

# Thymoma

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No potential conflicts to disclose with respect to this presentation

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# Clinical Presentation

Symptoms

Paraneoplastic syndromes



# Thymoma - Symptoms

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Usually indolent course, long-standing symptoms

- Asymptomatic 34%
- Myasthenia Gravis 35%
- Any systemic symptom 27%
  - Weight loss 7%
  - Fever 4%
- Any local symptom 38%
  - Dyspnea 12%
  - Chest Pain 19%
  - Cough 15%
  - Hoarseness 3%
  - SVC Syndrome 2%



# Associated “Parathymic” Conditions

Myasthenia Gravis 40-45%

Red Cell aplasia 2-5%

Hypo  $\gamma$  globulinemia 2-5%

Polymyositis 1-3%

SLE / RA 1 / 1%

Thyroiditis 0.8%

Sjogren’s Syndr. 0.8%

Ulcerative colitis 0.3%

Pernicious anemia 0.2%

Other cancer 15%

Raynaud’s Syndr

Regional enteritis

Dermatomyositis

Scleroderma

Takayasu’s Syndr

Cushings disease(2%)

Hyperthyroidism(1%)

Addison’s disease

Macrogenitosomia

Panhypopituitarism



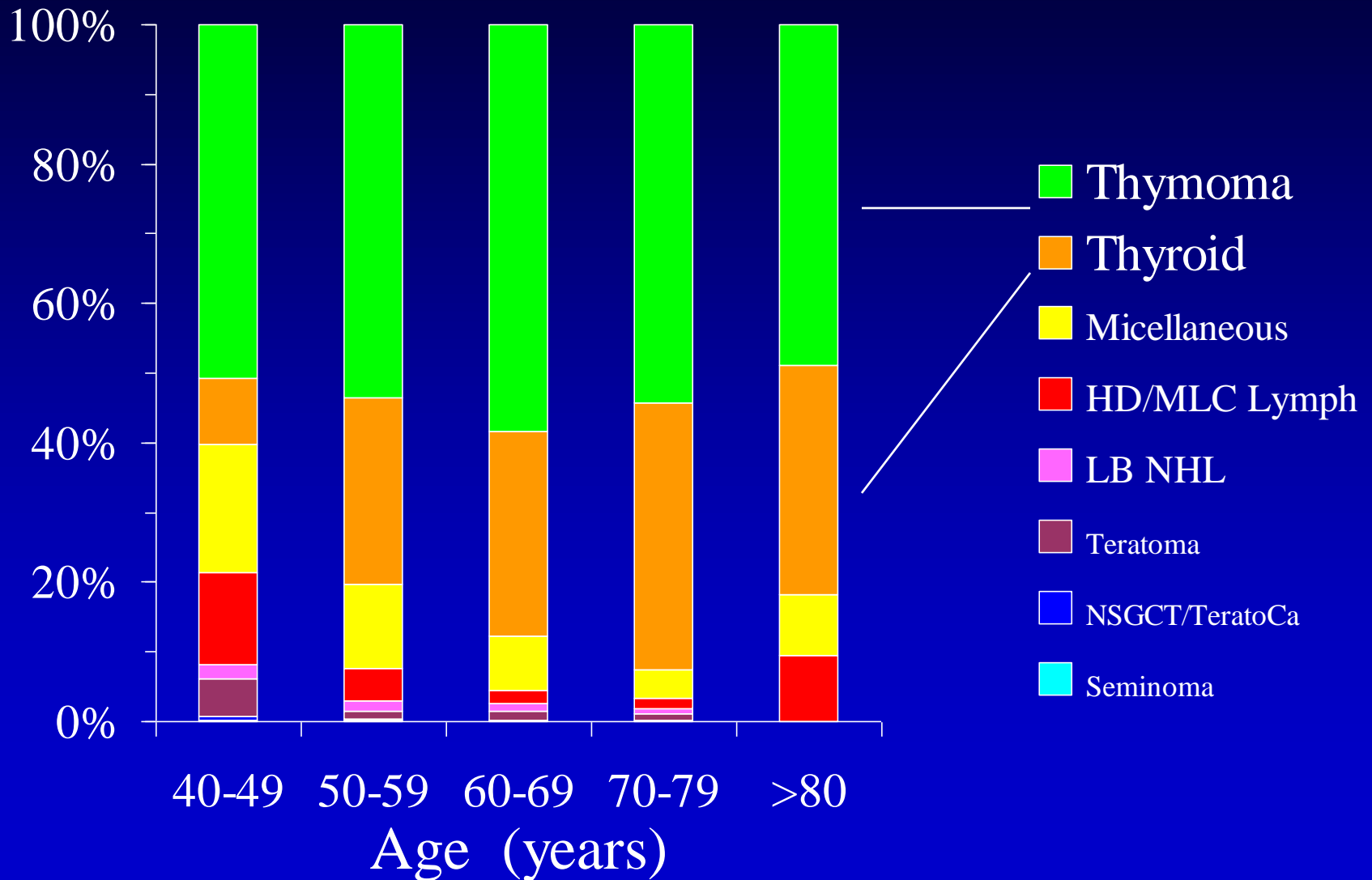
# Patient Evaluation

Making a Clinical Diagnosis

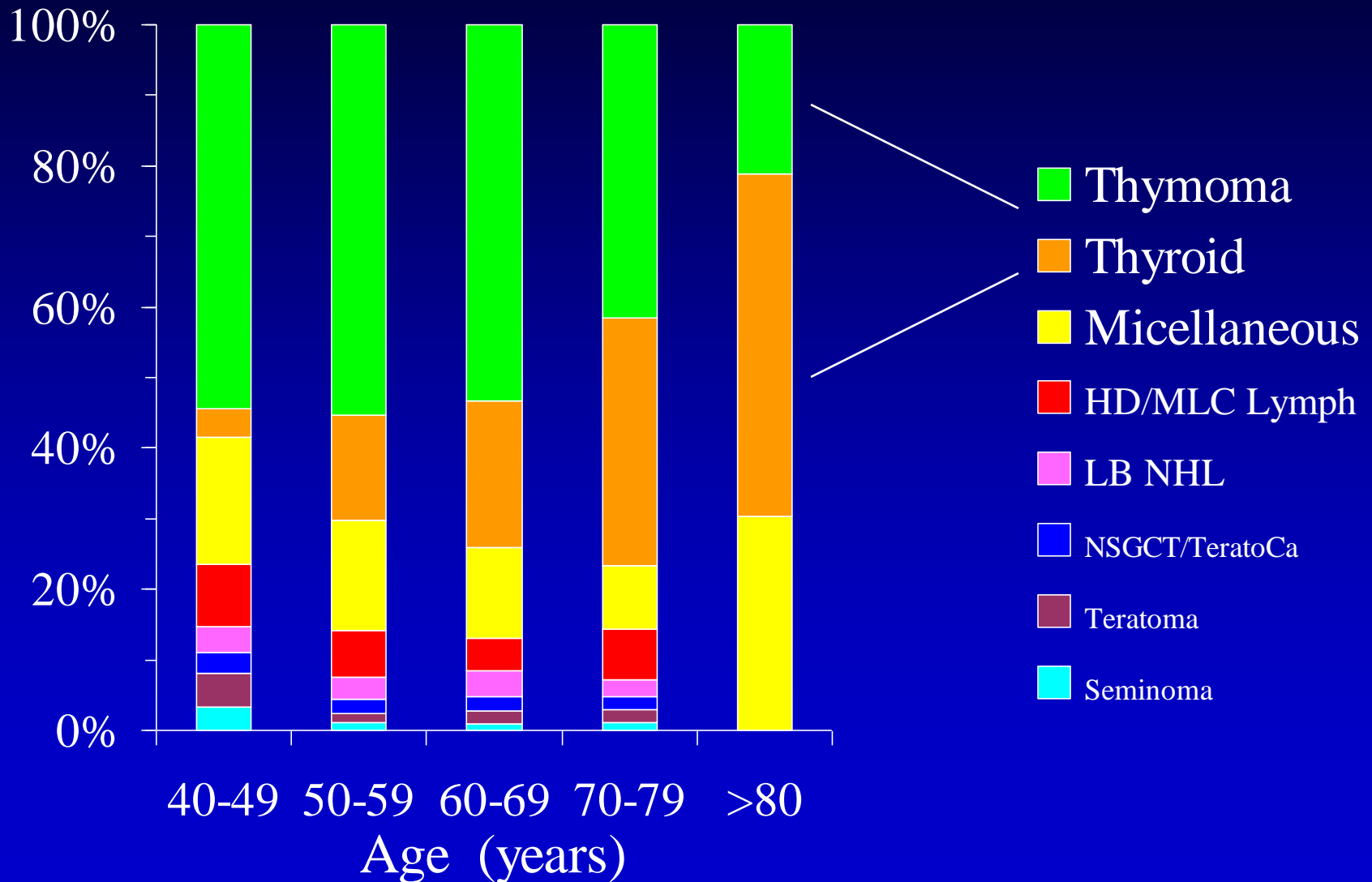
Biopsy



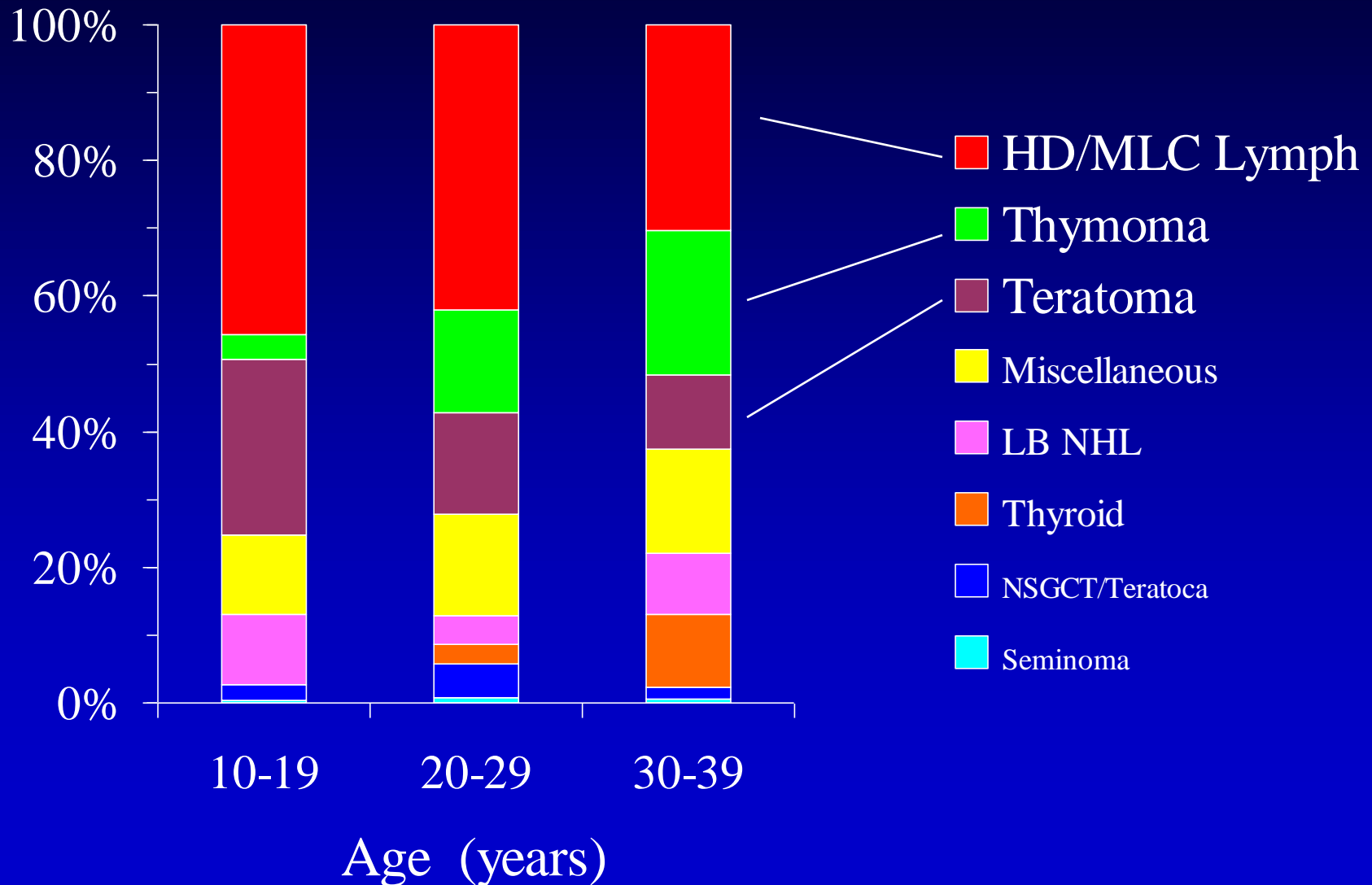
# Ant Mediast Tumors – Women > 40



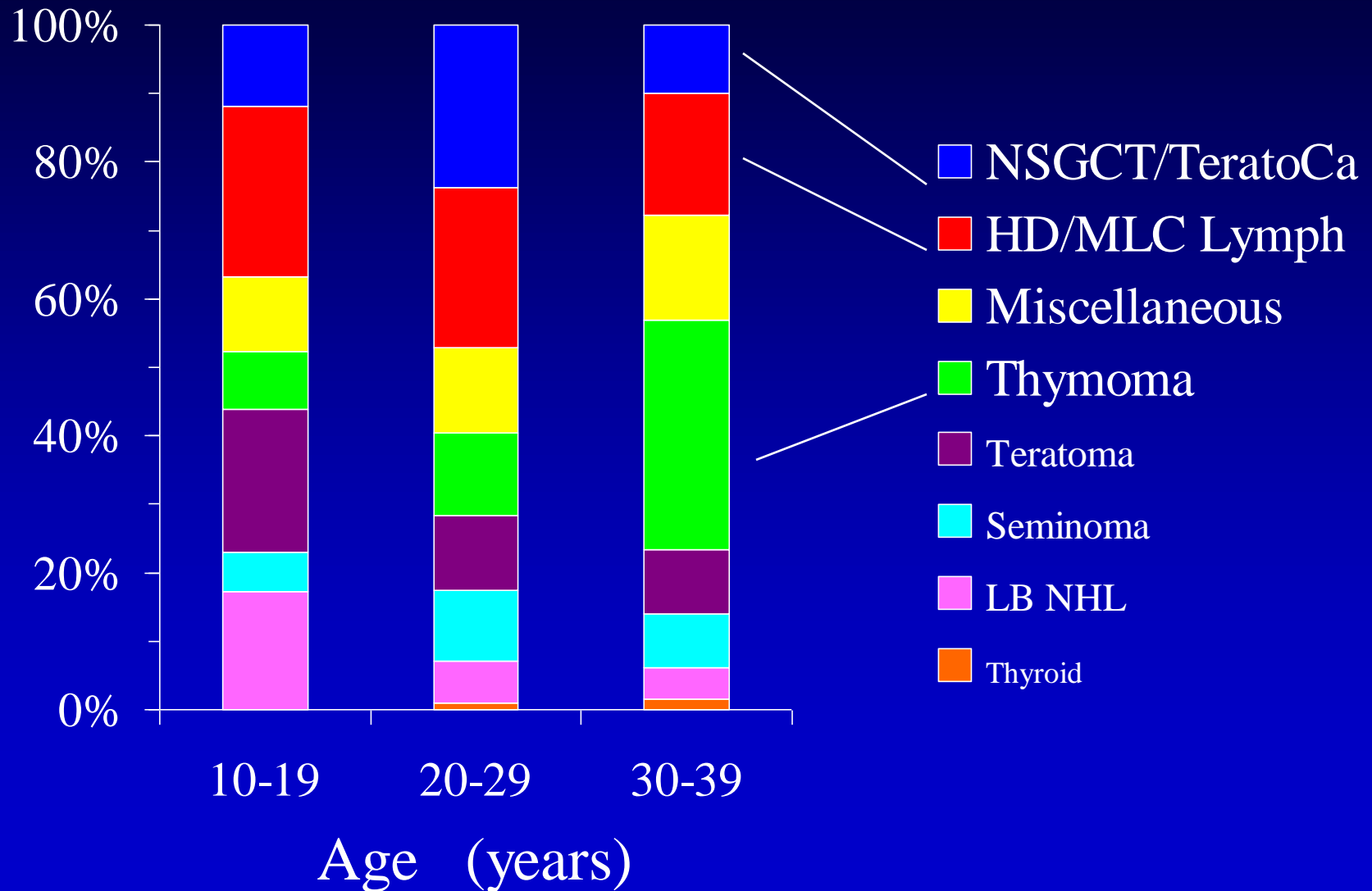
