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SUNY DOWNSTATE MEDICAL CENTER

SURGERY GRAND ROUNDS

February 28, 2013



VERENA LIU, MD
ROSEANNA LEE, MD

Case Presentation



- 35 year old male referred from PMD with an asymptomatic palpable right neck mass
- PMH/PSH: none
- Meds/Allergies: none
- Labs:
 - TFT normal
 - Ca 9.7



- CT Scan – 5 cm right thyroid nodule with subcentimeter cystic complex nodule in bilateral lobes
- Ultrasound
 - Right thyroid: 4.2 x 2.4 x 3.8cm heterogenous solid mass
 - Left thyroid: homogenous parenchyma
 - No cervical lymphadenopathy
- FNA of right thyroid nodule: multinodular goiter



- **Diagnosis**

- Right multinodular and substernal goiter with tracheal deviation and compression

- **Operation**

- Right total and substernal thyroidectomy and isthmusectomy

Pathology



- Papillary thyroid carcinoma (follicular variant) – 1.6 cm
- No extracapsular extension
- No lymphovascular invasion
- Surgical margins negative
 - Closest margin 2mm



Total
Thyroidectomy

vs

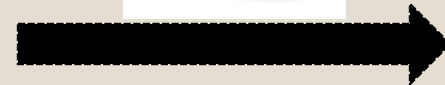
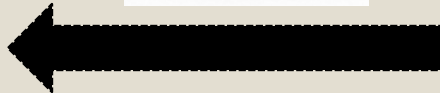
Lobectomy



Total
Thyroidectomy

vs

Lobectomy

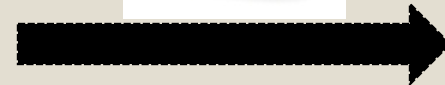
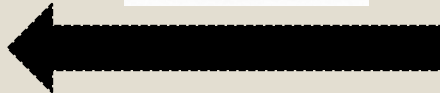




Total
Thyroidectomy

vs

Lobectomy



What this Debate is **NOT** about



- Bilateral clinically suspicious disease
- Aggressive variant
- Extrathyroidal extension
- Nodal or distant metastatic disease
- High risk patients defined by staging systems
- Prior history of irradiation to head and neck in childhood or radiation exposure
- Inherited syndromes associated with thyroid cancer

Our Debate



- **Young** patients with **small, unilateral, well-differentiated** thyroid cancers with **low risk** factors

Lobectomy for well differentiated Thyroid Cancer



VERENA LIU, MD
SUNY DOWNSTATE MEDICAL CENTER
SURGERY GRAND ROUNDS 2/28/2013

Thyroid Cancer

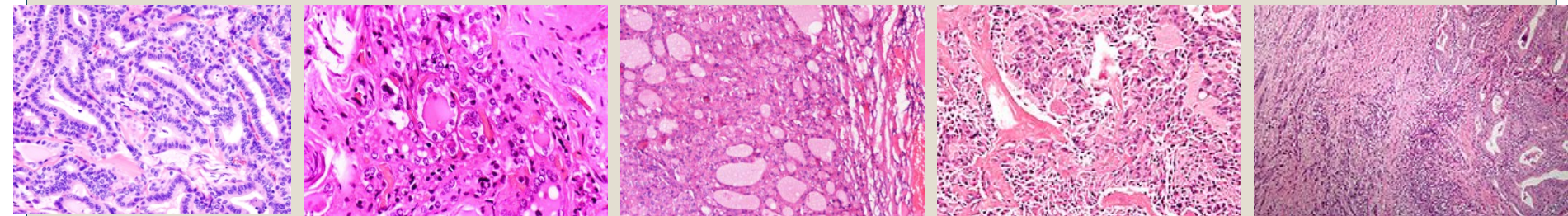


- Well differentiated Thyroid Cancer (follicular cell origin)

- Papillary 85%
- Follicular 10%
- Hürthle cell 3%

- Other

- Medullary thyroid cancer 4%
- Anaplastic thyroid cancer 2%



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Papillary Thyroid Carcinoma



- Risk factors: childhood radiation exposure, history of thyroid cancer in 1st degree relative, tumor syndrome
- 1:2.5 male-to-female ratio, peak incidence 30-50y
- High rate of multicentricity
- Early lymphatic spread
- Excellent prognosis: 95% 10 year survival

