PNEUMOLOGIA 2018

Milano, 14 – 16 giugno 2018 · Centro Congressi Palazzo delle Stelline

LA CHIRURGIA DEL TIMO

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Thymic surgery

Thymectomy in myasthenic patients

Thymectomy for oncological reasons

RATIONALE FOR THYMECTOMY IN MG

The thymus may play a role in pathogenesis of myasthenia (possible source of antigen to drive this autoimmune disease)

Most patients with MG and autoantibodies directed against the acetylcholine receptor (AChR) have thymic abnormalities: hyperplasia is found in 60 to 70% and thymoma in 10 to 15%

The disease often improves or disappears after thymectomy (Blalock 1936)

EXPECTED BENEFITS OF THYMECTOMY IN MG

- CLINICAL BENEFITS

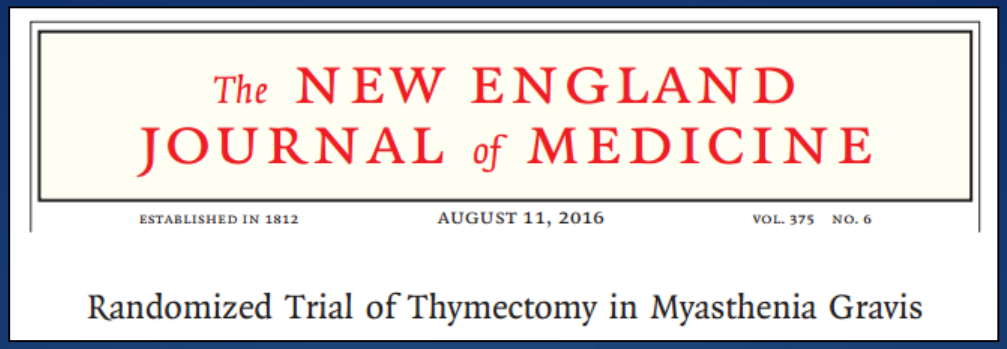
(REMISSION-IMPROVEMENT OF SYMPTOMS)

- REDUCTION OF MEDICATIONS

(ADVERSE EFFECTS – COSTS)

- MINIMAL INVASIVENESS AND LOW COMPLICATIONS

(RISK-BENEFIT BALANCE)



- The time-weighted average Quantitative Myasthenia Gravis score over a three-year period was significantly lower for the thymectomy group compared with the prednisone-alone group (6.15 versus 8.99, estimated difference 2.85, 95% CI 0.47-5.22).
- The average requirement for alternate-day prednisone over three years was significantly lower for the thymectomy group (44 versus 60 mg, estimated difference 16 mg, 95% CI 7-25).
- The proportion of subjects requiring immunosuppression with azathioprine was significantly lower for the thymectomy group (17 versus 48 percent, estimated difference 31 percent, 95% CI 16-47).
- The proportion of subjects hospitalized for MG exacerbations was significantly lower for the thymectomy group (9 versus 37 percent, estimated difference 28 percent, 95% CI 14-42).
- The proportion of subjects who achieved minimal manifestation status was significantly greater in the thymectomy group at 12 months (67 versus 37 percent) and at 36 months (67 versus 47 percent).

Surgical and neurologic outcomes after robotic thymectomy in 100 consecutive patients with myasthenia gravis

Giuseppe Marulli, MD, PhD, Marco Schiavon, MD, Egle Perissinotto, MD, Antonella Bugana, MD, Francesco Di Chiara, MD, Alessandro Rebusso, MD, and Federico Rea, MD

The Journal of Thoracic and Cardiovascular Surgery • March 2013

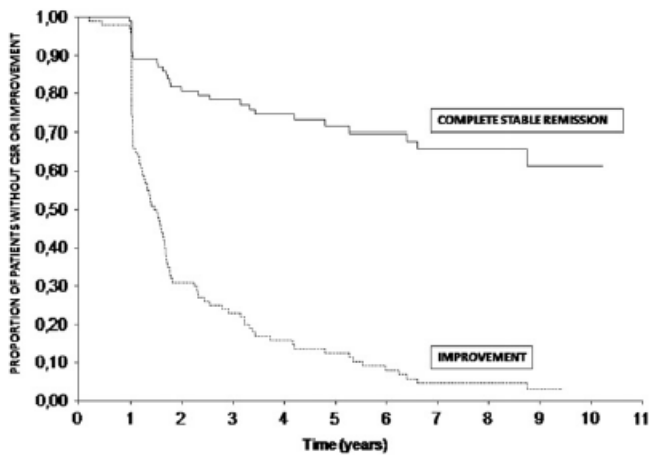


FIGURE 1. Cumulative probability of CSR and improvement. *CSR,* Complete stable remission.

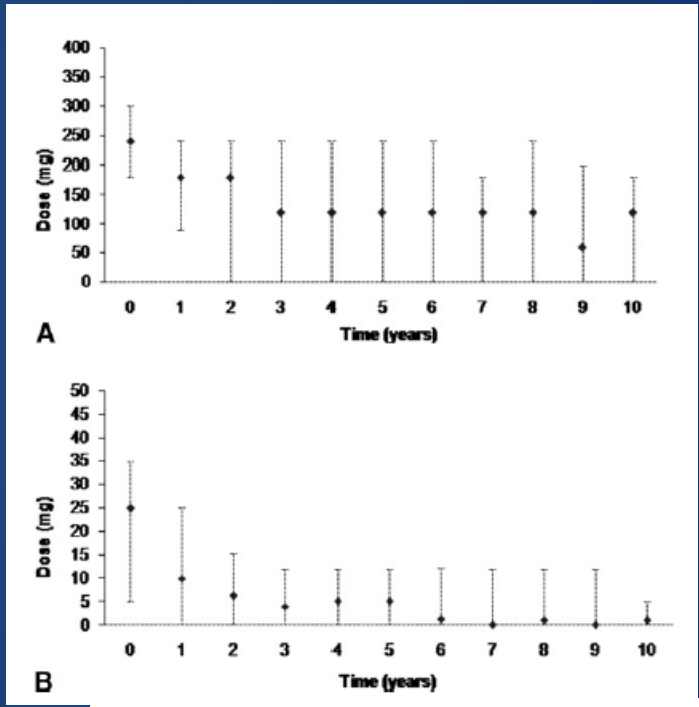
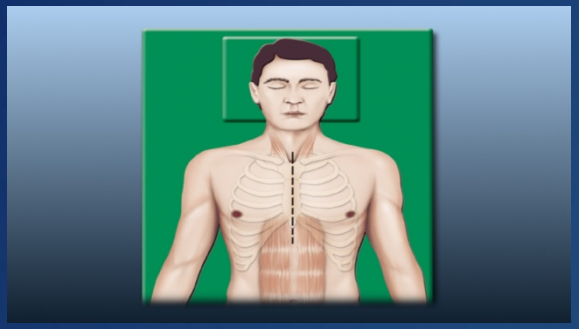
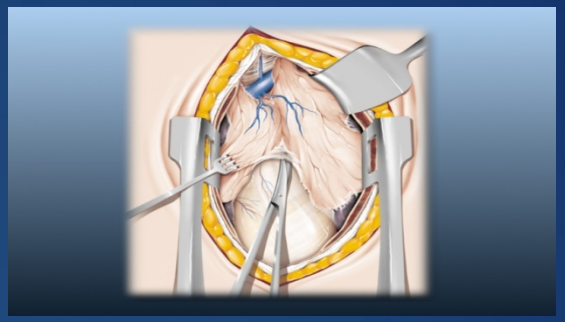


FIGURE 3. Postoperative reduction over time of the median dose of cholinesterase inhibitor (A) and prednisone (B) compared with the basal preoperative treatment

TRANS-STERNAL THYMECTOMY





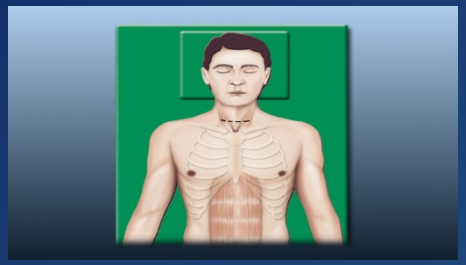
ADVANTAGES

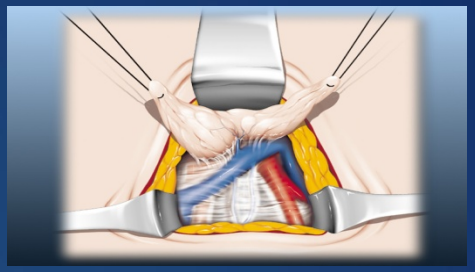
- Optimal exposition of the operative field
- Thymectomy easier and extended to the perithymic tissue
- Low probability of nervous and vascular injuries

DISADVANTAGES

- Invasive technique
- Longer hospitalization than minimally invasive techniques
- More complications
- Lesser acceptability by young patients

TRANS-CERVICAL THYMECTOMY





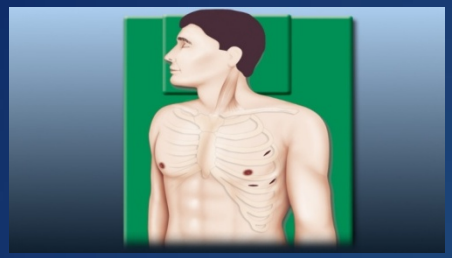
ADVANTAGES

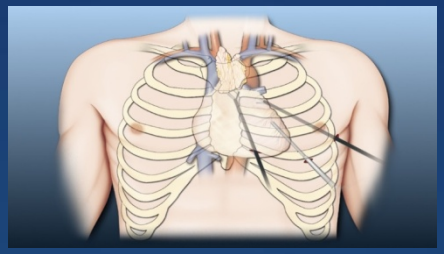
- Minimally invasive technique
- Short hospitalization and low costs
- Good cosmetic results
- Easily accepted by young patients
- Few complications, low pain and early improved pulmonary function

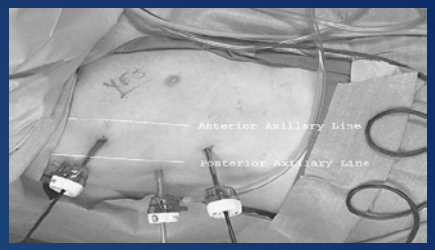
DISADVANTAGES

- Small surgical access
- Crowding of surgical instruments
- Impossibility to perform an extended thymectomy (thymus plus perithymic tissues)

THORACOSCOPIC THYMECTOMY







ADVANTAGES

- Minimally invasive technique
- Short hospitalization and low costs
- Optimal cosmetic results
- Easily accepted by young patients
- Minimal thoracic trauma and early improved lung function

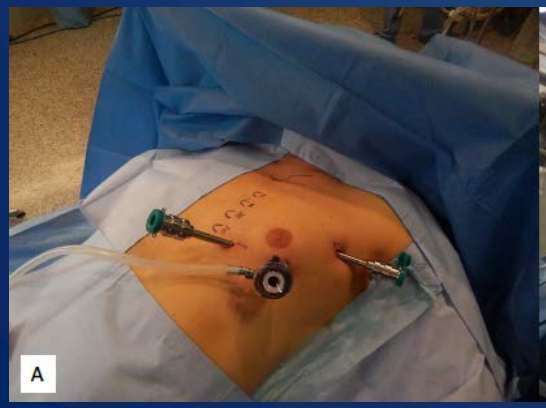
DISADVANTAGES

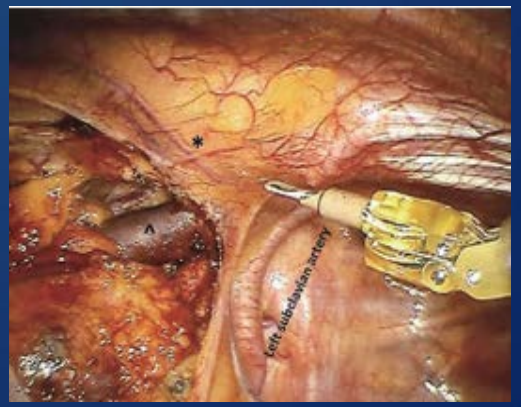
- 2-D view of the operative field
- Arms do not articulate making difficult the dissection of the neck and the access to the contralateral mediastinum
- Needs in some cases, of a cervical incision
- Impossibility to perform an extended thymectomy (thymus plus perithymic tissues)

Robotic Thymectomy

- Enhanced visualization (intuitive 3-D view)
- High dexterity of surgical instruments (360° of rotation and 7 degrees of freedom in the articulated movements)
- Tremor filtering

- Safe and comfortable dissection of vascular and nervous structures
- Better dissection in remote, fixed and difficult to reach areas of the neck and mediastinum





DISADVANTAGES OF ROBOTIC THORACOSCOPIC THYMECTOMY

Initial high costs

Early increased operative time (learning curve)

Absence of tactile feedback

Comparison of robotic and nonrobotic thoracoscopic thymectomy: A cohort study

Jens C. Rückert, MD, PhD, Marc Swierzy, MD, and Mahmoud Ismail, MD

(J Thorac Cardiovasc Surg 2011;141:673-7)

Results: There were no differences in age distribution and severity of myasthenia gravis. The dominant histologic finding was follicular hyperplasia of the thymus in both groups with a significantly higher percentage in the thoracoscopic thymectomy series (68% vs 45%, $P < .001$). After a follow-up of 42 months, the cumulative complete remission rate of myasthenia gravis for robotic and nonrobotic thymectomy was 39.25% and 20.3% ($P = .01$), respectively.

Conclusions: There is an improved outcome for myasthenia gravis after robotic thoracoscopic thymectomy compared with thoracoscopic thymectomy.

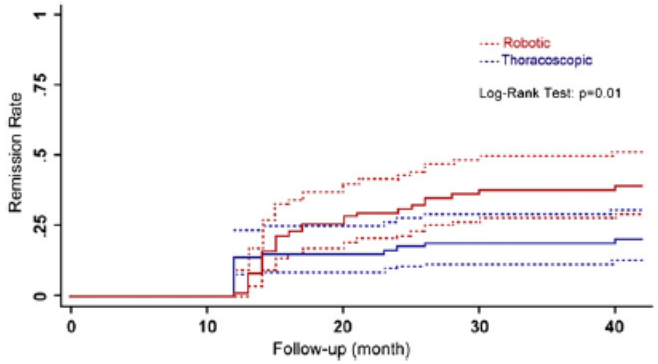


FIGURE 2. Cumulative complete remission rates of myasthenia gravis for robotic and nonrobotic thoracoscopic cohort groups analyzed by the Kaplan–Meier method.

It is difficult to compare the outcomes of the different operative techniques (confounding factors influenced both the controlled and the uncontrolled studies) but outcomes are probably similar (class iii evidence).