# Ant Mediast Tumors – Men > 40



# Ant Mediast Tumors – Age 10-39



# Ant Mediast Tumors – Age 10-39



# Ant Mediast Tumors – Age > 40

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## Clinical Approach:

- Thyroid is easy to recognize, extending down from neck on contrast-enhanced CT
- ~ 40% of pts w thymoma have Myasthenia Gravis, also RBC dysplasia, hypo- $\gamma$ -globulinemia
- No need to biopsy stage I,II thymoma
- Bx of stage III thymoma  $\rightarrow$  preop chemo is useful
- If it looks unusual or lymphoma  $\rightarrow$  biopsy



# Thymoma – Biopsy for Diagnosis

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## Dogma:

- Never biopsy a thymoma due to risk of seeding bx site and pleural space

## Data:

- Only 3 cases of seeding of biopsy site have been reported
- Pleural nodules are seen in advanced thymoma whether or not biopsy has ever been done
- Survival not affected by prior Bx by MV analysis
- Bx of stage III thymoma → preop chemo is standard in most centers with expertise in thymomas
- Yield of FNA ~60%, open Bx ~90%



# Thymoma: Presentation and Approach

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- Usually age  $>40$ , mass in Anterior mediastinum
- 33% asymptomatic, 30-50% have MG
- In most patients it is easy to differentiate from substernal thyroid, cyst, lymphoma
  - No need to biopsy stage I,II thymoma
  - Bx of stage III thymoma  $\rightarrow$  preop chemo is useful



# Classification

Staging

Histological Classification



# Masaoka Staging System

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- I Macroscopically encapsulated, no microscopic capsular invasion
- II
  - a Macroscopic invasion into surrounding fatty tissue or mediastinal pleura
  - b Microscopic invasion into the capsule
- III Macroscopic invasion into neighboring organs
- IVa Pleural or pericardial metastases
  - b Lymphogenous or hematogenous metastasis

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**Modifications:** Regnard: 1b adherence but no micro invasion

Verley/Regnard: divide III and IV according to  $R_0$  vs  $R_{1,2}$



# Histologic Classification: WHO

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- A Spindled epithelial cells, no atypia,
- AB Similar, but w foci of neoplastic lymphocytes
- B1 epithelioid cells, resembling cortex & medulla
- B2 epithelioid cells, w scattered neoplastic cells
- B3 epithelioid cells, w mild atypia  
(well differentiated thymic carcinoma)
  
- C Thymic Carcinoma



# Interobserver Variation in WHO type

Verghese Histopath 2008;53:218-23

95 consecutive Thymic Tumors,  
all with surgical specimen (no  
core Bx), over 1 year (2006)

17 pathologists with special  
interest in thoracic assigned  
each specimen to a WHO type  
(including thymic carcinoma)