Follicular Thyroid Cancer



- Increased incidence in geographic distributions associated with iodine deficiency
- 1:3 male-to-female ratio, peak incidence 40-60y
- Diagnosis of follicular cancer requires demonstration of cellular invasion of the capsule or vascular or lymphatic channels, not possible on FNA
- Lymph node involvement unusual (<10%)
- Earlier hematogenous spread to bone and lungs
- Prognosis less favorable than papillary thyroid cancer

Hürthle Cell Cancer



- Variant of follicular thyroid cancer
- Peak incidence 60-75y
- contains an abundance of oxyphilic cells, or oncocytes
- Lymph nodes metastasis is associated with poor prognosis
- Worse prognosis overall than follicular thyroid carcinoma

Prognostic Factors



	Low Risk	High Risk
Age	< 40	> 40
Gender	female	male
Extent	No local extension, intrathyroidal, no capsular invasion	Capsular invasion, extrathyroidal extension
Metastasis	none	Regional or distant
Size	< 2cm	> 4cm
Grade	Well differentiated	Poorly differentiated

AGES- Age, pathologic grade, extent, size

AMES- Age, Metastasis, extent, size

Papillary carcinoma FNA positive^a

- Consider chest x-ray
- Thyroid ultrasound, including lateral neck, if not previously done
- CT/MRI for fixed, bulky, or substernal lesions (avoid iodinated contrast, unless essential)
- Evaluate vocal cord mobility

- Indications for total thyroidectomy: (any present)
- Age < 15 y or > 45 y^b
 - Radiation history
 - Known distant metastases
 - Bilateral nodularity
 - Extrathyroidal extension
 - Tumor > 4 cm in diameter
 - Cervical lymph node metastases
 - Aggressive variant^c

- Indications for total thyroidectomy or lobectomy: (all present)
- Age 15-45 y^b
 - No prior radiation
 - No distant metastases
 - No cervical lymph node metastases
 - No extrathyroidal extension
 - Tumor < 4 cm in diameter
 - No aggressive variant^c

- Total thyroidectomy
If lymph node(s) palpable or biopsy positive:
- Central neck dissection (level VI)
 - Lateral neck dissection (levels II-IV, consider level V, sparing spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle); consider preservation of the cervical sensory nerves
- If node(s) negative, consider prophylactic central neck dissection (level VI; category 2B)^d

Total thyroidectomy (most common; category 2B)

or
Lobectomy + isthmusectomy (category 2B)

- Aggressive variant^c
- Macroscopic multifocal disease
- Positive isthmus margins
- Cervical lymph node metastases
- Gross extrathyroidal extension

- Negative margins
- No contralateral lesion

See Postsurgical Evaluation (page 1235)

Completion of thyroidectomy

- Consider thyroglobulin measurement
- Consider levothyroxine therapy to keep TSH low or normal^e

ATA Guidelines



- For patients with thyroid cancer >1 cm, the initial surgical procedure should be a near-total or total thyroidectomy unless there are contraindications to this surgery. Thyroid lobectomy alone may be sufficient treatment for small (<1 cm), low-risk, unifocal, intrathyroidal papillary carcinomas in the absence of prior head and neck irradiation or radiologically or clinically involved cervical nodal metastases. Recommendation rating: A

Patient Selection: Who is a Candidate for thyroid lobectomy?



- Age → *<45 or low risk tumor*
- Distant metastasis → none
- Size → *<1cm or <4cm*
- Extent of primary tumor → no extrathyroidal inv.
- Histologic grade/ type → low grade
- Multicentricity → no clinical/sono
- Cervical lymph node metastasis → none
- History of Radiation exposure → none

Lobectomy for WDTC



- Retrospective Review of 889 Patients with WDTC (T1T2 N0) operated on between 1986 and 2005 at MSKCC
- Patients with extrathyroidal extension, lymph node metastasis, distant metastasis and nodules in contralateral lobe (>0.5mm) were excluded

Table I. Patient, tumor and treatment characteristics

<i>Characteristics (N = 889)</i>	<i>n (%)</i>
Age	
<45 yr	425 (48)
>45 yr	464 (52)
Gender	
Male	188 (21)
Female	701 (79)
pT stage	
T1	637 (72)
T2	252 (28)
Pathology	
Papillary	800 (90)
Follicular	52 (6)
Hürthle cell	37 (4)
Risk group	
Low	374 (42)
Intermediate	457 (51)
High	58 (7)
Surgery	
Lobectomy	361 (41)
Total thyroidectomy	528 (59)