(Meyer et al., 2009)

IDEALLY, THE LESS INVASIVE SURGICAL TECHNIQUES ARE DESIRABLE, ASSUMING THE RESULTS ARE EQUIVALENT

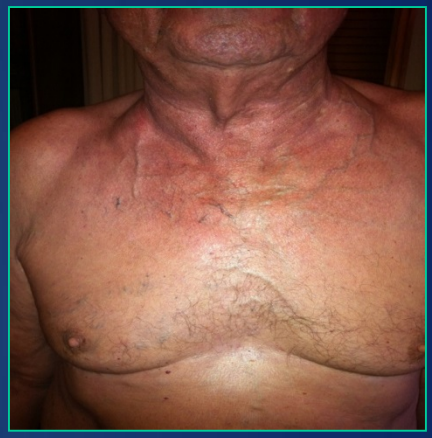
Thymectomy in myasthenic patients

Thymectomy for oncological reasons

THYMOMA

SIGNS AND SYMPTOMS:

Asymptomatic in 30-50% (incindental finding in ChestXR)



Local symptoms and signs:

- anterior thoracic pain (tumor necrosis);
- cough;
- dyspnoea and/or impaired swallowing;
- superior Vena Cava Syndrome;
- supraventricular tachyarrhythmias;
- dyspnoea (← diaphragmatic palsy← phrenic nerve involvement);
- dysphonia (← recurrent nerve involvement).

Systemic signs:

- fever;
- weight loss;
- **Paraneoplastic syndromes**

REVIEW

Thymic Tumors

Frank C. Detterbeck, MD, and Alden M. Parsons, MD

Department of Surgery, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Thymic tumors include thymic carcinoma, which exhibit aggressive behavior, and thymomas, which manifest a more indolent course. Complete resection is the mainstay of treatment, and there appears to be little benefit to partial resection. Postoperative radiotherapy may be useful in incompletely resected patients. Preoperative chemotherapy appears to increase the rate of complete resection and survival of patients with a stage III or IVa thymoma and should strongly be considered in such cases.

(Ann Thorac Surg 2004;77:1860–9)

Because of the indolent course and sporadic occurrence of tumors of the thymus, clinical management has been based largely on observations in only a few patients from single-institution experiences. A larger body of literature now provides further insight into the biologic behavior of thymomas, and suggests that many previously held beliefs are not substantiated by data. New concepts regarding the clinical approach to thymic tumors are emerging as a result of a more evidence-based approach. This article reviews existing data and trends in the management of thymic tumors.

have adopted the Groupe d'Étude des Tumeurs Thymiques system [3], which is similar to the Masaoka system but also includes the completeness of resection. Although this may be of prognostic value, it does not lend itself to clinical staging of patients before treatment to select the optimal approach.

Histologic Classification

One can distinguish three groups of thymic tumors: (1) those with no cytologic features of malignancy [4–6]; (2) an intermediate group, sometimes called well-differentiated thymic carcinoma (WDTC), that have the

THYMOMA-THYMIC CARCINOMA

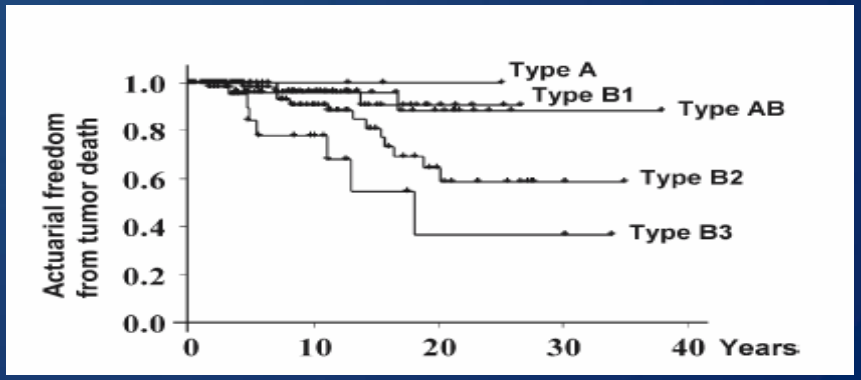
WHO CLASSIFICATION

Table 1. World Health Organization Histologic Classification

A	A tumor composed of a population of neoplastic thymic epithelial cells having spindle/oval shape, lacking nuclear atypia, and accompanied by few or no nonneoplastic lymphocytes.
AB	A tumor in which foci having the features of type A thymoma are admixed with foci rich in lymphocytes.
B1	A tumor that resembles the normal functional thymus in that it combines large expanses having an appearance practically indistinguishable from normal thymic cortex with areas resembling thymic medulla.
B2	A tumor in which the neoplastic epithelial component appears as scattered plump cells with vesicular nuclei and distinct nucleoli among a heavy population of lymphocytes. Perivascular spaces are common and sometimes very prominent. A perivascular arrangement of tumor cells resulting in a palisading effect may be seen.
B3	A type of thymoma predominantly composed of epithelial cells having a round or polygonal shape and exhibiting no or mild atypia. They are admixed with a minor component of lymphocytes, resulting in a sheetlike growth of the neoplastic epithelial cells.
C	A thymic tumor exhibiting clear-cut cytologic stypia and a set of cytoarchitectural features no longer specific to the thymus, but rather analogous to those seen in carcinomas of other organs. Type C thymomas lack immature lymphocytes; whatever lymphocytes may be present are mature and usually admixed with plasma cells.

The WHO classification system

WHO Type	Old terminology [2]	Biological behaviour
A	Medullary thymoma	indolent
AB	Mixed type	
B1	Predominantly cortical	
B2	Cortical	
B3	Well-differentiated thymic carcinoma	
C	Squamous cell carcinoma Undifferentiated carcinoma Sarcomatoid carcinoma Lymphoepithelioma-like carcinoma	aggressive



Masaoka Staging System

Table 1 **Modified Masaoka Clinical Staging of Thymoma**

Masaoka Stage	Diagnostic Criteria
Stage I	Macroscopically and microscopically completely encapsulated
Stage II	A. Microscopic transcapsular invasion B. Macroscopic invasion into surrounding fatty tissue or grossly adherent to but not through mediastinal pleura or pericardium
Stage III	Macroscopic invasion into neighboring organs (i.e. pericardium, great vessels, lung) A. Without invasion of great vessels B. With invasion of great vessels
StageIV	A. Pleural or pericardial dissemination C. Lymphogenous or hematogenous metastasis

Koga et al: Pathol.Int. 1994; 44: 359-367

SURGICAL PRINCIPLES

- Exploration of entire mediastinum.
- Complete resection of tumor and thymus (including cervical horns) with *en-bloc* resection of any involved structures.
  - Pleura, pericardium, lung, SVC, etc.
- Resection of pleural implants, if possible.
- If involved, resection of one phrenic nerve is usually tolerated.
  - Diaphragm plication recommended.
- Areas of any residual disease should be marked with radio-opaque clips

Port and Ginsberg, Chest Surg Clin N Amer 2001; 11: 421-37

RADICALITY

MOST IMPORTANT PROGNOSTIC FACTOR

R0 RESECTION MAY BE ACHIEVED IN 100% OF STAGE I, 85% OF STAGE II, 47% OF STAGE III AND 26% OF STAGE IVa.

Table 2. Survival According to Extent of Resection

	Rea et al [26]	Zhu et al [49]	Nakagawa et al [30]	Regnard et al [47]	Kim et al [23]	Okumura et al [25]
Surgery	132	175	130	307	108	273
Complete resection	81.8%	72.0%	95.0%	84.7%	81.5%	94.5%
5-yr SR	82.5%	88.4%	96.0%	—	c. 95%	c. 98%
10-yr SR	71.0%	—	94.0%	76.0%	c. 85%	c. 95%
Incomplete resection	9.1%	13.7%	5.0%	9.8%	18.5%	3.30%
5-yr SR	16.0%	43.2%	33.0%	—	c. 55%	—
10-yr SR	9.0%	—	33.0%	28.0%	c. 35%	c. 60%
Biopsy/gross disease	9.1%	14.4%	—	5.5%	—	1.6%
5-yr SR	33.0%	73.5%	—	—	—	—

SR = survival rate.

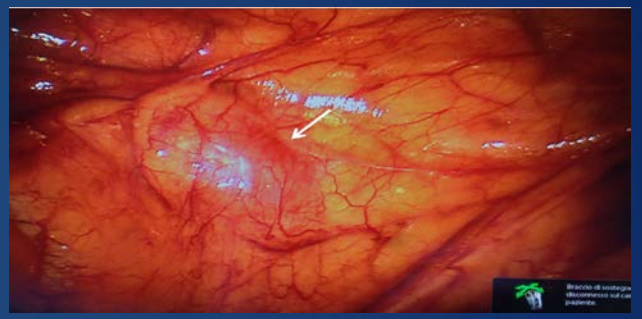
SURVIVAL AFTER R0 RESECTION IS SIGNIFICANTLY HIGHER THAN R1/2 OR BIOPSY. NOT CLEAR YET IF DEBULKING IS SUPERIOR TO BIOPSY (Detterbeck, 2004)

MASAOKA EARLY STAGES (I-II)

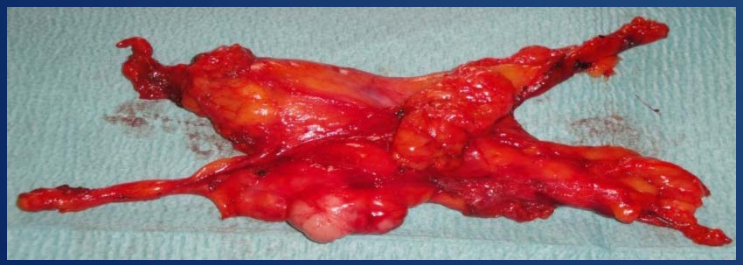
- SURGERY IS THE CORNERSTONE OF TREATMENT
- CONTROVERSIAL ISSUES:
  - ROLE OF MINIMALLY INVASIVE THYMECTOMY
  - THYMECTOMY VS THYMOMECTOMY
  - ROLE OF ADJUVANT RT FOR STAGE II

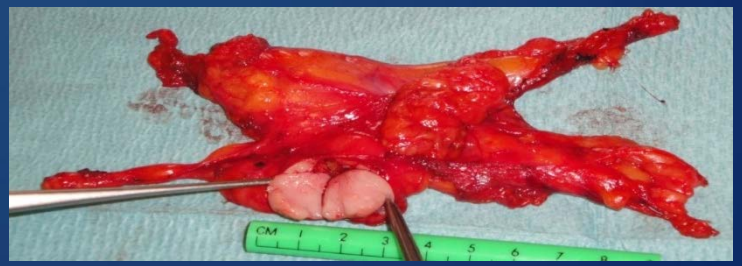
SURGICAL TECHNIQUE

- **intraoperative evaluation** (no invasion of contiguous structures, no macroscopic gross transcapsular invasion)



- **"no-touch" technique**
- **"en-bloc" resection** of thymus and perithymic fat tissue (plus mediastinal fat tissue for MG pts)

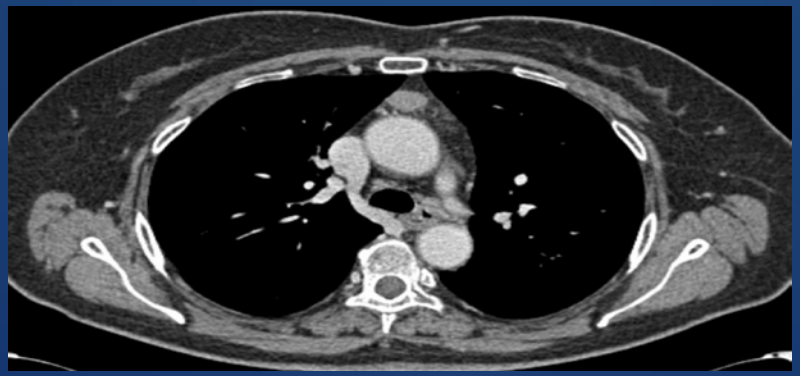




Toker A, Sonett J, Zielinski M, Rea F, Tomulescu V, Detterbeck FC. Standard terms, definitions, and policies for minimally invasive resection of thymoma. J Thorac Oncol 2011; 6:S1739-42.

Preferred radiological characteristics to be eligible for thoracoscopic/robotic thymectomy

- location of the tumor in the anterior mediastinum
- tumor encapsulation
- dimension < 3 cm
- a distinct fat plane between the tumor and surrounding structures
- no mass compression effect
- existence of residual normal appearing thymic tissue
- unilateral tumor predominance



CHENG YJ - SURG TODAY 2007

Table 1 Review of the published studies on thoracoscopic and robotic thymectomy for thymoma

Author	Patients (N)	SA	Masaoka stage I/II	TS (cm)	5-year survival (%)	FU (months)	RR (%)	OC (%)	OT (min)	POS (days)
Roviaro *et al*. (2)	22	uVATS	22	–	–	–	4.5	4.5	75*	6*
Cheng *et al*. (7)	44	uVATS	27/17	7.7*	100	34.6*	0	0	194*	7.6*
Odaka *et al*. (8)	22	uVATS	–	–	–	21.6*	0	0	194*	4.6*
Agasthian *et al*. (9)	50	uVATS	25/25	5*	100	58*	2	0	150*	5*
Pennathur *et al*. (20)	18	bVATS	5/13	3.5*	100	27**	0	0	–	2.9*
Takeo *et al*. (21)	34	bVATS	15/19	5.2*	100	65*	2.8	0	219*	10.5*
Kimura *et al*. (22)	45	uVATS	41/4	4.8*	100	–	6.7	0	197*	14*
Liu *et al*. (23)	76	uVATS	57/19	9.2*	100	61.9*	2.6	1.3	141.7*	7.1*
Ye *et al*. (24)	125	uVATS	80/45	3.2*	–	41**	0.8	3.2	170**	8**
Sakamaki *et al*. (25)	71	uVATS	40/31	3.5**	97	48**	1.4	5.6	–	–
Mussi *et al*. (26)	13	robotic	7/6	3.3*	100	14.5**	0	7.7	139*	4*
Marulli *et al*. (27)	79	robotic	30/49	3.7*	90	51.7*	1.3	1.3	165*	4.4*
Ye *et al*. (28)	23	robotic	21/2	2.9*	100	16.9*	0	0	97*	3.7*
Keijzers *et al*. (29)	37	robotic	20/13	5.1*	100	36**	2.7	13.5	149*	3**
Present series	134	robotic	46/71	4.4*	97	48*	0.7	8.9	146*	4**

Featured Article

Multi-institutional European experience of robotic thymectomy for thymoma

Giuseppe Marulli[1], Jos Maessen[2], Franca Melfi[3], Thomas A. Schmid[4], Marlies Keijzers[2], Olivia Fanucchi[3], Florian Augustin[4], Giovanni M. Comacchio[1], Alfredo Mussi[1], Monique Hochstenbag[2], Federico Rea[1]

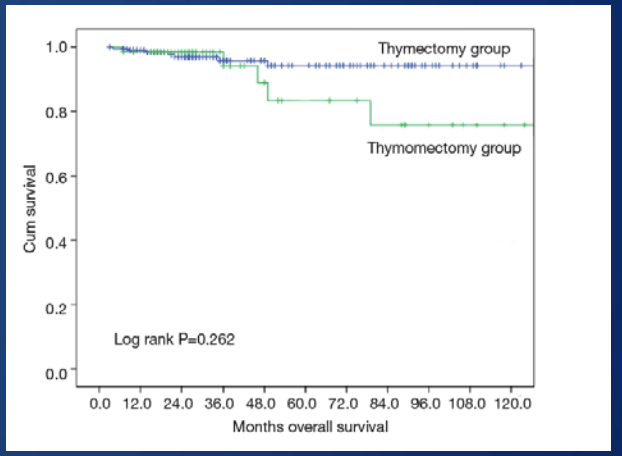
Ann Cardiothorac Surg 2016;5(1):18-25

GOOD RESULTS BUT LACK OF LONG TERM FOLLOW-UP!!

