented
Lin <i>et al.</i> (2005) [6], Am J Med Sci	Twenty patients with (carcinoma) stages IVa and IVb; debulking with chemo/radiotherapy, debulking with chemotherapy, debulking with radiotherapy, only chemo/radiotherapy, only chemotherapy	Chemotherapy played an important role in the advanced stages of thymoma	15% survival at 22-month median follow-up	Chemotherapy played an important role in the advance stages of thymoma
Retrospective (level 3 evidence)		No difference		Histology of the tumour has an importance prognostic significance
Liu <i>et al.</i> (2002) [7], Ann Thorac Surg	Thirty-five patients (carcinoma) stages III, IV; debulking, full resection, biopsy	Debulking did not increase survival significantly	Three-year survival 38%	Respectability and stage were the main predictors of the survival
Retrospective (level 3 evidence)			Five-year survival 27%	
			Median survival: complete resection 35 months, debulking 25 months, biopsy 17.4 months	
Urgesi <i>et al.</i> (1990) [8], Radiother Oncol	Thirty-six patients stages III (21) and IVa (15) had debulking compared with 8 patients, (5) stage III and (3) stage IVa biopsy only	Patients with subtotal resection in stage III had better survival and less recurrence compared with biopsy only	Proportion of patients with macroscopical residual disease was 44% in stage III	Total resection showed best results
Retrospective (level 3 evidence)				Better outcome with debulking in unresectable stage III
				Marginal difference with debulking in stage IVa
Liu <i>et al.</i> (2006) [9], Eur J Surg Oncol	Forty-three patients with stage III/IVa; debulking or partial resection/biopsy only	Significantly better survival in the group with debulking compared with biopsy only	Survival in debulking group was 106 months and in biopsy group 57.2 ( $P = 0.03$ )	Maximal debulking surgery should be attempted for locally advanced disease even if complete resection is not possible
Retrospective (level 3 evidence)			Five-year 71 vs 35%, 10 years 53 vs 18%	

Continued

Table 1: Continued

Author, date and study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Lin <i>et al.</i> (2004) [10], J Chin Med Assoc Retrospective (level 3 evidence)	Twenty-seven patients with stages III and IVa	Debulking and high-dose irradiation showed significantly better survivals ( $P = 0.021$ )	Five-year survival 54%, 10-year survival 35%	Debulking followed by high-dose irradiation improves survival
Kondo <i>et al.</i> (2003) [11], Ann Thorac Surg Retrospective (level 3 evidence)	A total of 1320 patients with all stages of thymoma and thymic carcinoma; total resection, subtotal resection, inoperable	Debulking improved survival in thymoma but not in thymic carcinoid	Five-year survival 65 vs 35% for thymoma ( $P = 0.002$ ), 30 vs 24% for carcinoma ( $P = 0.2$ )	Total tumour resection and cell type are the most important prognostic factors  Value of irradiation and debulking in thymic carcinoma not proven

papers were identified that provided the best evidence to answer this question. These are presented in Table 1.

## RESULTS

The most important predictive factor in survival after surgery for thymoma is complete resection, however, factors such as the stage of the tumour, cell-type, the presence of myasthenia gravis that enables early detection, and adjuvant chemo/radiotherapy have been shown to influence the survival post resection. The role of surgery and tumour debulking in advanced stages of thymoma is controversial. Out of 10 studies that we analysed, 6 showed no difference in the survival; Ciernik *et al.* [2] reported his retrospective review of 31 patients with stage III and IV thymoma that had incomplete macroscopic resection of thymoma followed by irradiation. His 5- and 10-year survival data failed to show any difference between biopsy only and subtotal resection. Tumours greater than 10 cm correlated with a worse prognosis, and a similar outcome was observed after treating stage IVa and IVb thymoma. However, debulking surgery in his series did not include artificial vascular grafting and may not have been extensive. Curran *et al.* [3] also showed no difference in survival and recurrence rates between biopsy/partial resection and debulking surgery, and suggested that the advantage of aggressive debulking is a reduced size of the radiotherapy ports that can protect the adjacent organs from irradiation postoperatively.

The oldest paper reporting results of debulking surgery for thymoma was published in 1984 by Cohen *et al.* [4], who reported a 5-year survival of 35% and showed no difference in the histological cell-type, partial resection and debulking surgery, but showed better survival with irradiation in the local control of thymoma. Their results were in accordance with a report by Akoum *et al.* [5], who showed a 5-year survival of 44%, and no difference between debulking surgery and partial resection.

Two other reports on carcinoma of the thymus showed no survival benefit with debulking surgery; Lin *et al.* [6] reported only 15% survival after 22 months in 20 patients with stage IVa

and IVb disease and revealed that histology was an important prognostic factor in thymic tumours. Similarly, Liu *et al.* [7] failed to show any advantages with debulking for carcinoma of thymus.

Urgesi *et al.* [8] on the other hand, showed that the difference between the patients with stage III thymoma who had subtotal resection and those only biopsied was significant ( $P < 0.01$ ), but in stage IVa only marginally better survival after debulking was observed. Similarly, two reports in recent years showed significantly better outcome with debulking compared with biopsy or partial resection with 5-year survival rate to be 70 and 35%, respectively [9, 10]. Authors reported that maximum debulking followed by irradiation improves survival significantly. Results of a large number of patients with thymoma undergoing various treatments have been published, which showed a significant survival difference between subtotal resection and inoperable cases of thymoma, but showed no difference in cases of thymic carcinoma [11].

A systemic review on the treatment of all stages thymoma [12] published guidelines on the role of surgery in the advanced stages of thymoma; based on their recommendations, the main aim of surgery should be complete removal of the thymoma with wide surgical margins, and in advanced stages of thymoma, surgery should only be recommended if pleural and pericardial metastases can be resected. With this in mind, debulking surgery as the initial step in the management of stage III and IV thymomas is not recommended. Moreover, if at thoracotomy it is confirmed that total resection is not possible, then maximal debulking with appropriate vascular reconstruction, and avoidance of bilateral phrenic nerve resection should be carried out and clips should be placed to mark the residual tumour to facilitate postoperative radiotherapy.

## CLINICAL BOTTOM LINE

In patients with thymoma, complete surgical resection is the main determinant of the outcome and survival postoperatively. However, in advanced stages of thymoma, complete resection is not possible without damaging the main organs. Current data do

not support a statistically significant benefit with debulking surgery only; however, there is a trend towards some positive results with debulking of the advanced thymic tumours followed by radiotherapy. But there is no survival benefit with debulking surgery only, especially with thymic carcinomas that have a more aggressive nature compared with the other thymic tumours.

On the other hand, the effect of high-dose irradiation in prolonging survival is invaluable; however, extensive irradiation has its own complications and it is possible that maximum resection prior to radiotherapy minimizes irradiation damage to the surrounding organs, therefore decreasing the complications of radiotherapy and resulting in a better outcome. Therefore, debulking surgery for thymoma followed by radiotherapy may be offered to some individuals with large tumours; however, the risks of surgery in these patients should be weighed over the risks of radiotherapy alone before this option is offered to the patient.

**Conflict of interest:** none declared.

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