Risk Stratification



High Risk	High risk patient with high risk tumor		374 (42%)
Intermediate Risk	High risk patient with low risk tumor	Low risk patient with high risk tumor	457 (51%)
Low Risk	Low risk patient with low risk tumor		58 (7%)

High risk patients:

>45y

High risk tumor:

pT3/4, distant metastasis, high grade (follicular, Huerthle Cell)

Results



Table III. Patient characteristics, tumor characteristics, and outcomes stratified by surgical group

<i>Variable</i>	<i>Lobectomy</i> n = 361 n (%)	<i>Total thyroidectomy</i> n = 528 n (%)	<i>P value</i>
Age			
<45 yr	195 (54)	230 (44)	.002
>45 yr	166 (46)	298 (56)	
Gender			
Male	82 (23)	106 (20)	.345
Female	279 (77)	422 (80)	
pT stage			
pT1	249 (69)	388 (73)	.143
pT2	112 (31)	140 (27)	
RAI			
No	360 (99.7)	333 (63)	<.001
Yes	1 (0.3)	195 (37)	
Pathology			
Papillary Ca	310 (86)	490 (93)	<.001
Follicular Ca	36 (10)	16 (3)	
Hürthle cell Ca	15 (4)	22 (4)	
10-yr local recurrence	0 (0)	0 (0)	1
10-yr neck recurrence	0 (0)	5 (0.8)	.96
10-yr distant recurrence	0 (0)	5 (3)	.05
10-yr deaths of any cause	18 (7)	27 (9)	.64
10-yr disease-specific deaths	0 (0)	1 (1.5)	.246

RAI, Radioiodine ablation.

Results



Table IV. 10-year overall survival for lobectomy and total thyroidectomy groups stratified by pT, pT size, and risk group

Variable	n (%)	Overall 10-yr survival (%)		P value
		Lobectomy	Total thyroidectomy	
pT stage				
T1	632 (71)	92	89	.78
T2	252 (29)	96	94	.62
pT size (cm)				
<1	354 (40)	89	93	.27
1-2	283 (32)	94	87	.11
2-3	164 (18)	98	94	.93
3-4	88 (10)	94	92	.53
Risk group				
Low	374 (42)	97	96	.58
Intermediate	457 (51)	90	85	.36
High	58 (7)	90	96	.35