Thymectomy vs Thymomectomy

Thymectomy versus tumor resection for early-stage thymic malignancies: a Chinese Alliance for Research in Thymomas retrospective database analysis

Journal of Thoracic Disease, Vol 8, No 4 April 2016



- Improvement rate of MG higher after thymectomy than thymomectomy
- 10-yrs OR and RR similar in the two groups
- In pts wth Masaoka 2 thymoma, reccurrence was significantly less after thymectomy than thymomectomy (2,9% vs 14,5%, p=0,001)

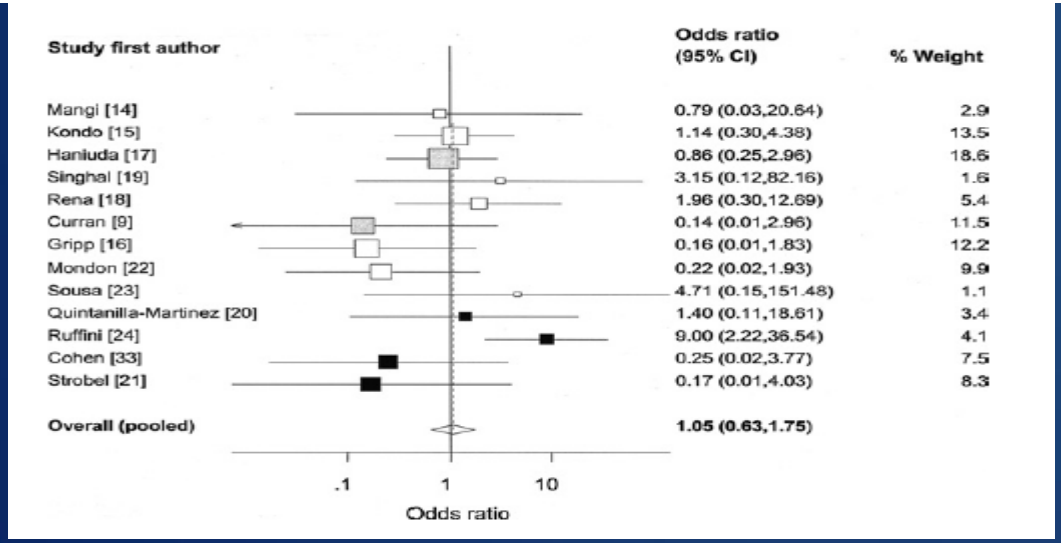
Conolusions: Thymectomy, instead of tumor resection alone, should still be recommended as the surgical standard for thymic malignancies, especially for stage II tumors and those with concomitant MG.

Ajuvant radiotherapy for Stage II Thymoma

Adjuvant Radiotherapy for Thymic Epithelial Tumors: A Systematic Review and Meta-Analysis

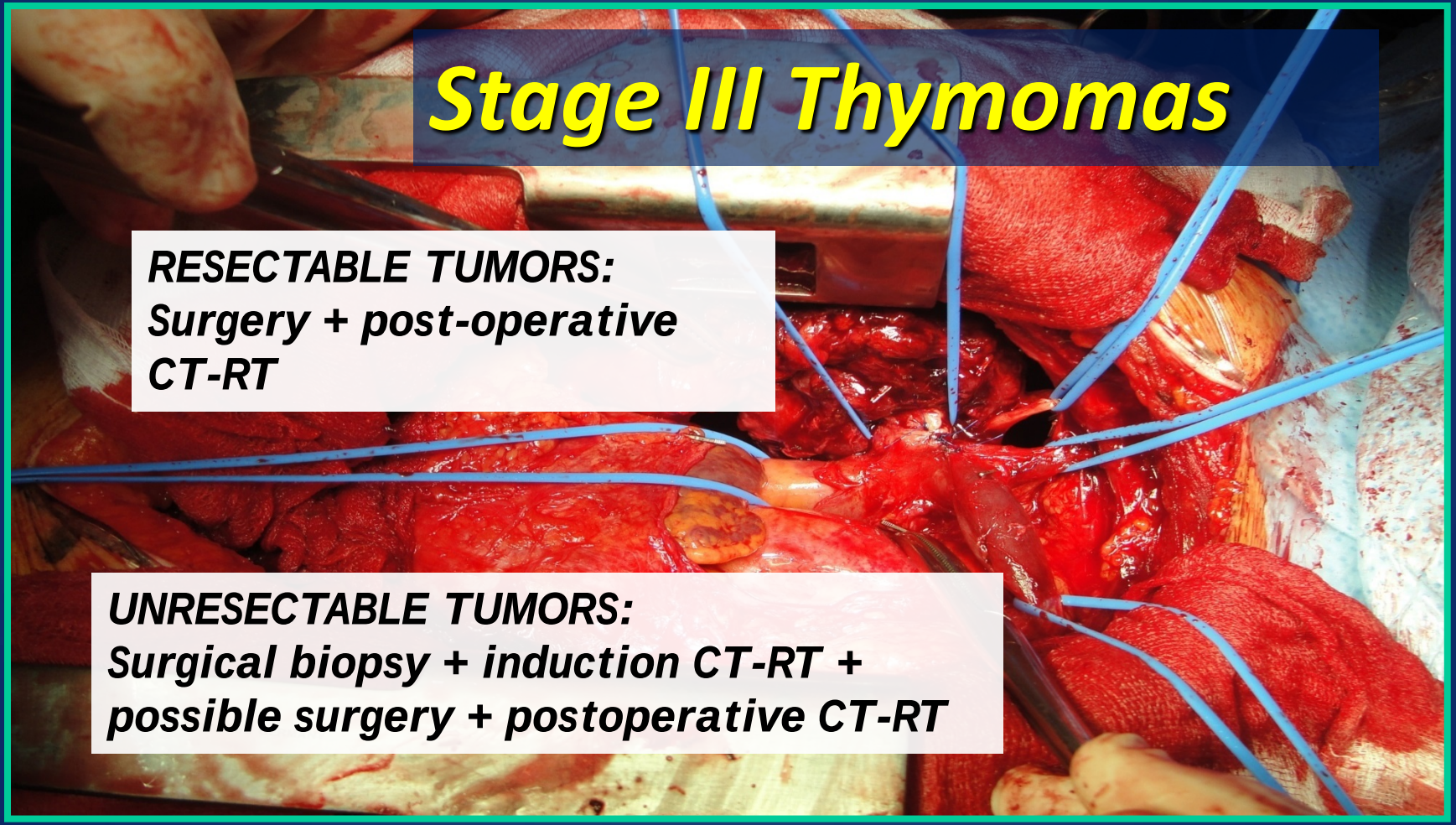
Robert J. Korst, MD, Amanda L. Kansler, MPH, Paul J. Christos, MPH, MS, and Sanjay Mandal, MD

Daniel and Gloria Blumenthal Cancer Center, Paramus, Division of Thoracic Surgery, Department of Surgery, Valley Hospital/ Valley Health System, Ridgewood, New Jersey; and Division of Biostatistics and Epidemiology, Department of Public Health, Weill Medical College of Cornell University, New York, New York



(Ann Thorac Surg 2009;87:1641–7)

NO CLEAR EVIDENCE OF BENEFIT YET!



Stage III Thymomas

RESECTABLE TUMORS:
Surgery + post-operative CT-RT

UNRESECTABLE TUMORS:
Surgical biopsy + induction CT-RT + possible surgery + postoperative CT-RT

MASAOKA STAGE III

RADICALITY IS THE MOST IMPORTANT PROGNOSTIC FACTOR IN THYMIC TUMORS AND SHOULD BE THE AIM OF SURGICAL RESECTION

❖ TYPE OF INVASION

- ➢ PERICARDIUM/ NERVES
- ➢ LUNG
- ➢ SVC/ ANONIMOUS VEINS
- ➢ PULMONARY ARTERY
- ➢ AORTA/ SUPRAORTIC BRANCHES
- ➢ TRACHEA
- ➢ CHEST WALL

RADICALITY

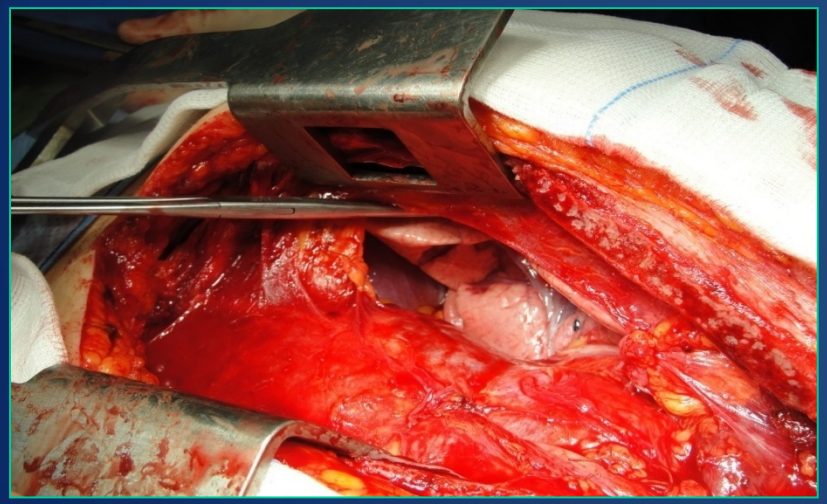
❖ INDUCTION TREATMENT

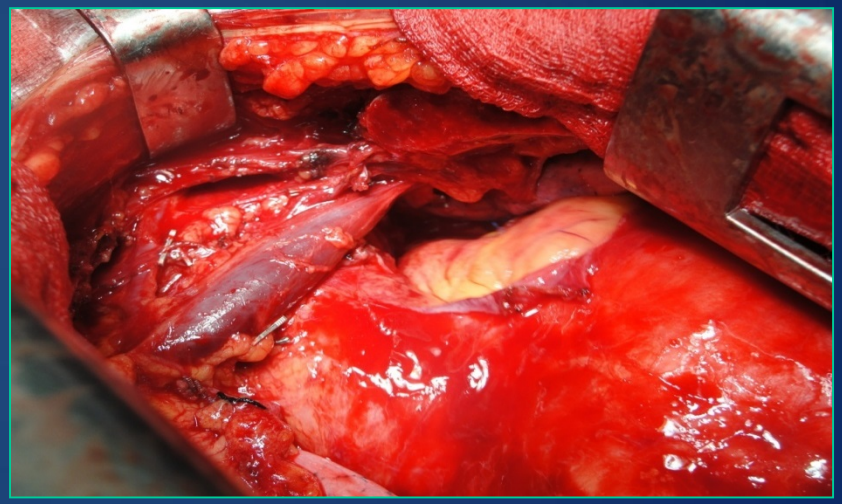
❖ SURGICAL ACCESS

❖ TYPE OF VASCULAR RESECTION AND RECONSTRUCTION

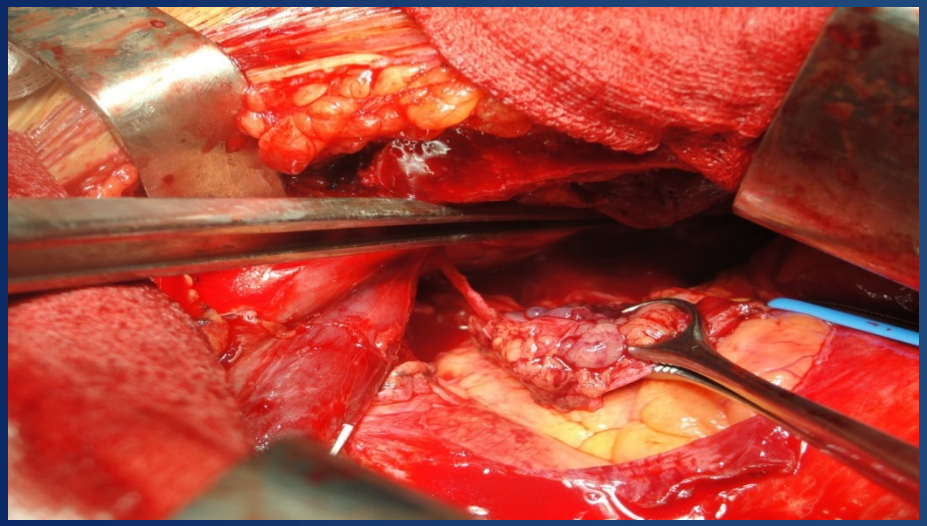
❖ CIRCULATORY SUPPORT AND MANAGEMENT

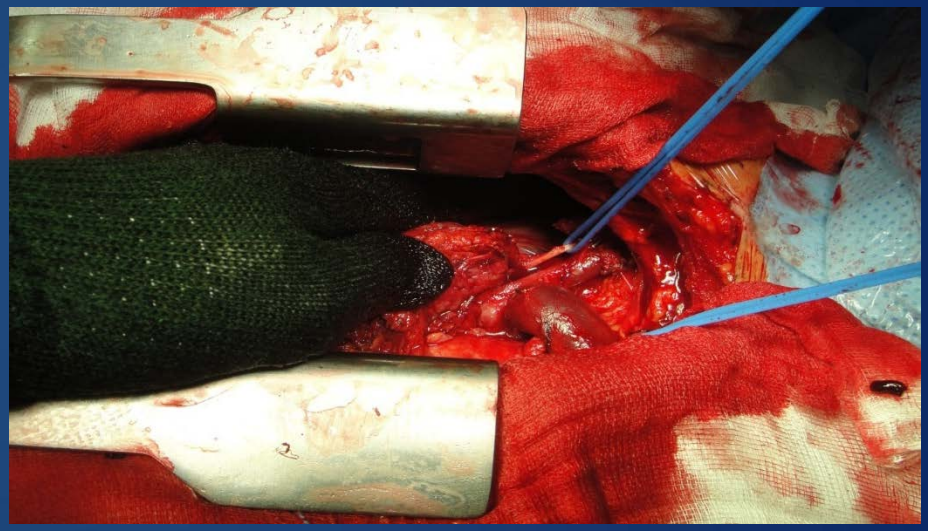
Pericardium and mediastinal pleura are easily resected, without the need of any replacement