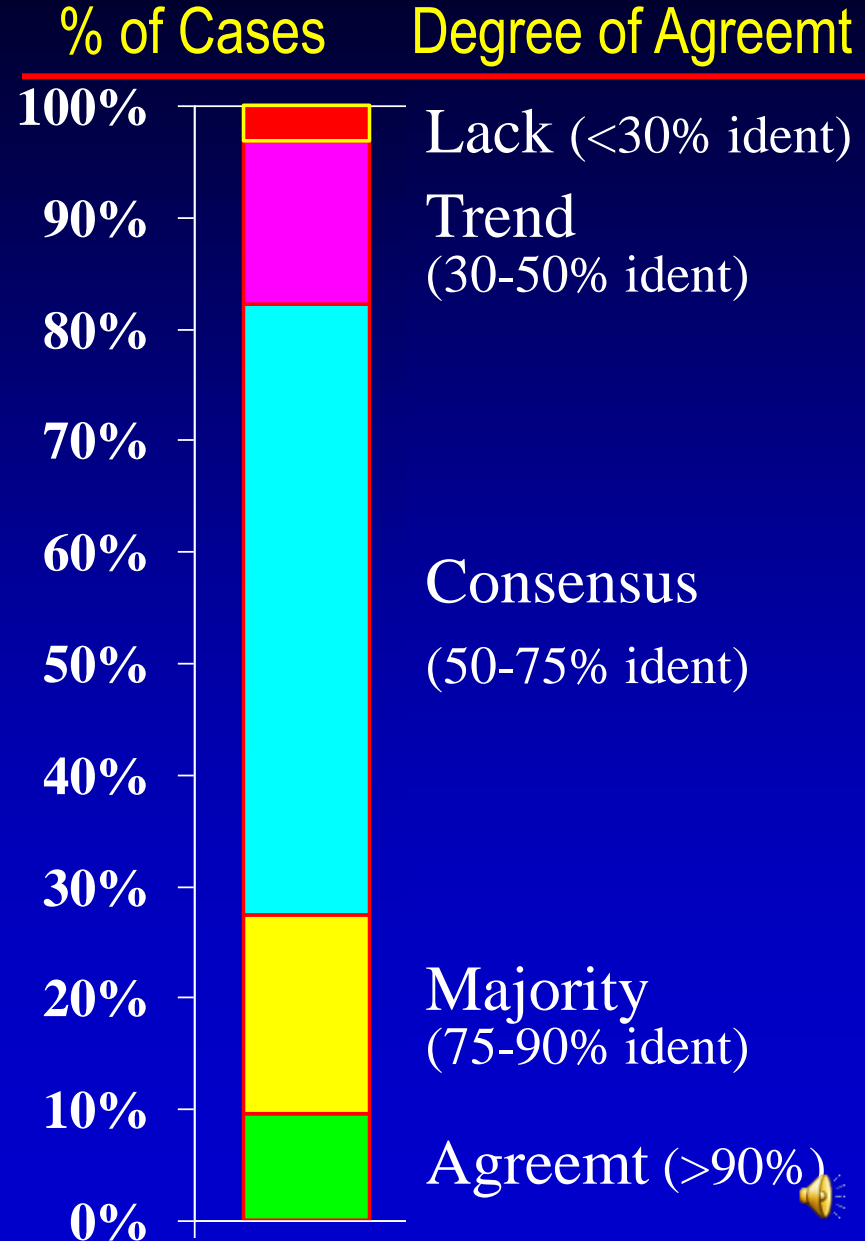
No mixed classifications allowed

Overall:  $\kappa = 0.45$

B3 vs. C  $\kappa = 0.48$

A-B2 vs. B3,C  $\kappa = 0.62$

Most difficulty: B1 vs. B2 vs. B3



# Treatment

Natural History

Surgery - General

Stage I, II

Stage III, IVa

Prognostic Factors



# Thymoma – Natural History

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- Indolent Course

Present retrospectively in 77% of 31 pts (mean 6 yrs)

Long interval to recurrence (1-32 yrs, mean 5 yrs)

- At Presentation:

10% pleural or pericardial implants, 3% nodal mets, 6 % distant mets

- Recurrence Pattern

56% pleural/pericardial implants, 31% distant, 14% nodes

- There is no such thing as a benign thymoma!

Distant metastases have been consistently reported for each stage, and for each histologic type



# Thymoma – Surgical Resection

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- Op Mortality 2% overall, 0-1% in recent series
- Sternotomy (rarely thoracotomy)
  - VATS or transcervical for stage I is controversial
- Complete thymectomy
  - Recommended by most larger centers
  - 2<sup>nd</sup> Thymoma found in 3%
  - Sometimes MG develops later after partial thymectomy
- Complete Resection (with invaded structures)
  - Probably little benefit from debulking



# Rate of R<sub>0</sub> Resection by Stage

Incl Crit: > 50 pts	N	I	II	III	!Va	IVb
Regnard	307	100	100	50	----63----	
Fang	204	100	100	-----75----		
Okumura	194	100	100	89	0	0
Nakahara	141	100	100	73	----0----	
Blumberg	118	100	73	56	78	
Kondo	100	100	100	72	50	47
Curran	99	100	100	20		
Masaola	96	100	100	64	0	0
Gamonedes	65	100	43	0	----13----	
Kaiser	50	100	63	21		
Average		100	88	49	----29----	

# Recurrence Rate after Resection

Study	n	I	II	III	IVa
Kondo	1089	1	4	27	39
Regnard	307	4	7	16	58
Maggi	241	2	13	30	25
Verley	200	6	36	-----38-----	
Wright	179	0	2	31	45
Ströbel	179	2	3	27	-
Cowen	149	0	7	23	25
Wilkins	136	8	10	24	0
Nakagawa	130	3	2	28	27
Monden	127	3	13	27	54
Blumberg	118	4	21	47	80
Ruffini	114	5	10	30	33
Quintanilla	105	0	13	13	0
Ogawa	103	0	10	44	-
Kondo	100	3	8	50	67