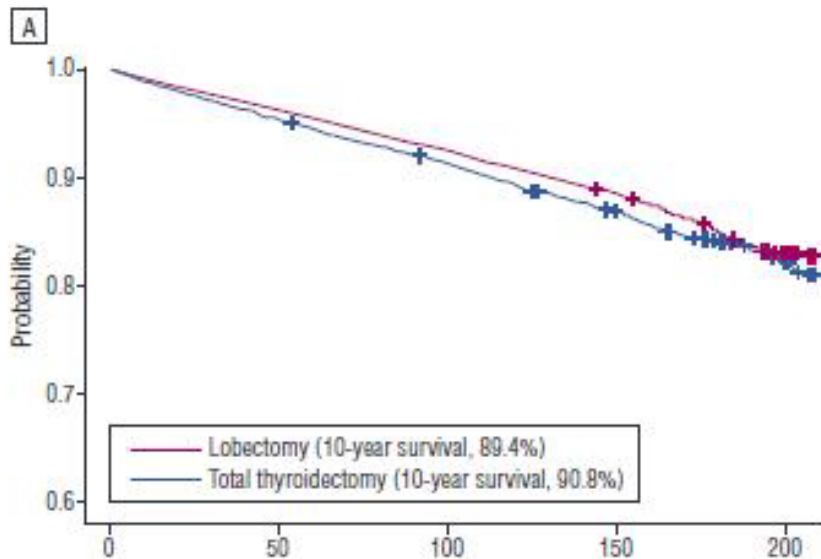
Lobectomy for WDTC



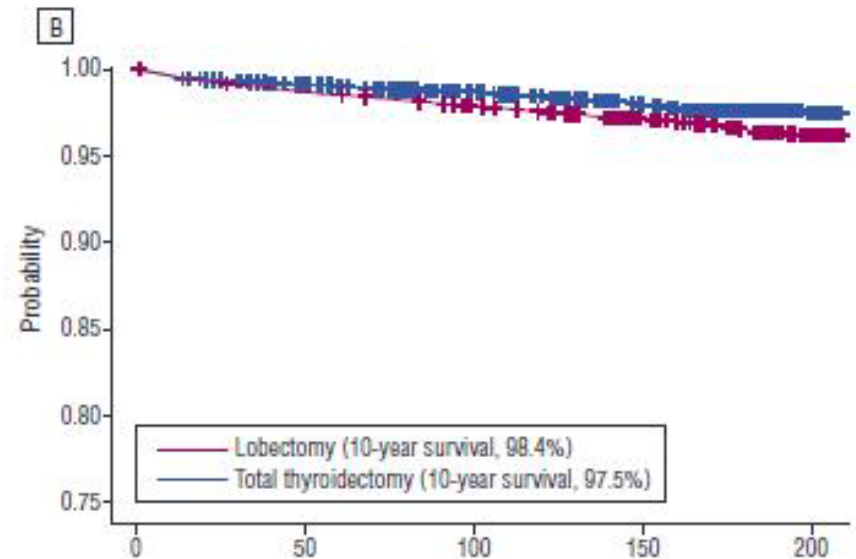
- Population-based cohort analysis using SEER database, including 22 724 patients with papillary thyroid cancer from 1988-2001
- Mean follow-up 109 months

	Lobectomy	TT
Patients:		
Number	1172 (19.7)	3825 (22.8)
Female	4792 (80.2)	12935 (77.2)
Age	46 (18-91)	43 (18-96)
Tumor:		
< 1.0	2657 (44.6)	3885 (23.2)
1.0-1.9	1335 (22.4)	5067 (30.2)
2.0-2.9	950 (15.9)	3942 (23.5)
3.0-3.9	488 (8.2)	1972 (11.8)
4.0-8.0	497 (8.3)	1788 (10.7)
>8.0	37 (0.6)	106 (0.6)
Localized	4990 (83.7)	11824 (70.5)
Loc invasive	944 (15.8)	4728 (28.2)
Metastasis	30 (0.5)	208 (1.2)
Pos LN	556 (9.3)	4666 (27.8)

Results



A: Overall Survival



B: Disease Specific Survival

Short-Term Outcomes after Thyroidectomy



- Cohort Analysis using NIS database, including 13 854 patients undergoing thyroid lobectomy or total thyroidectomy for cancer from 1999 to 2003

	Lobectomy	TT
Patients:		
Number	4238	9616
Age (mean)	49.7	47.5
Female	3318 (78%)	7224 (75%)
Hospitals:		
Small	422 (30%)	1004 (70%)
Large	2617 (29%)	6515 (71)
Rural	390 (43%)	518 (57%)
Urban	3847 (30%)	9098 (70%)
Teaching	2388 (28%)	6164 (72%)
Non-Teaching	1849 (35%)	3452 (65%)

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Complication Rate for Unilateral vs Total Thyroidectomy

TABLE 2. *Complication Rate for Unilateral Thyroid Lobectomy Compared with Complete Thyroidectomy*

Complication	Unilateral Thyroid Lobectomy Number (%)	Complete Thyroidectomy Number (%)	P Value
Myocardial infarction	4 (0.1)	9 (0.1)	0.9888
Cerebrovascular accident	0 (0.0)	4 (0.04)	—
Pulmonary embolus	2 (0.04)	7 (0.1)	0.5858
Pneumonia	16 (0.4)	45 (0.5)	0.4588
Renal failure	3 (0.1)	5 (0.1)	0.6714
Wound hematoma	34 (0.8)	97 (1.0)	0.2472
Wound infection	6 (0.1)	9 (0.1)	0.4288
Hypocalcemia	149 (3.5)	1,015 (10.6)	<0.0001
Hypoparathyroidism	11 (0.3)	132 (1.4)	<0.0001
Esophageal perforation	0 (0.0)	1 (0.01)	—
Tracheal/laryngeal perforation	0 (0.0)	0 (0.0)	—
Unilateral VCP	26 (0.6)	104 (1.1)	0.0085
Bilateral VCP	4 (0.1)	41 (0.4)	0.0016
TOTAL	255 (6.0)	1,469 (15.3)	0.0001

VCP, vocal cord paralysis.