Phrenic nerve can be resected
en bloc with the thymoma
Care should be done in MG patients






Wedge resections are the commonest procedures; sometimes lobectomy is also performed

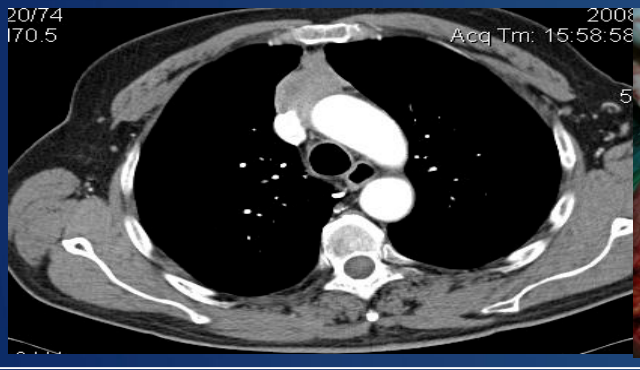
VASCULAR INVASION

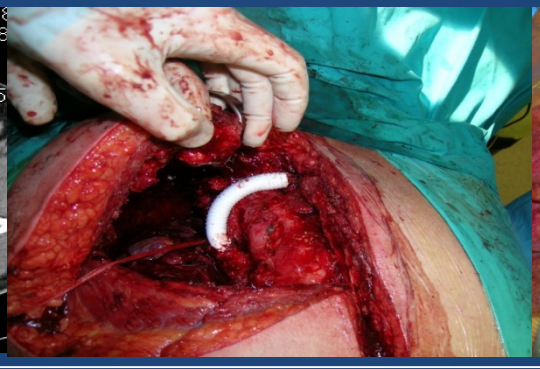
NEGATIVE PROGNOSTIC FACTOR

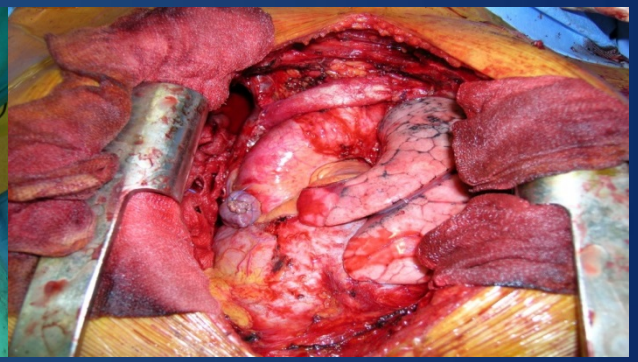
↓ **R0 RESECTION**

↑ **LOCAL RECURRENCE**

↑ **DISTANT M1**







Results of surgical treatment of thymomas with special reference to the involved organs.

CONCLUSION: Although the Masaoka staging system is a valuable prognostic factor, **the category of stage III is heterogeneous and consists of 2 groups with distinct prognoses depending on involvement of the great vessels.**

J Thorac Cardiovasc Surg. 1999 Mar;117(3):605-13.

ELSEVIER

European Journal of Cardio-thoracic Surgery 39 (2011) e1—e7

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Surgical treatment of stage III thymic tumors: a multi-institutional review from four Italian centers☆

Giuseppe Marulli[a,*], Marco Lucchi[b], Stefano Margaritora[c], Giuseppe Cardillo[d], Alfredo Mussi[b], Giacomo Cusumano[c], Francesco Carleo[d], Federico Rea[a]

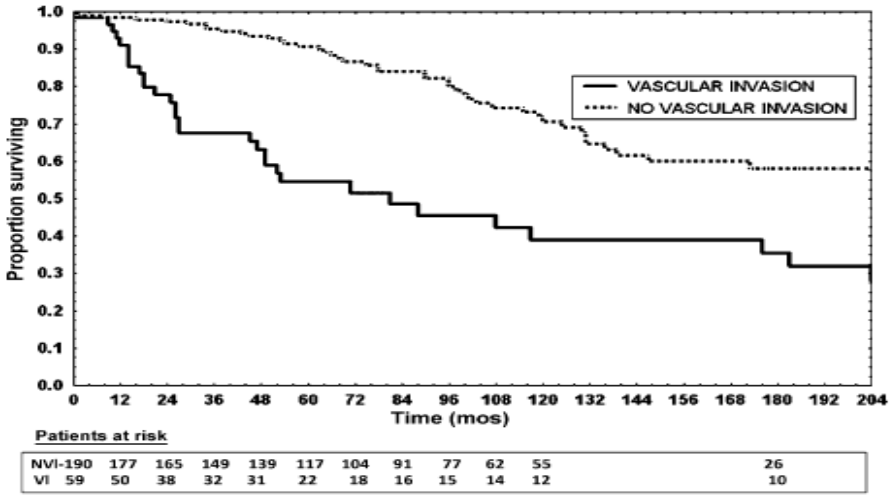


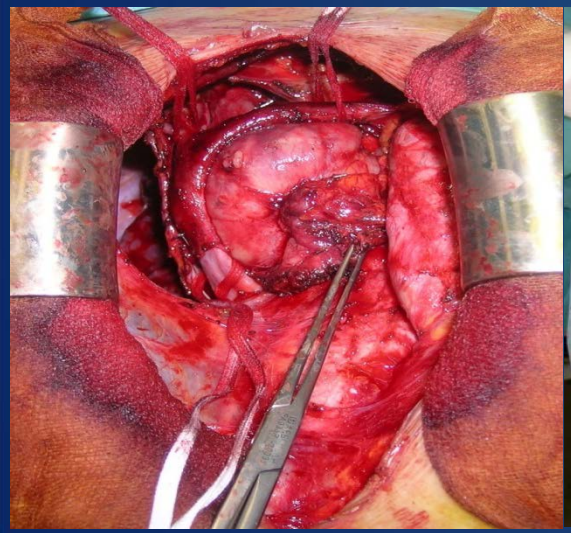
Table 4. Site of recurrences on the basis of involved organs.

Involved organs			Recurrence (total)	Site of recurrence (*n*)
V	L	P		
+	—	—	4 (12)	Med (1) — Dis (3)
—	+	—	16 (70)	Pl (8) — Dis (4) — Pl + L (2) Med + Dis + Pl (1) — Dis + Pl (1)
—	—	+	14 (61)	Pl (7) — Dis (4) — Med (2) — L (1)
+	+	—	2 (3)	Pl (1) — Dis (1)
+	—	+	0 (2)	
—	+	+	7 (28)	Pl (3) — Dis (1) — Med (1) Pl + L (1) — PH + Dis (1)
+	+	+	0 (5)	
Total			43 (181)	

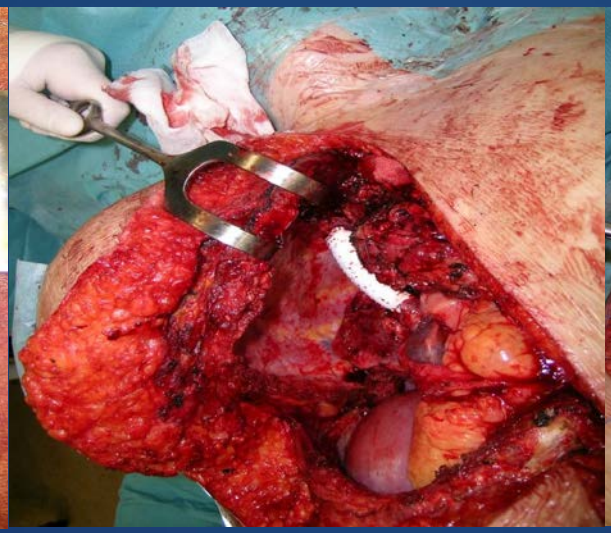
V: great vessels; L: lung; P: pericardium; Med: mediastinum; Dis: distant; and Pl: pleural.

SURGICAL ACCESS

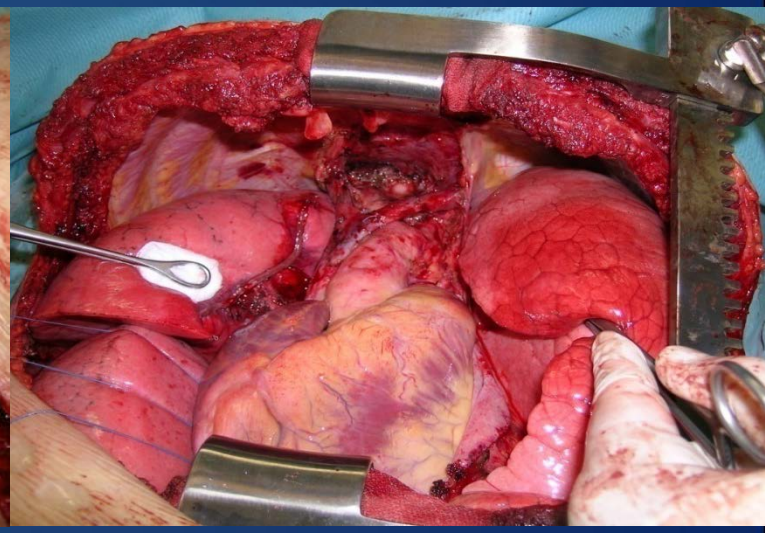
MEDIAN STERNOTOMY



HEMICLAMSHELL



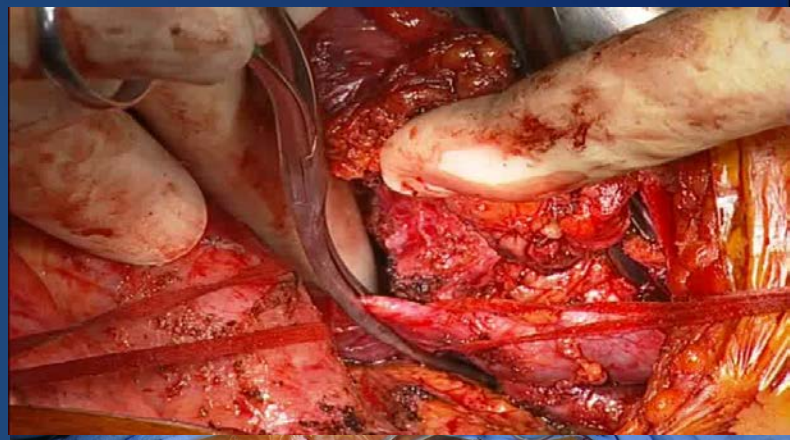
CLAMSHELL

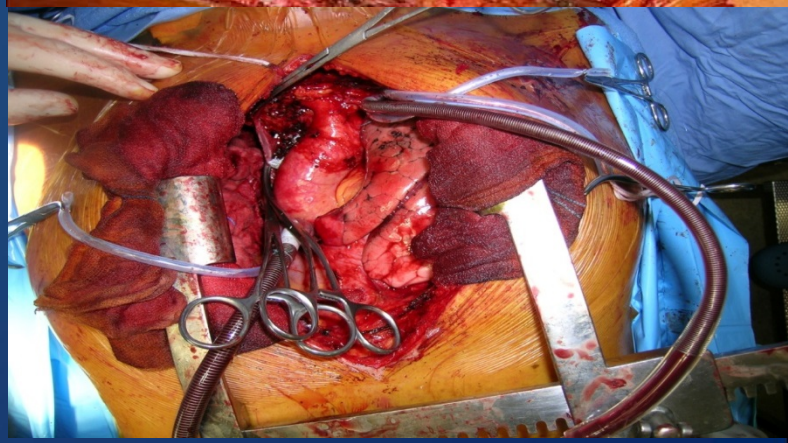


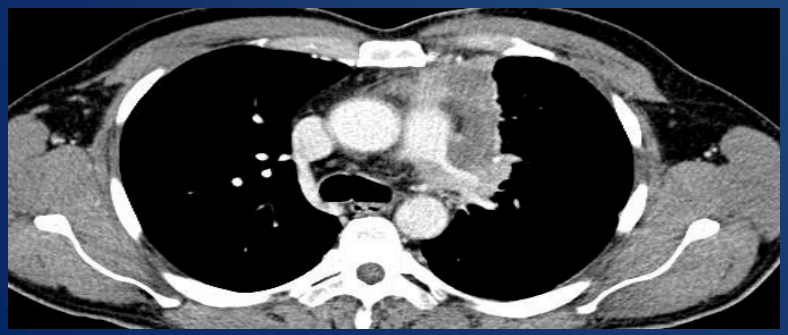
SUPERIOR VENA CAVA SYSTEM RECONSTRUCTION