Inclusion criteria: Studies reporting recurrence by stage in  $\geq 100$  pts



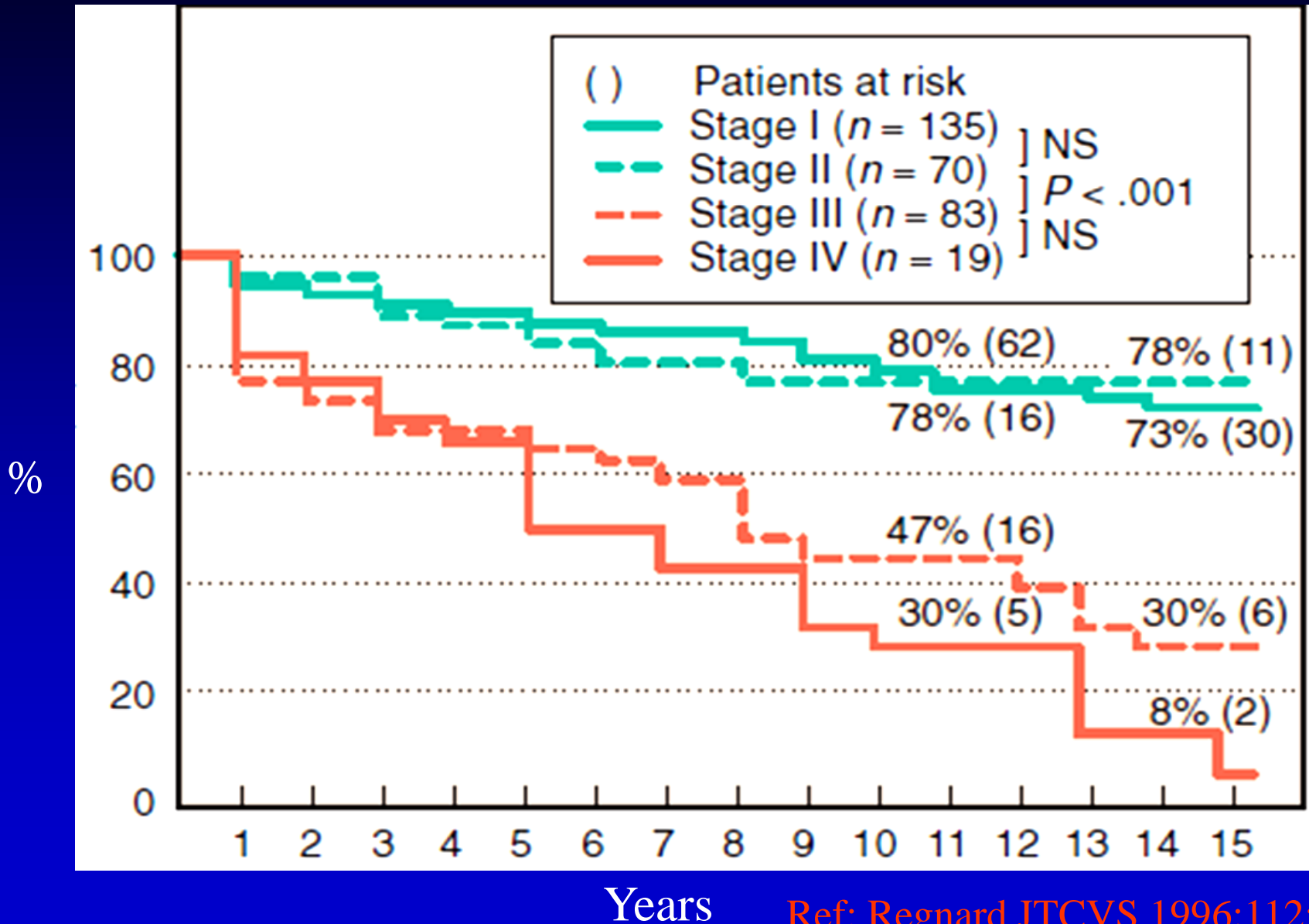
# 10-yr Overall Survival after Resection

Study	n	I	II	III	IVa
Regnard	307	80	78	47	30
Maggi	241	87	60	64	40
Verley	200	80	42	-----23-----	
Chen	200	90	82	37	-
Ströbel	179	100	91	84	47
Nakahara	141	100	84	77	47
Wilkins	136	75	50	44	40
Blumberg	118	86	54	26	-
Quintanilla	116	100	100	60	0
Pan	112	87	69	58	22
Ogawa	103	100	90	48	-
Kondo	100	100	100	69	-
Average		90	75	56	38

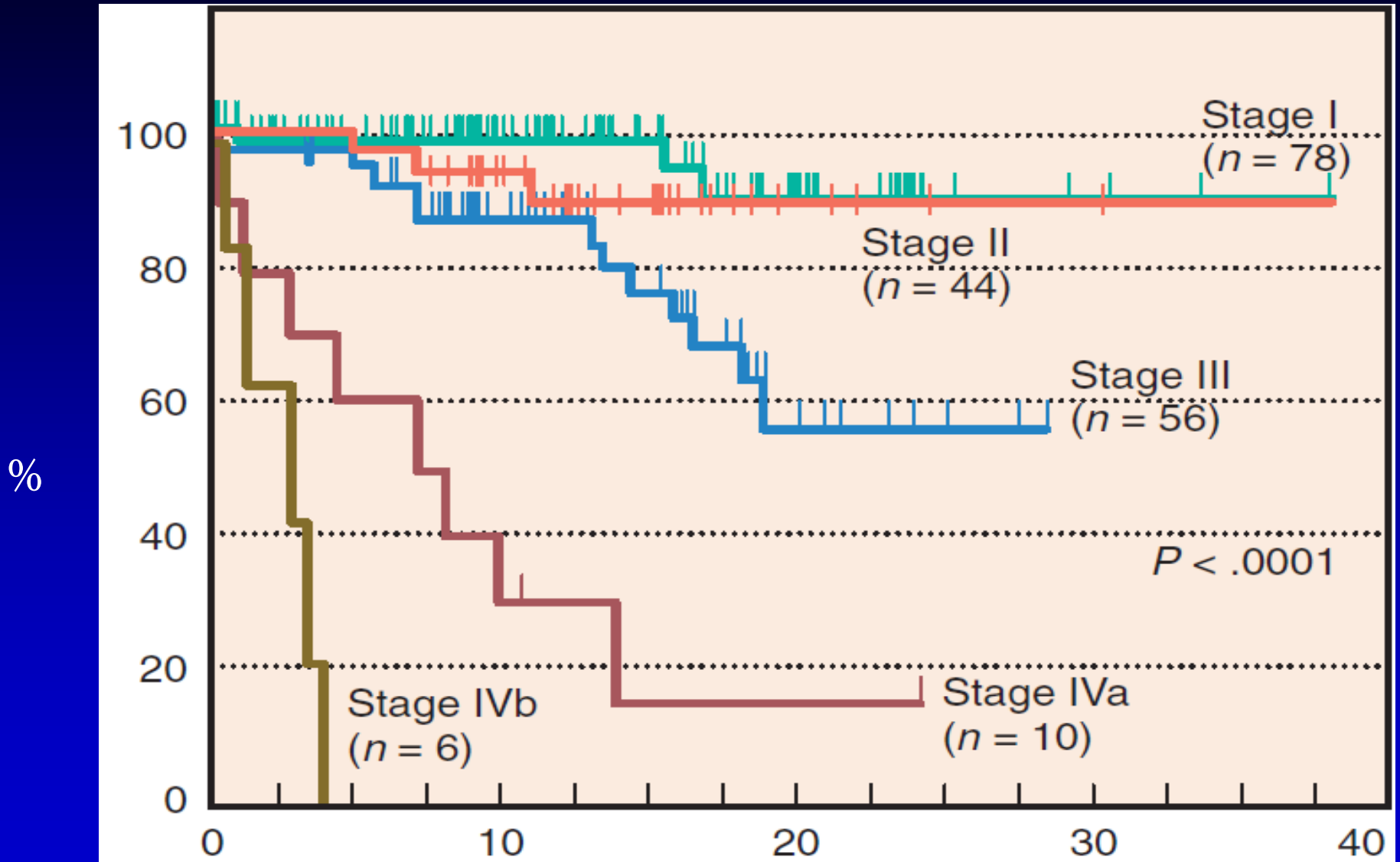
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# Overall Survival