TABLE 3. *Length of Stay, Total Charges, and Mortality Rate in Patients Undergoing Unilateral Thyroid Lobectomy and Complete Thyroidectomy for Malignancy*

Outcomes	Unilateral Thyroid Lobectomy Number (%)	Complete Thyroidectomy Number (%)	P Value
Length of Stay; days (range)	1 (0–83)	2 (0–62)	0.0001
Total charges; \$ (mean)	9,379	11,432	0.0001
Mortality; number (%)	9 (0.2)	12 (0.1)	0.22

Summary



- Patients with WDTC <4 cm without distant metastasis, lymph node metastasis, contralateral nodules and high grade tumor can be managed with thyroid lobectomy with similar excellent long term outcomes (OSS >90% at 10y)
- Thyroid lobectomy is associated with lower complications rates (hypocalcemia, hypoparathyroidism) compared to total thyroidectomy
- Recurrence in opposite lobe arises in less than 5% of patients and can be treated surgically
- Thyroid lobectomy is the appropriate treatment for small well-differentiated thyroid cancer in low risk patients

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- Nixon et al. Thyroid lobectomy for treatment of well differentiated intrathyroid malignancy. *Arch Otolaryngol Head Neck Surg.*2012;151(4):571-79
- Mendelsohn et al. Surgery for Papillary Thyroid Carcinoma. Is Lobectomy Enough? *Arch Otolaryngol head neck surg.*2010;136(11):1055-1061
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- Tuttle et al. Thyroid Cancer. *J Natl Comp Canc Netw* 2010;8:1228-1274
- Cooper et al. Revised American Thyroid Association Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2009;19(11):1167-1214
- Townsend: Sabiston Textbook of surgery 19th edition