Options to allow reconstruction

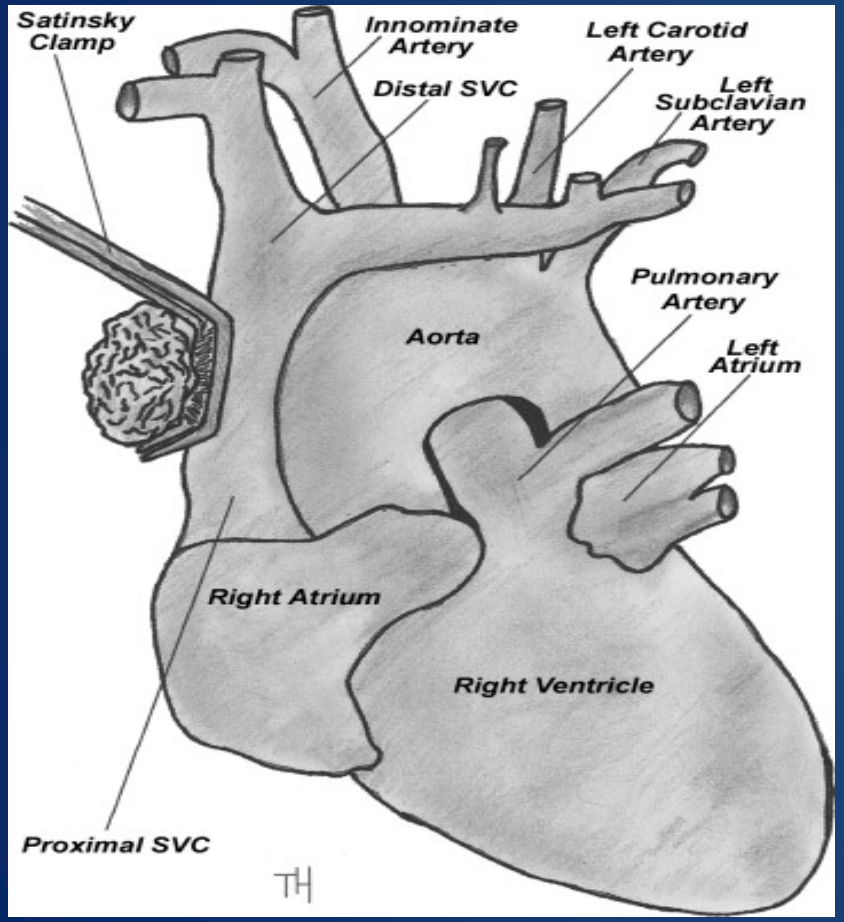
- DIRECT SVC CROSSCLAMPING
- VASCULAR SHUNTS
- CARDIOPULMONARY BYPASS

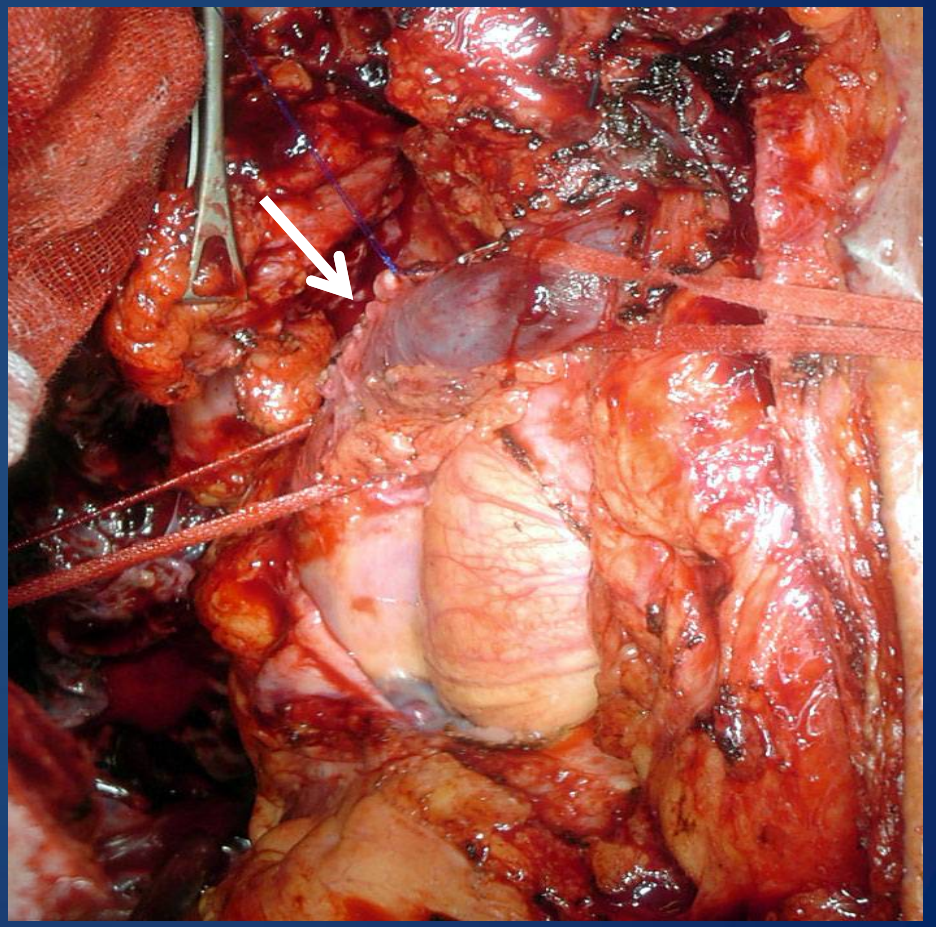




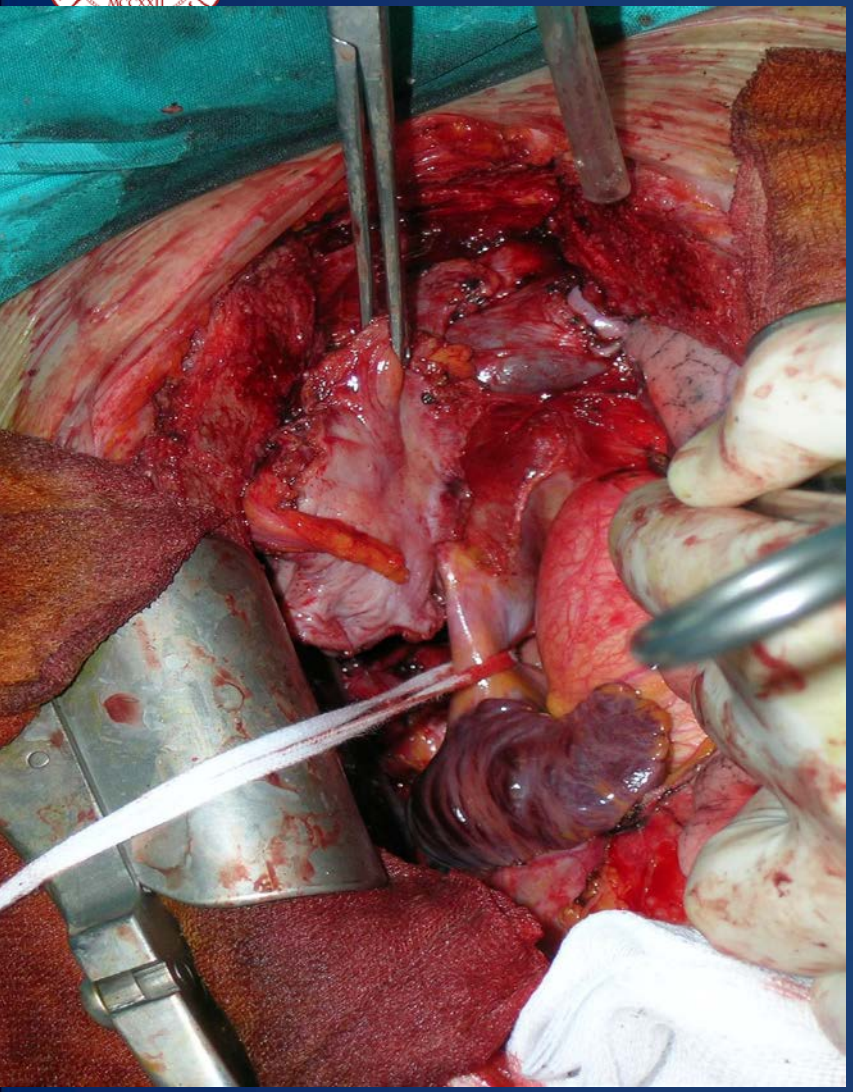


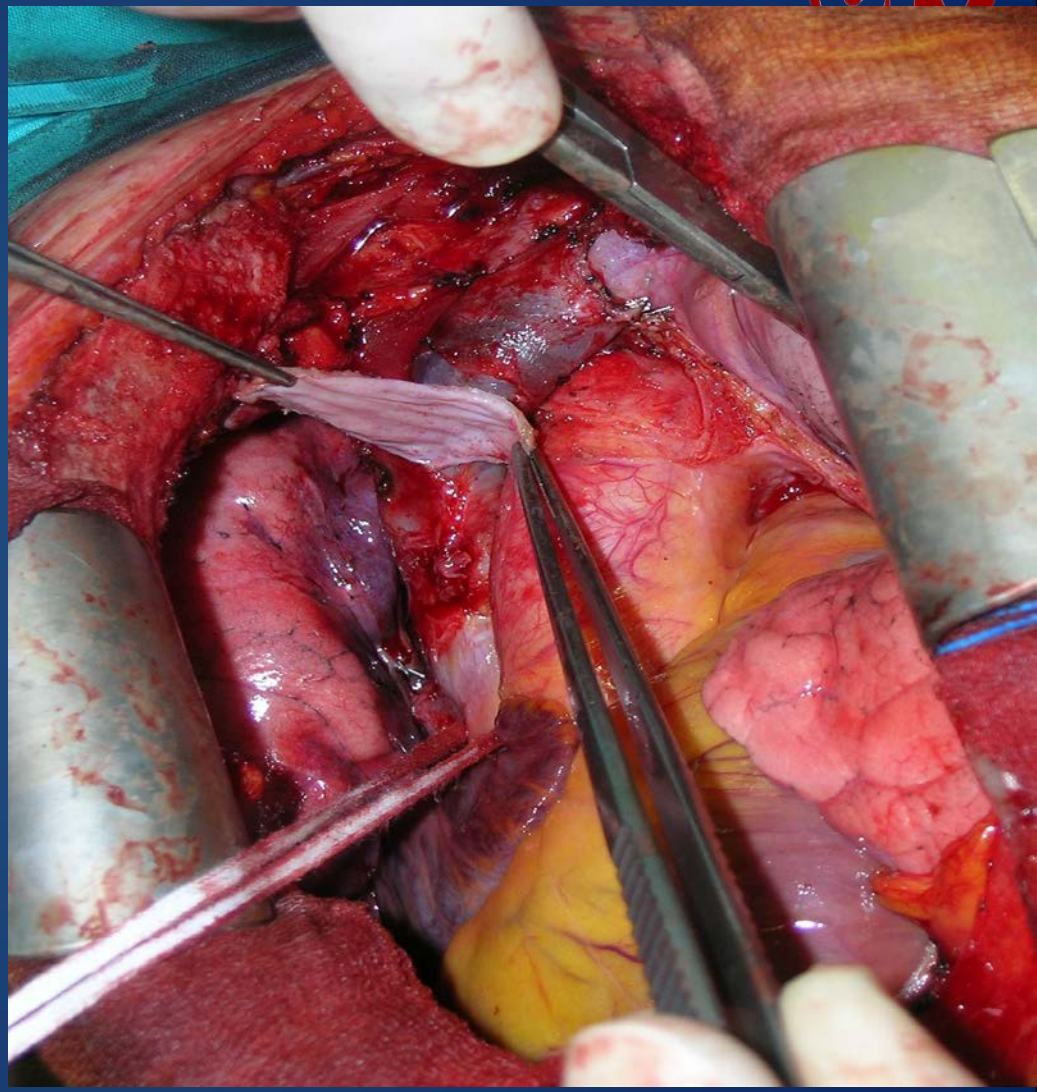
LONGITUDINAL SUTURE OF SVC

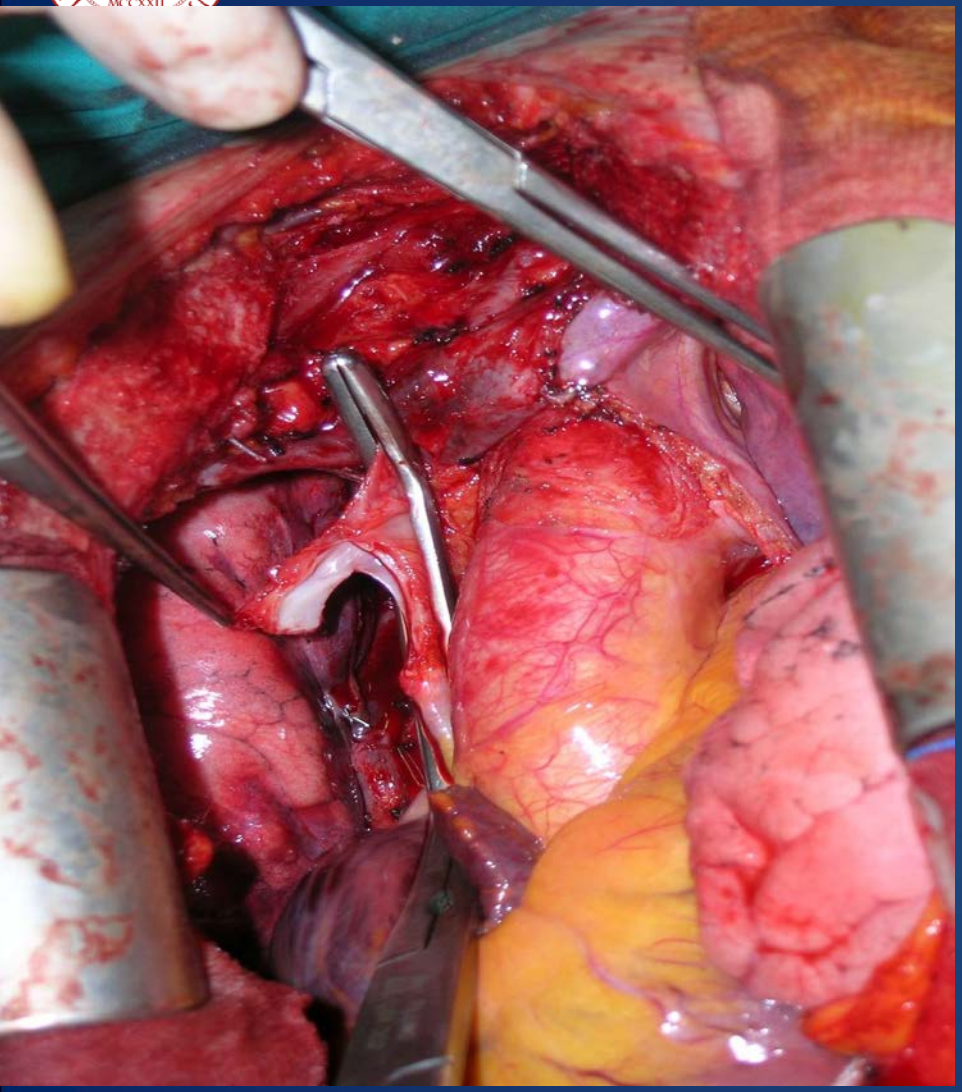


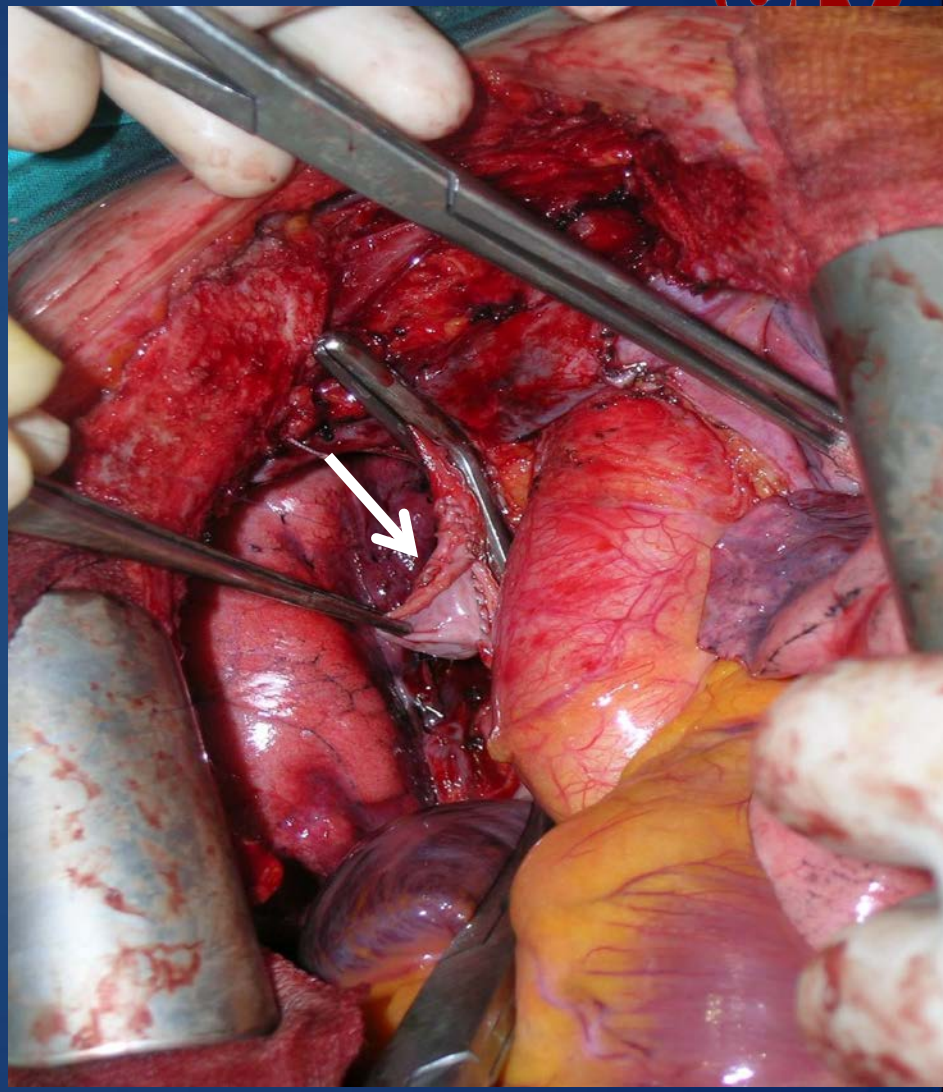