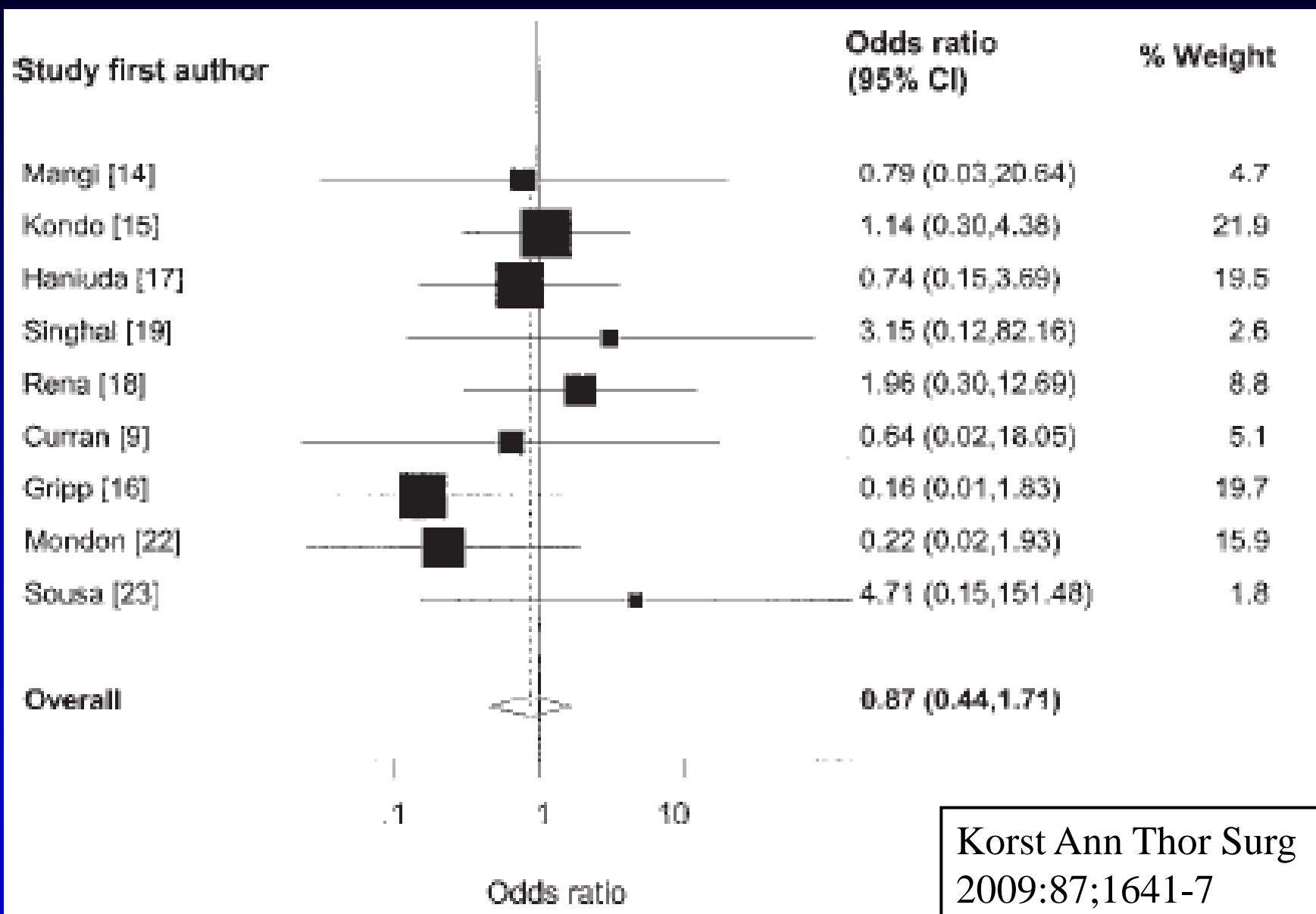
# Disease Free Survival



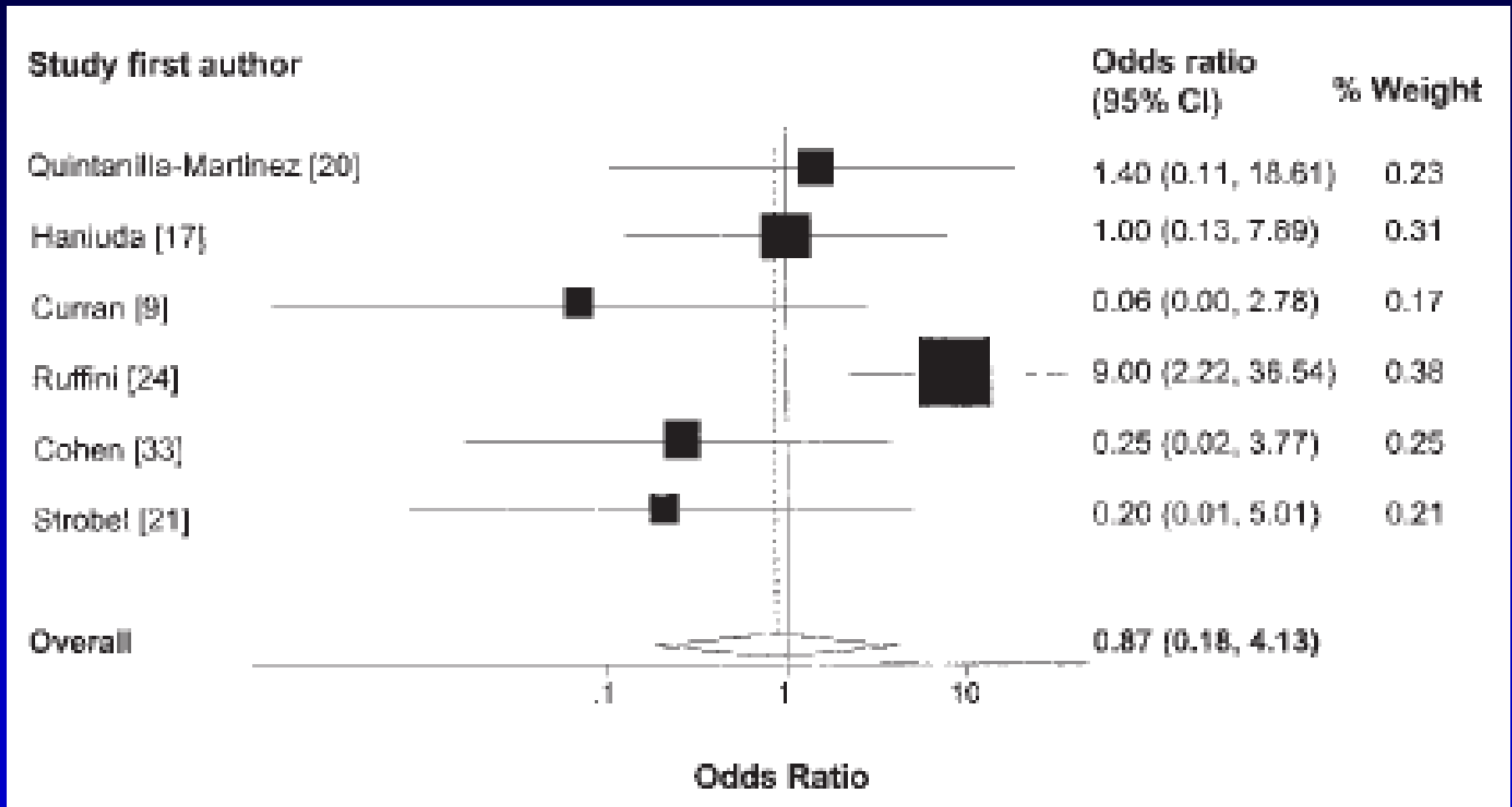
Years

Ref: Okumura JTCVS 1999;117:605-13

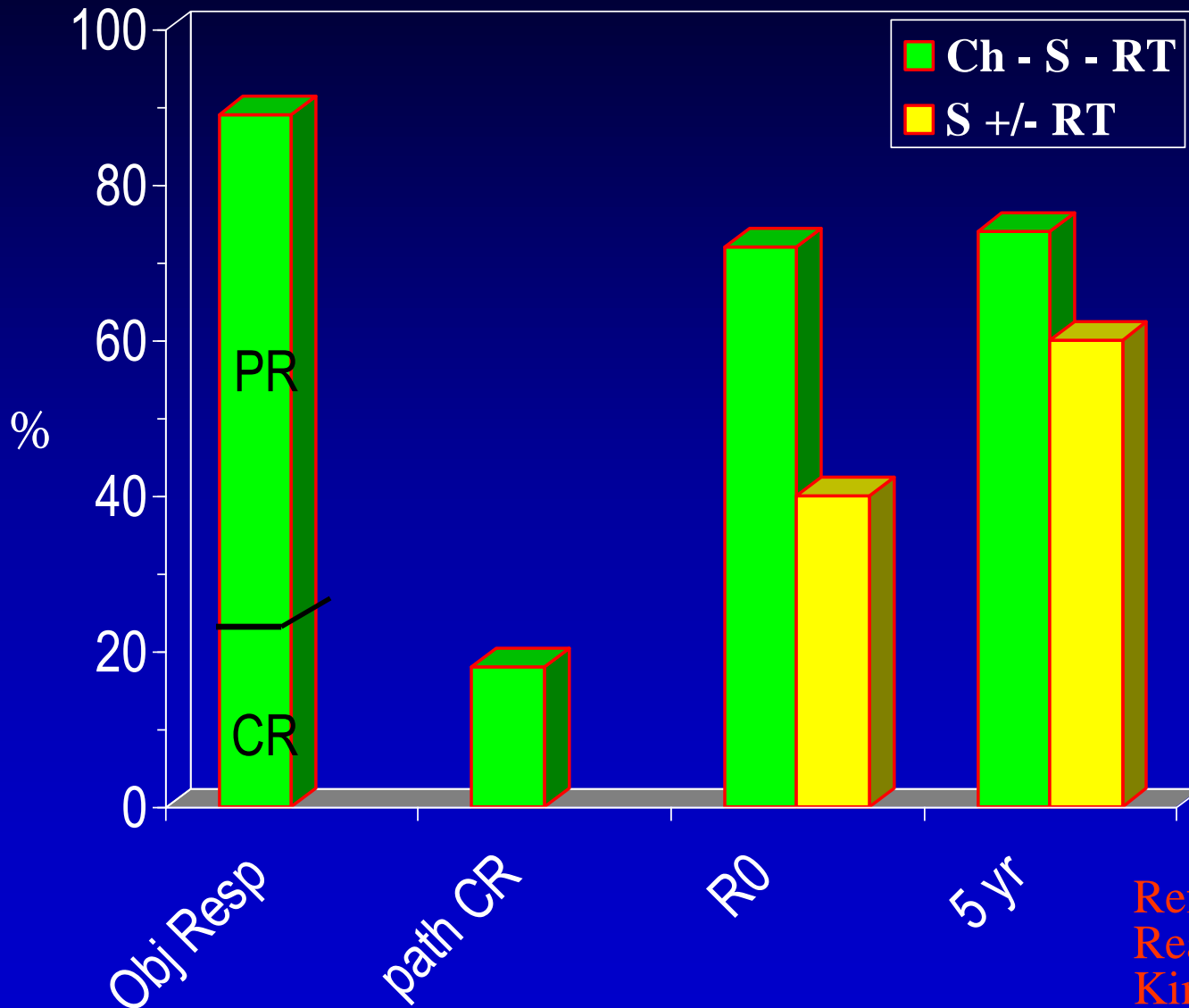
# Systematic Review of RT: Stage II



# Systematic Review of RT: Stage III



# Pre-op Chemo Stage III, IVa



## Pre-op Chemo

6 studies, 106 pts

66% III, 34% IV

Also adj RT( $\pm$ Ch)

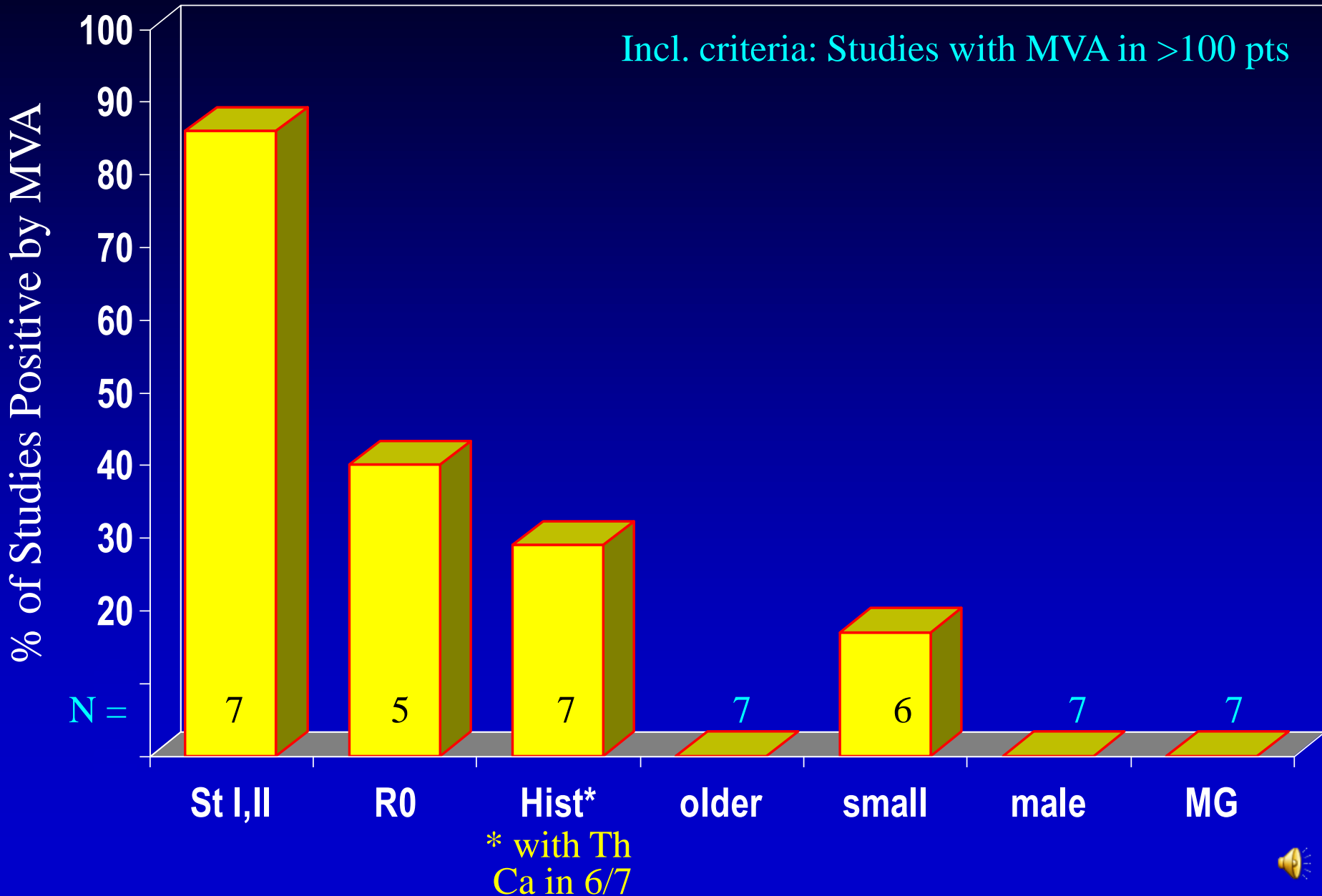
References: Lucchi 2005,  
Rea 2004, Venuta 1997,  
Kim 2004, Rea 1993,  
Macchiarini 1991