SVC RECONSTRUCTION WITH PERICARDIAL PATCH

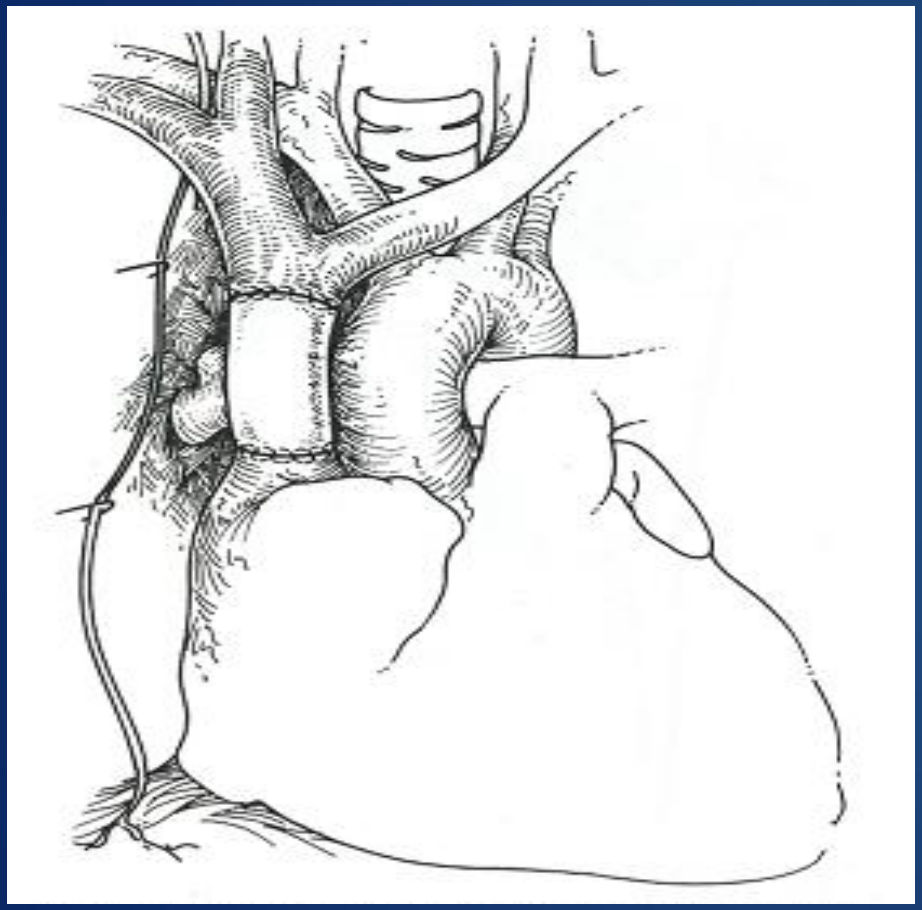


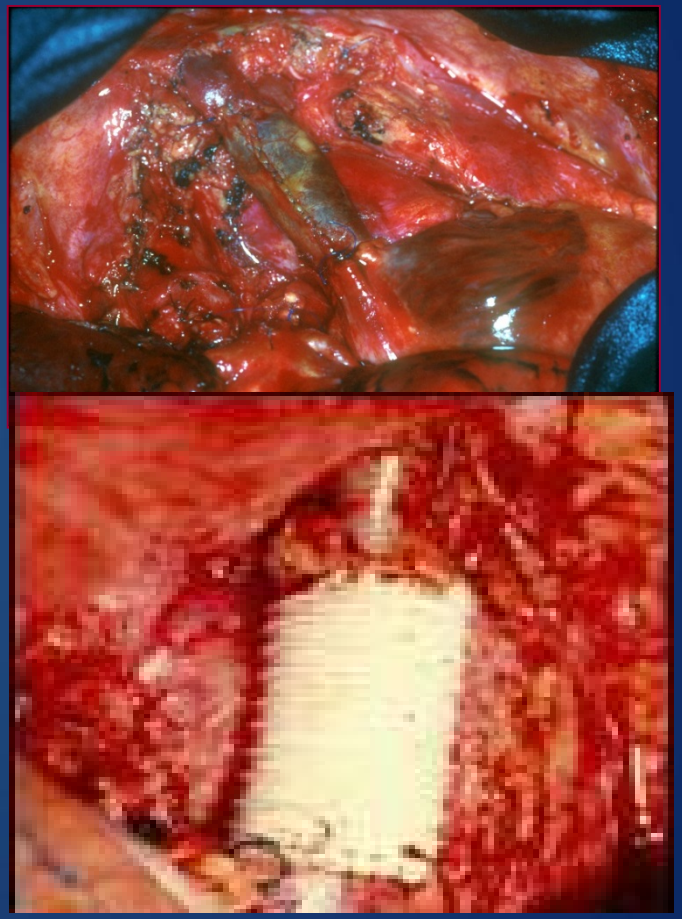




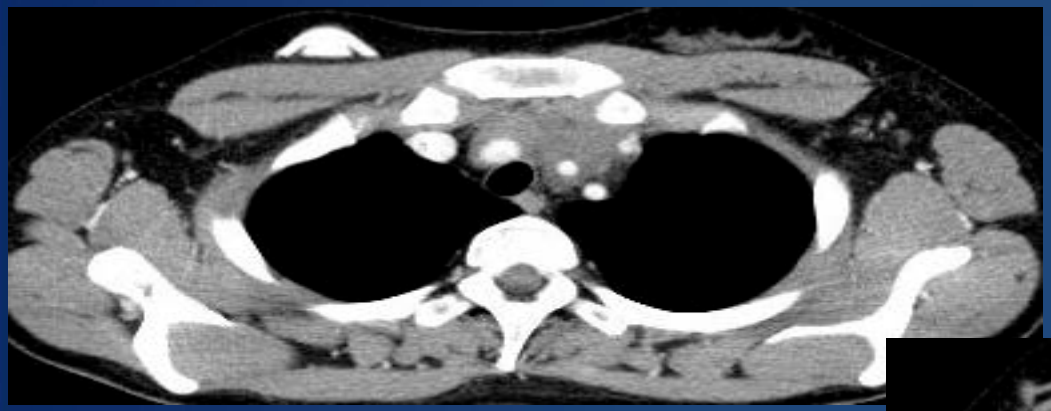


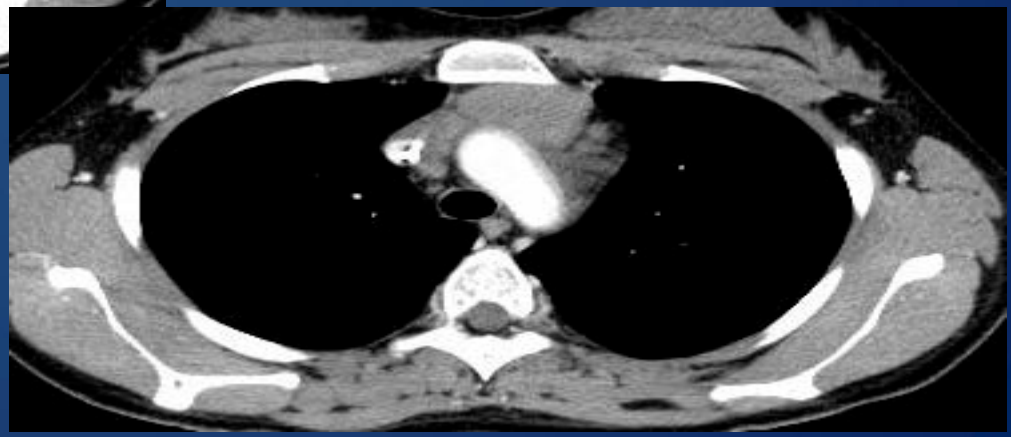
TRUNCULAR REVASCULARIZATION OF SVC



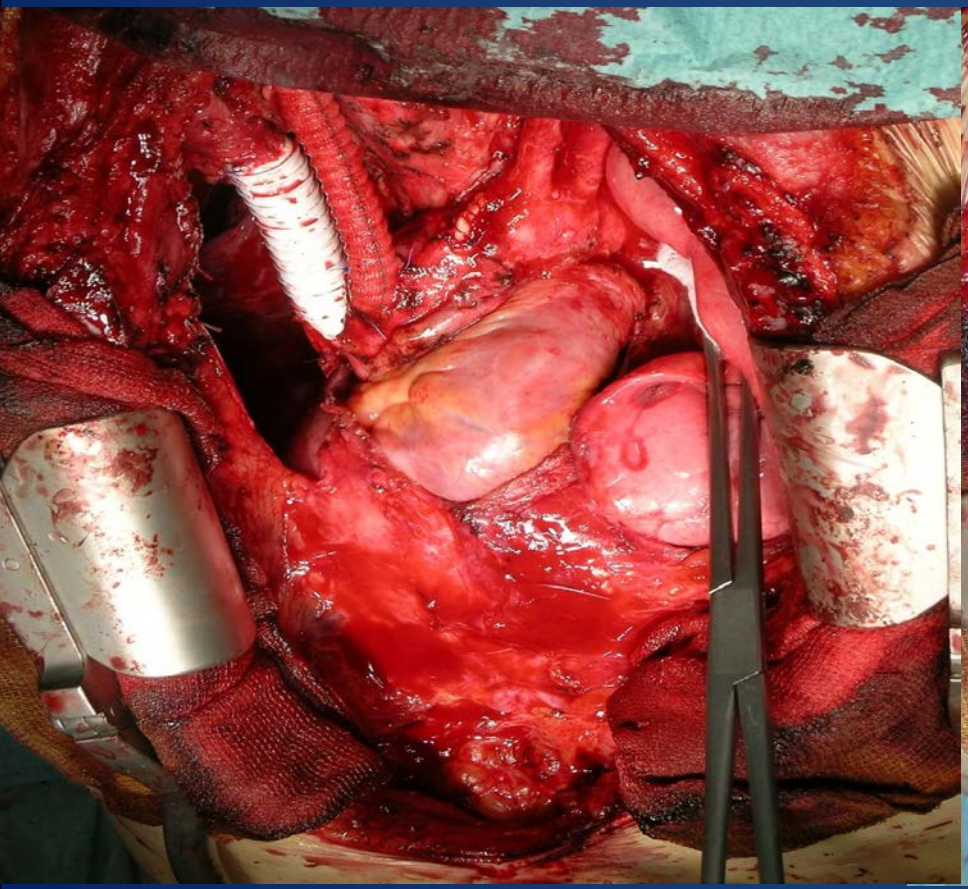


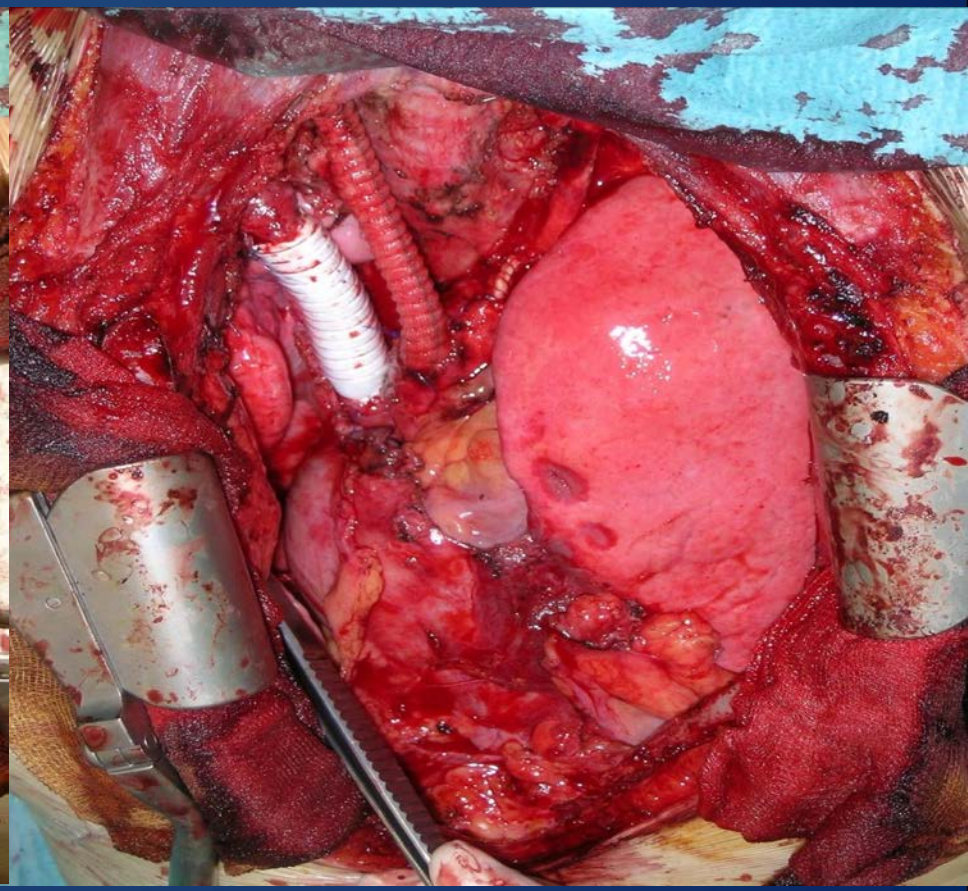
SVC AND RIGHT INNOMINATE ARTERY INVOLVEMENT