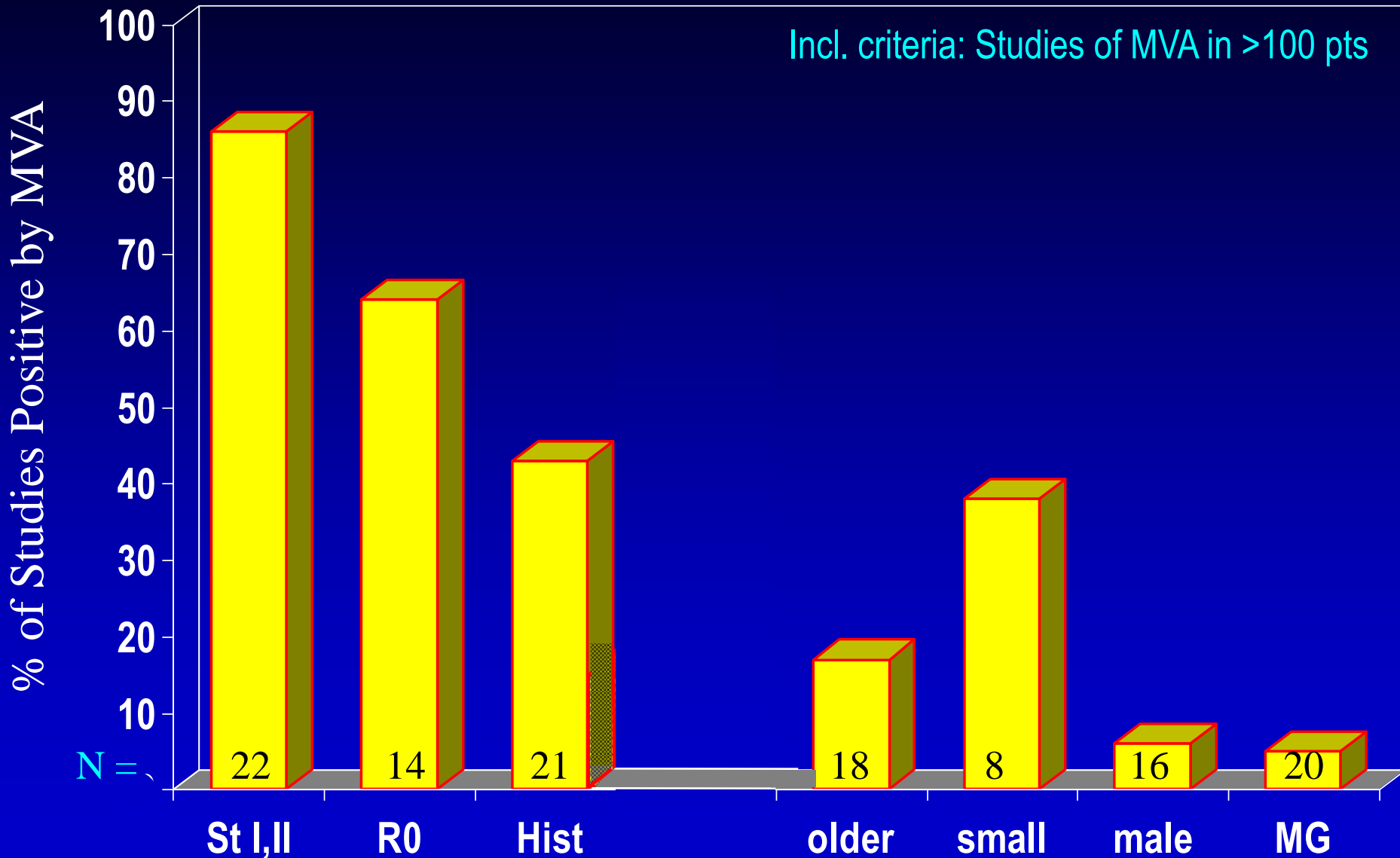
# Prognostic Factors



# Factors associated with ↓ Recurrence



# Factors associated with ↑ Survival



# Summary of Prognostic Factors

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- Masaoka stage is clearly the MOST important independent prognostic factor in studies using multivariate analysis (MVA)
- R0 resection is next most consistent factor in MVA
- WHO histologic type: questionable reproducibility, prognostic value by MVA appears low  
(but thy carcinoma appears to have worse prognosis)
- Other factors that have been studied by MVA do not seem to be useful



# Conclusions



# Common Dogma NOT supported by Data

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- Pre-op biopsy should be avoided because it causes seeding
- Postop RT is needed to prevent pleural seeding
- Microscopic assessment is not useful (stage, invasion)
- WHO histologic type is a major prognostic factor (only thy carcinoma is consistently worse)



# Thymoma: Presentation and Approach

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  - No need to biopsy stage I,II thymoma
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# Thymoma: Treatment

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- Surgery is the Mainstay of Tmt
- For stage I and II, R<sub>0</sub> resection rates are ~100%, and recurrence rate <10%
- Adjuvant RT
  - No role in R<sub>0</sub> resected Stage I,II
  - Controversial role in R<sub>0</sub> resected Stage III
  - Probably useful in R<sub>1</sub> resection
- Preop Chemo → Surg → RT in Stage III, IVa
  - Good response, ↑ R<sub>0</sub> rates, ↑ Survival



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