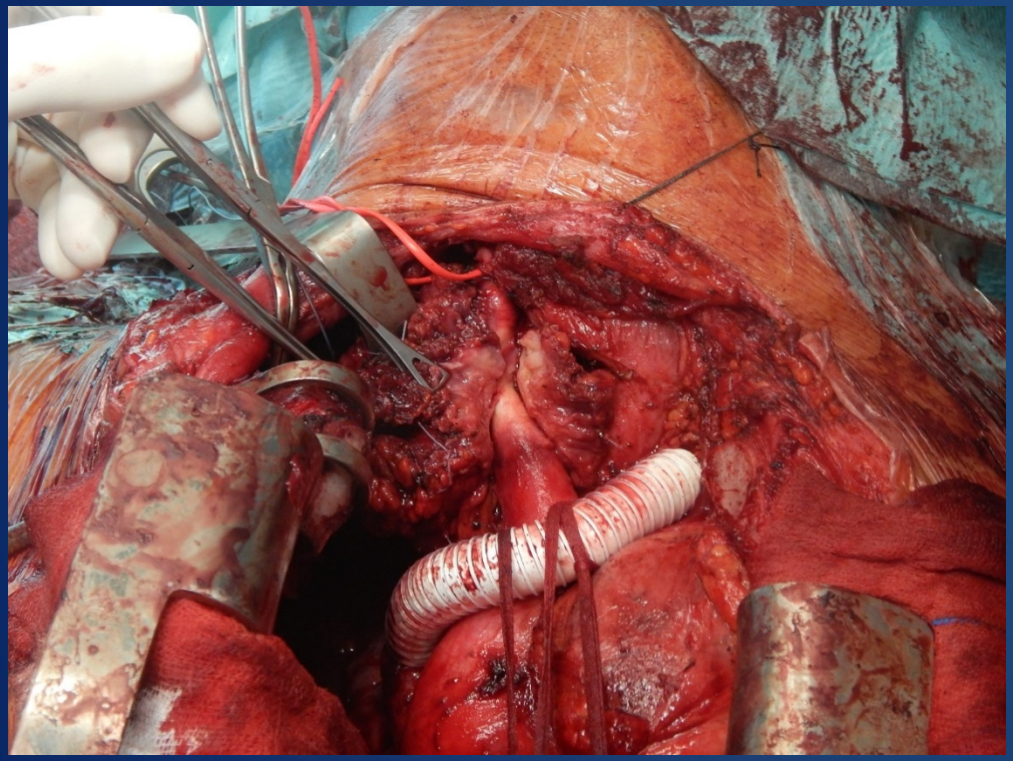


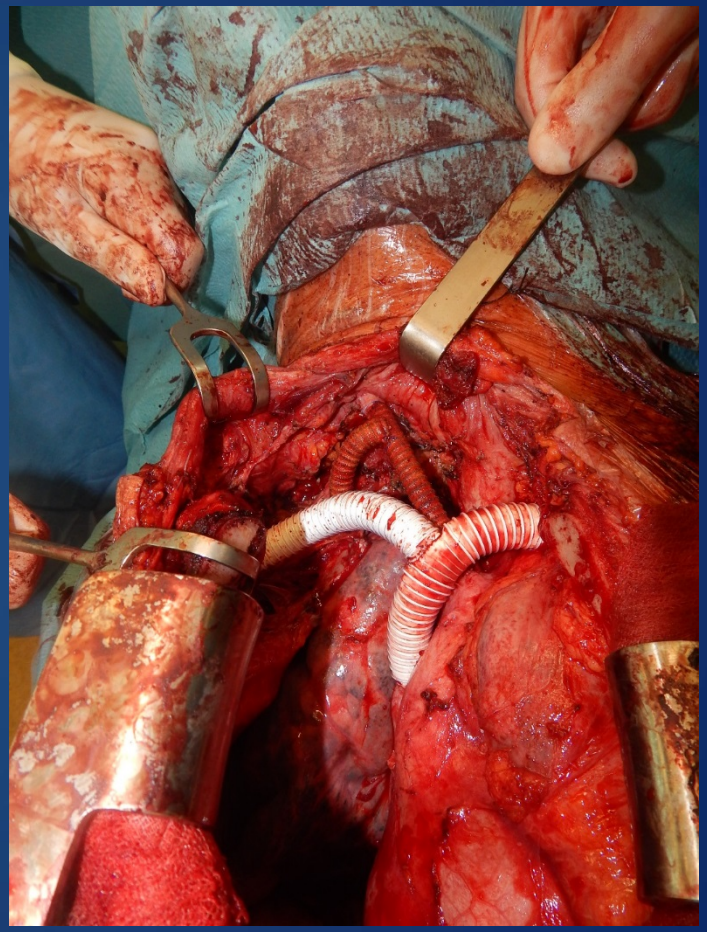
DOUBLE PROSTHETIC REPLACEMENT OF SVC AND RIGHT INNOMINATE ARTERY



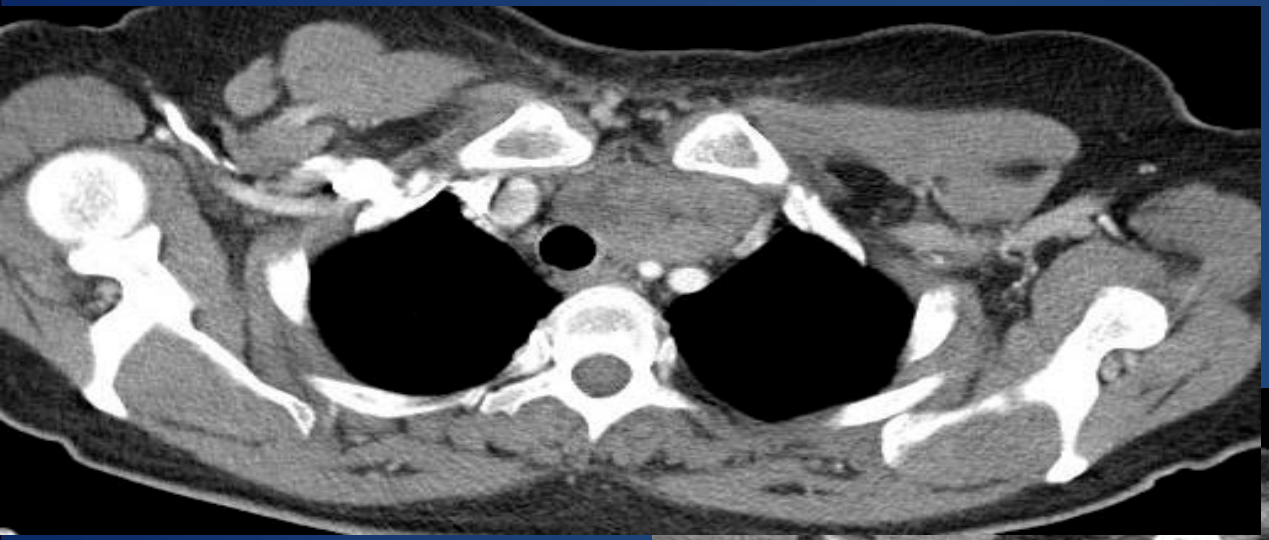


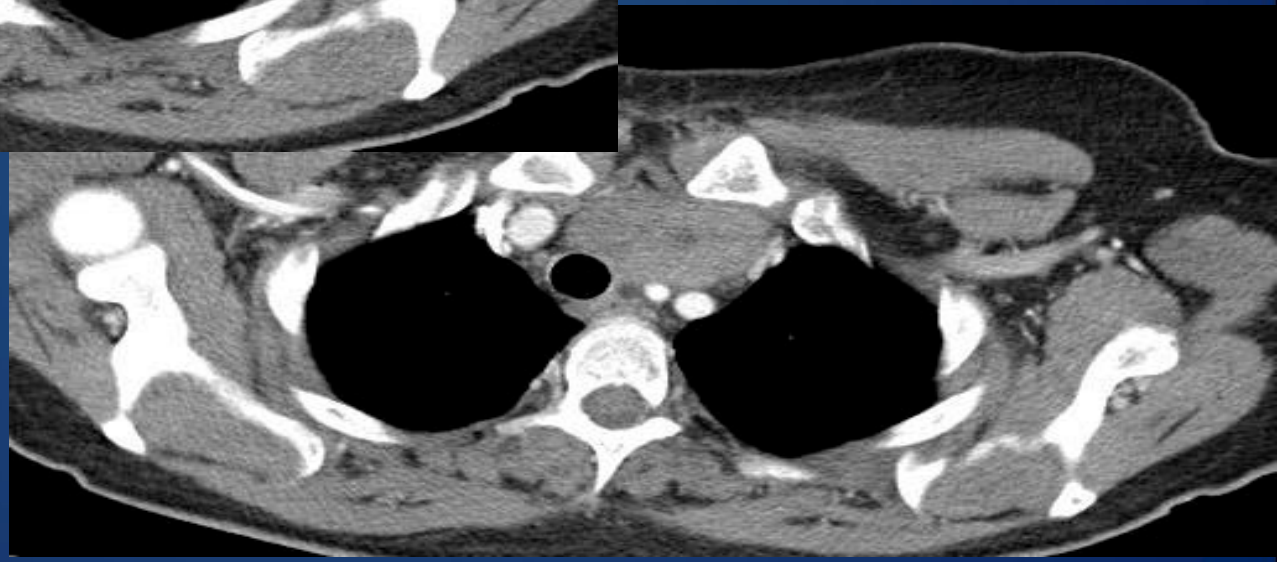
PROSTHETIC REPLACEMENT OF SVC AND INNOMINATE VEINS AND INNOMINATE ARTERY



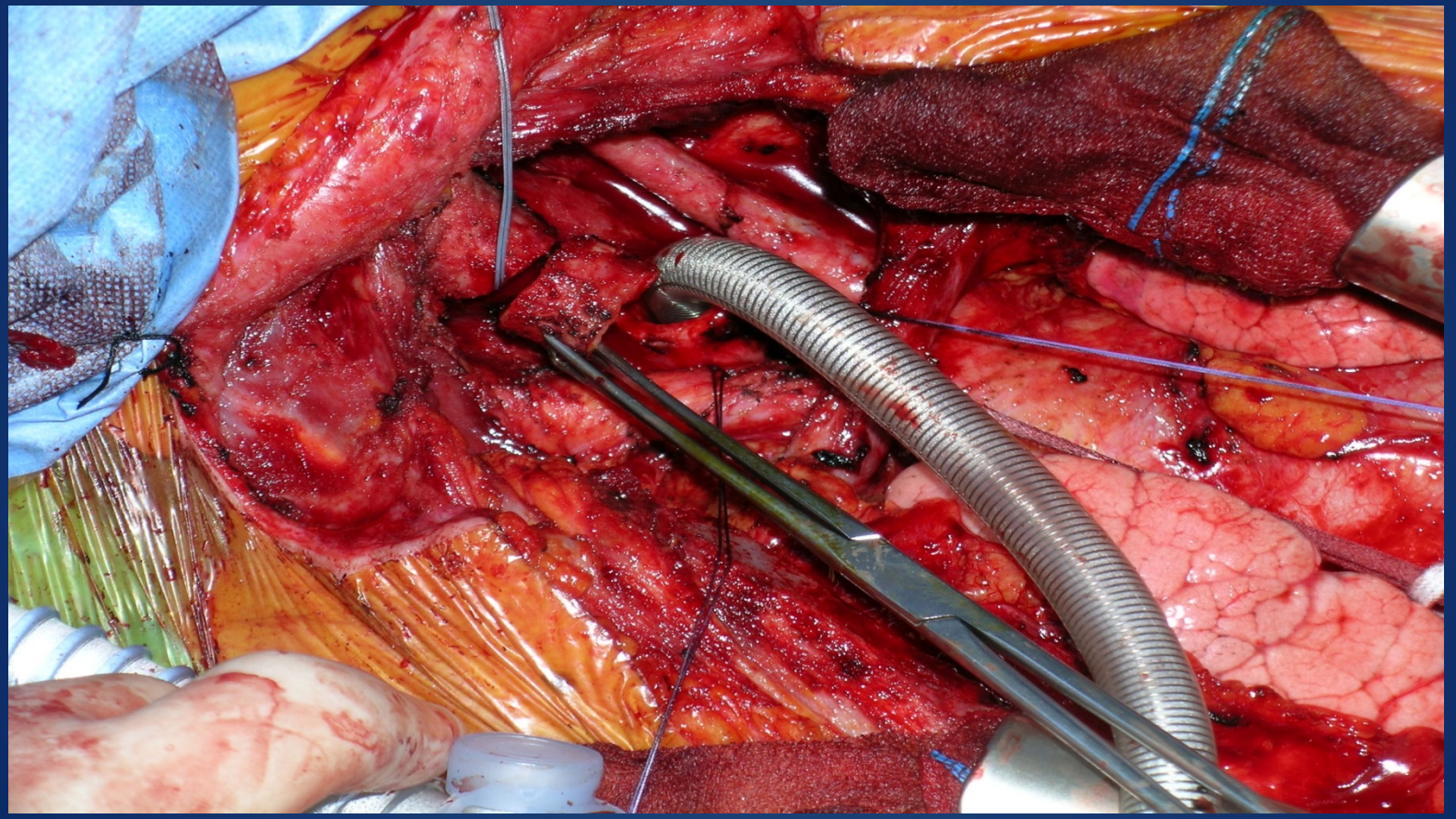


TRACHEAL INVOLVEMENT





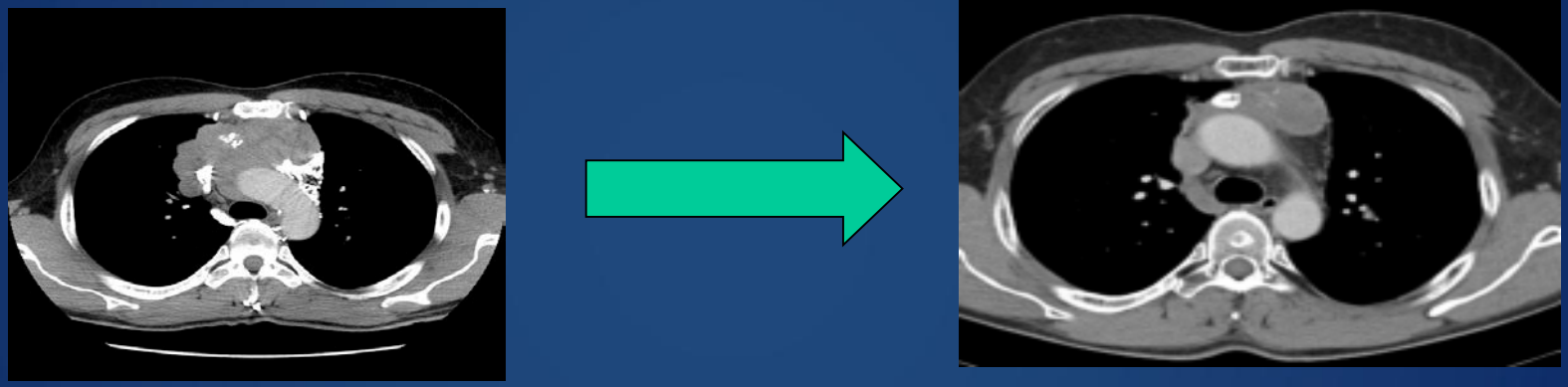
TRACHEAL RESECTION AND ANASTOMOSIS



INDUCTION THERAPY

THEORETICAL ADVANTAGES

a) facilitate and increase the surgical resection by reducing the mass and downstaging the tumor;



b) prevent local and systemic relapses;

c) better assess the activity and the efficacy of the drugs;

d) improves survival?

Thymoma: state of the art

Thomas CR, Wright CD, Loehrer PJ.

J Clin Oncol 1999, 17: 2280

Platinum based CT

Shrinkage 50 - 80%

Lung Cancer 72 (2011) 68–72

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Multidisciplinary approach for advanced stage thymic tumors: Long-term outcome

Federico Rea[a,*], Giuseppe Marulli[a], Francesco Di Chiara[a], Marco Schiavon[a], Egle Perissinotto[b], Cristiano Breda[a], Adolfo Gino Favaretto[c], Fiorella Calabrese[d]

Last decade experience on multidisciplinary treatment of advanced stage thymoma and thymic carcinoma.

Author [Ref.]	Year	*n* patients	Stage III/IVa	IC (*n*; %; type)	RR (%)	CR (%)	5–10-year survival	Recurrence (%)	Adjuvant therapy
Venuta et al. [10]	2003	45	45/0	15 (33%) 7 PAC, 8 PEV	66.6%	88.9%	80–78%	24.5%	CT + RT
Kim et al. [11]	2004	22	11/11[a]	22 (100%) PAC	77%	76%	95–79%	11.5%	CT + RT
Bretti et al. [13]	2004	63	43/20	25 (39.6%) 7PE, 18ADOC	72%	50.8%	NA	NA	RT
Lucchi et al. [14]	2005	56	40/16	36 (64.2%) PEV	66.6%	66%	66–46%	62.2%	RT37 CT + RT 18 CT1
Huang et al. [22]	2007	18	0/18	18 (100%) 10 PAC, 3 VIP, 3 CP,2 PE	67%	67%	78–65%	25%	RT7 CT5
Wright et al. [23]	2008	10	7/3	10 (100%) PE + RT	40%	80%	69–NA	37.5%	CT7
Cardillo et al. [24]	2010	61	34/27	31 (50.8%) PAC	58%	85.3%	NA–50.6%	11.5%	RT34
Present series	2010	75	51/24[a]	38 (50.6%) ADOC	68.4%	81.3%	70–57%	34.4%	RT37 CT + RT 25 CT4

CT, chemotherapy; RT, radiotherapy; IC, induction chemotherapy; RR, response rate; CR, complete resection; ADOC, cisplatin, doxorubicin, vincristine, cyclophosphamide; PE, cisplatin, etoposide (VP-16); PEV, cisplatin, epirubicin, etoposide; PAC, cisplatin, doxorubicin, cyclophosphamide; CP, carboplatin, paclitaxel; VIP, etoposide, ifosfamide, cisplatin; NA, not available.

[a] Stages IVa and IVb.

Lung Cancer 93 (2016) 88–94

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Induction therapy followed by surgical resection in Stage-III thimic epithelial tumors: Long-term results from a multicentre analysis of 108 cases

Giuseppe Cardillo[a], Marco Lucchi[b], Giuseppe Marulli[c], Maurizio Infante[d], Giovanni Leuzzi[e], Alfredo Mussi[b], Francesco Carleo[a], Francesco Facciolo[f], Emanuele Voulaz[d], Federico Rea[c], Cristian Rapicetta[g], Filippo Lococo[g,*]

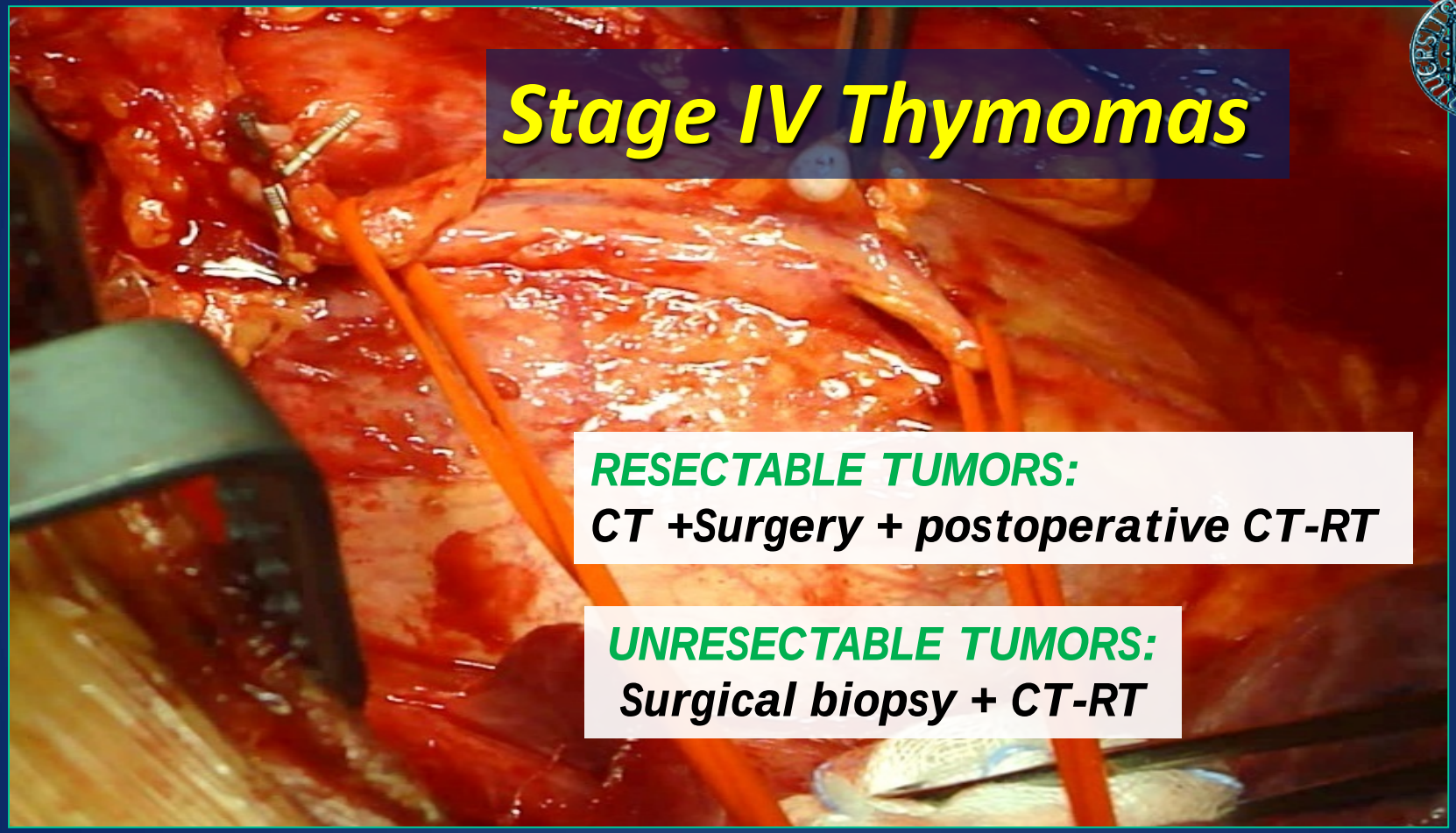
3.2. *Neo-adjuvant and adjuvant therapy*

Induction chemotherapy was administered to all patients with the regimens reported above.

Mean IT length was 4 months (range 2–6); chemo was well tolerated with no episodes of major toxicity. Pathologic response to IT on surgical specimen (presence of necrosis) was observed in 36 cases (33.3%) and a complete pathological response (necrosis > 90%) in 21 cases (19.4%).

Results: Mean age and male/female ratio were 51 ± 13 years and 61/47, respectively. World Health Organization (WHO) histotype was: A in 6 pts (5.6%), AB in 18 (16.7%), B1 in 15 (13.9%), B2 in 26 (24.1%), B3 in 23 (21.3%), and thymic carcinoma in 20 (18.5%). Thirty-day mortality was 1.8%. A total of 81 (75%) had R0-resection, 11 (10.2%) R1 and 16 (14.8%) R2-resection. Adjuvant therapy was performed in 71 patients. During the follow-up a relapse of disease was observed in 38 pts(35.2%). Five-years DFS and LTS were 69.3% and 79.3%, respectively. At univariate analysis, WHO-type B3/C ("high-risk") TETs ($p = 0.001$) and recurrence of disease ($p = 0.02$) were predictors of poor LTS while only a slight correlation was found for R-status and "CHT-regimen type" ($p = 0.097$ and $p = 0.067$, respectively). At multivariate analysis WHO "high-risk" TETs (H.R.5.73;C.I.:1.77–18.57) and ADOC-regimen (H.R.2.84;C.I.:1.37–5.86) were independent predictors of poor survival.

Conclusions: A multimodal treatment for Stage-III thymic tumors may achieve a rewarding survival. WHO-Histology seems to be the most important prognostic factor.



Stage IV Thymomas

RESECTABLE TUMORS:

CT +Surgery + postoperative CT-RT

UNRESECTABLE TUMORS:

Surgical biopsy + CT-RT

Results of surgical treatment of Stage IVa thymic tumors

Author	Year	Pts No.	5-year survival	10-year survival
Masaoka	1991	11	50%	0%
Maggi	1991	21	59%	40%
Regnard	1996	19	60%	30%
Yagi	1996	5	67%	33%
Wilkins	1999	5	40%	40%
Kondo	2003	103	71%	48%
Nakagawa	2003	11	47%	47%
Lucchi	2005	16	NR	46%
Wright	2006	5	75%	50%
Huang	2007	18	78%	65%
Cardillo	2010	27	NR	28%
Margaritora	2010	14	76%	52%
Average			**62%**	**40%**

Feasibility of multimodality therapy including extended resections in stage IVA thymoma

James Huang, MD,[a] Nabil P. Rizk, MD,[a] William D. Travis, MD,[b] Venkatraman E. Seshan, PhD,[c] Manjit S. Bains, MD,[a] Joseph Dycoco, BA,[a] Robert J. Downey, MD,[a] Raja M. Flores, MD,[a] Bernard J. Park, MD,[a] and Valerie W. Rusch, MD[a]

Objective: Extended resections for advanced-stage thymomas are not commonly performed because of the potential morbidity in the face of unclear survival or palliative benefit. We reviewed our experience with multimodality treatment for Masaoka stage IVA thymomas for feasibility and outcomes.

Methods: We conducted a retrospective review of a single-institution surgical database. Data included patient demographics, preoperative staging and treatment, perioperative events, pathologic findings, and postoperative outcomes.

Results: During the period from 1996 to 2006, 18 patients who had Masaoka stage IVA thymoma underwent surgical resection. All patients received preoperative chemotherapy. Four patients with extensive pleural involvement underwent concomitant extrapleural pneumonectomy and postoperative hemithoracic radiation. Complete resection was achieved in 12 (67%) patients. There was no operative mortality. With a median follow-up of 32.2 months (range 1.4–129.9 months), 3-year, 5-year, and 10-year survivals were 91%, 78%, and 65%, respectively, and median survival has not yet been reached.

Conclusion: Multimodality therapy including extended surgical resection can be performed in select patients with stage IVA thymoma with low morbidity and mortality and can result in excellent long-term survival.

J Thorac Cardiovasc Surg 2007;134:1477-84

Pleuropneumonectomy for the Treatment of Masaoka Stage IVA Thymoma

Cameron D. Wright, MD

Division of Thoracic Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Background. The treatment of locally advanced Masaoka stage IVA thymoma is not standardized and is problematic.

Methods. A single-institution retrospective study was made of 5 patients with World Health Organization B3 thymomas who underwent pleuropneumonectomy for locally advanced thymoma. Two patients had recurrent thymoma and 3 presented de novo with stage IVA disease. Patients had a variety of induction and adjuvant treatments.

Results. There was no operative mortality, and only 1 patient had a major complication. Several patients had relatively prolonged disease-free survival. The median survival was 86 months, and the Kaplan-Meier survival was 75% (95% confidence interval: 53% to 97%) at 5 years and 50% (95% confidence interval: 25% to 75%) at 10 years.

Conclusions. Pleuropneumonectomy can be performed safely in patients with advanced thymomas and may improve survival. Highly selected patients might be cured with this approach if a complete resection is performed. While the optimal multimodality strategy for these patients is unknown, induction chemotherapy followed by resection then chemoradiotherapy seems promising.

(Ann Thorac Surg 2006;82:1234–9)

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European Journal of Cardio-thoracic Surgery 39 (2011) e133—e138

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Long-term outcome of pleuropneumonectomy for Masaoka stage IVa thymoma☆

Dominique Fabre*, Elie Fadel, Sacha Mussot, Olaf Mercier, Boriana Petkova, Benjamin Besse, James Huang, Philippe G. Dartevelle

Marie-Lannelongue Hospital, Le Plessis Robinson, Paris-Sud University, Orsay, France

Received 6 September 2010; received in revised form 22 December 2010; accepted 23 December 2010

Abstract

patients at 26 and 87 months, respectively, which was treated medically without success. Conclusions: Pleuropneumonectomy for Masaoka stage IVa thymoma is associated with a high morbid-mortality rate. However, included in a multimodality strategy and in highly selected patients this procedure may provide good long-term survival.

radiotherapy, or both was performed in 14 (82%) patients. **Results:** Eight patients (47%) experienced a major postoperative complication, including four broncho-pleural fistulae (23%). There were no operative deaths and the 30-day mortality was 17.6% (3/17). But two patients died at 2 and 3 months, increasing the postoperative mortality to 29.4% (5/17). Complete resection was achieved in 11 (65%) patients. By univariate analysis, myasthenia gravis was the only risk factor for broncho-pleural fistulae. With a median survival of 76 months and median follow-up of 59 months (range, 1—262 months), 5-year and 10-year survivals were 60% and 30%, respectively. During follow-up, a recurrence occurred in two patients at 26 and 87 months, respectively, which was treated medically without success. **Conclusions:** Pleuropneumonectomy for Masaoka stage IVa thymoma is associated with a high morbid-mortality rate. However, included in a multimodality strategy and in highly selected patients this procedure may provide good long-term survival.

Keywords: Thymoma; Masaoka stage IVa; Extrapleuralpneumonectomy; Survival

Summary

- Mini-invasive thymectomy has an important role in myasthenia gravis patients.
- Surgery remains the mainstay of therapy for Stage I – III thymic tumors
- Minimally invasive techniques probably reasonable for stage I tumors, but long-term follow up lacking
- Complete thymectomy / en-bloc tumor resection required
- For advanced stages recommended treatment in high volume centers with multidisciplinary approach

Padova

Grazie