Total Thyroidectomy for Well-Differentiated Thyroid Cancer

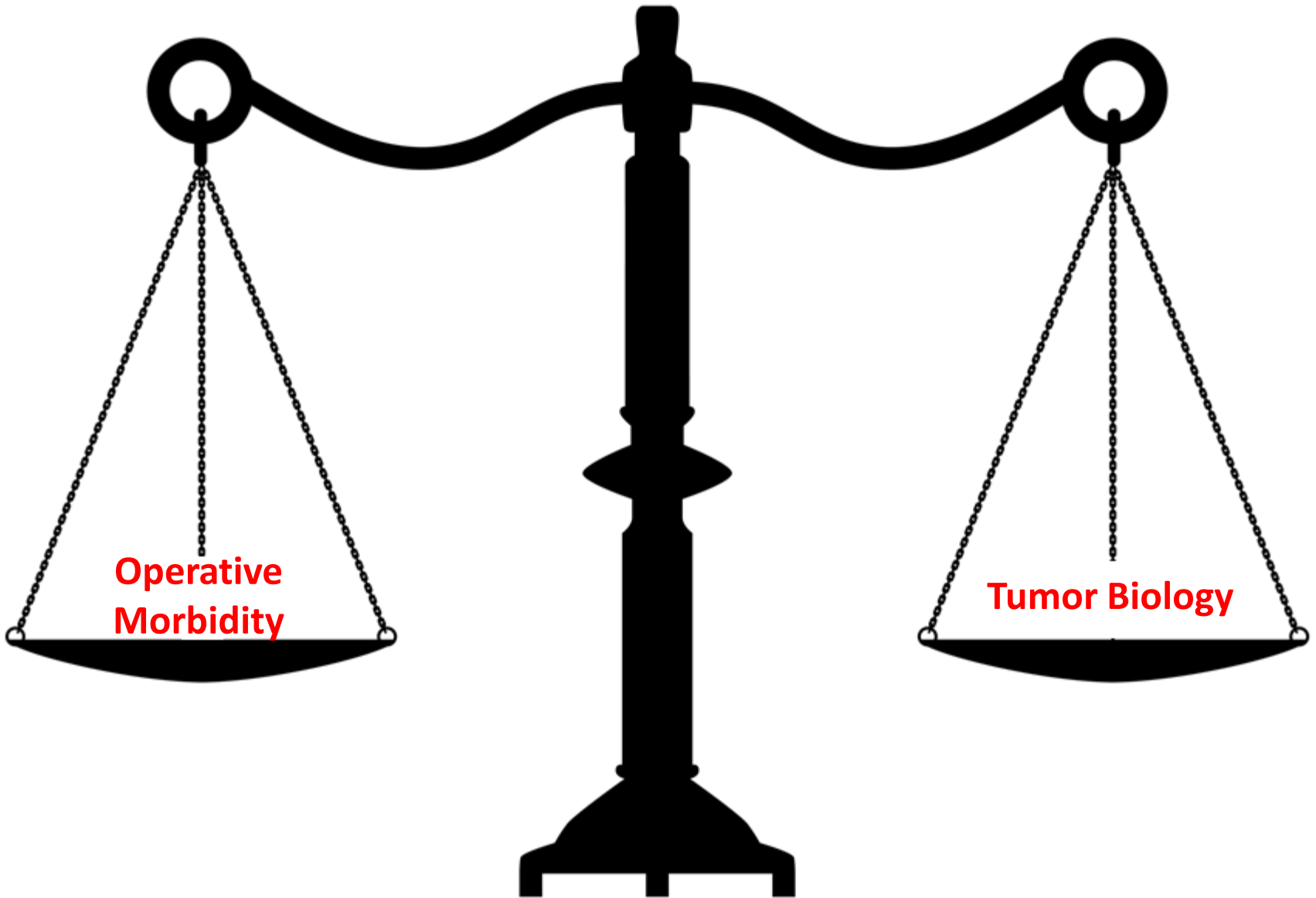


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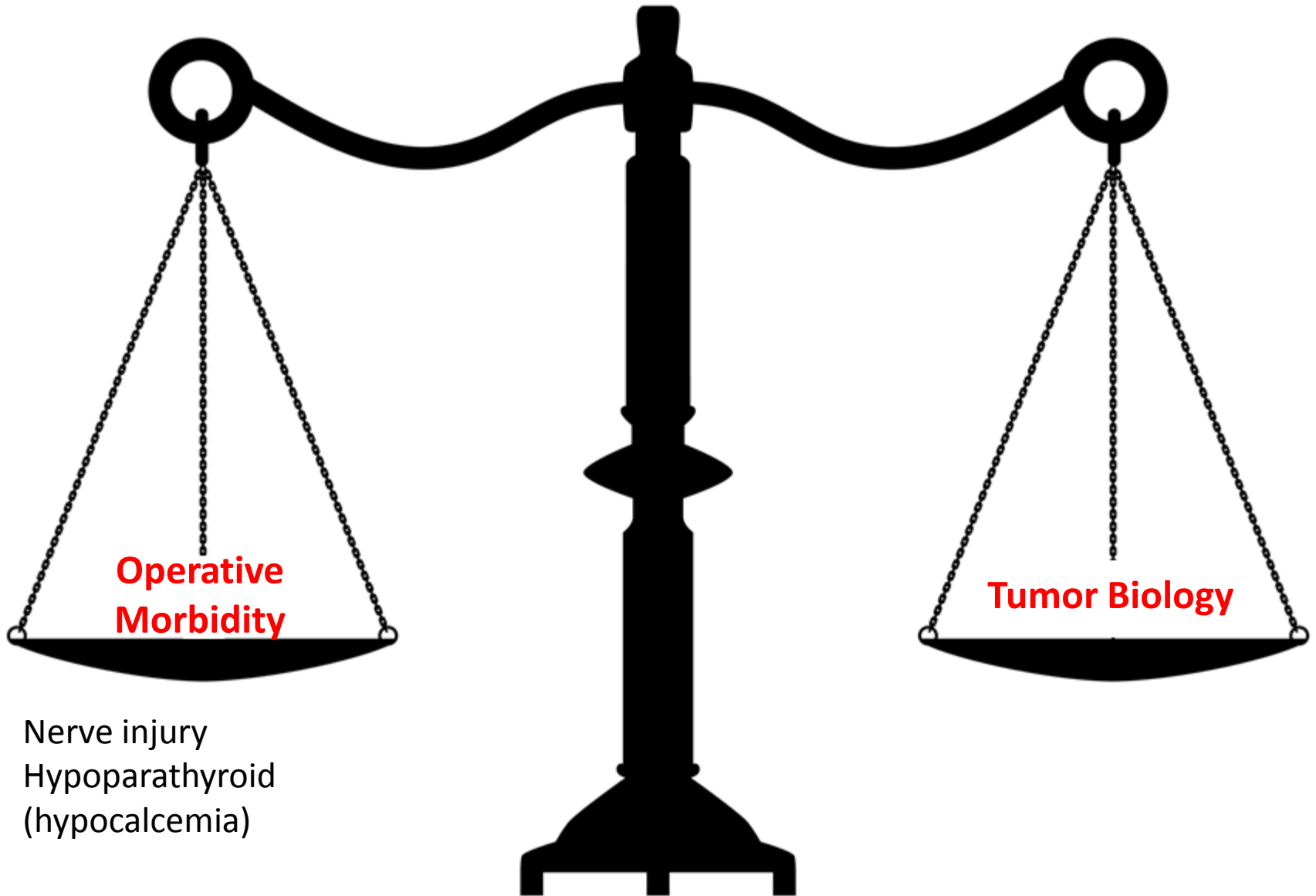


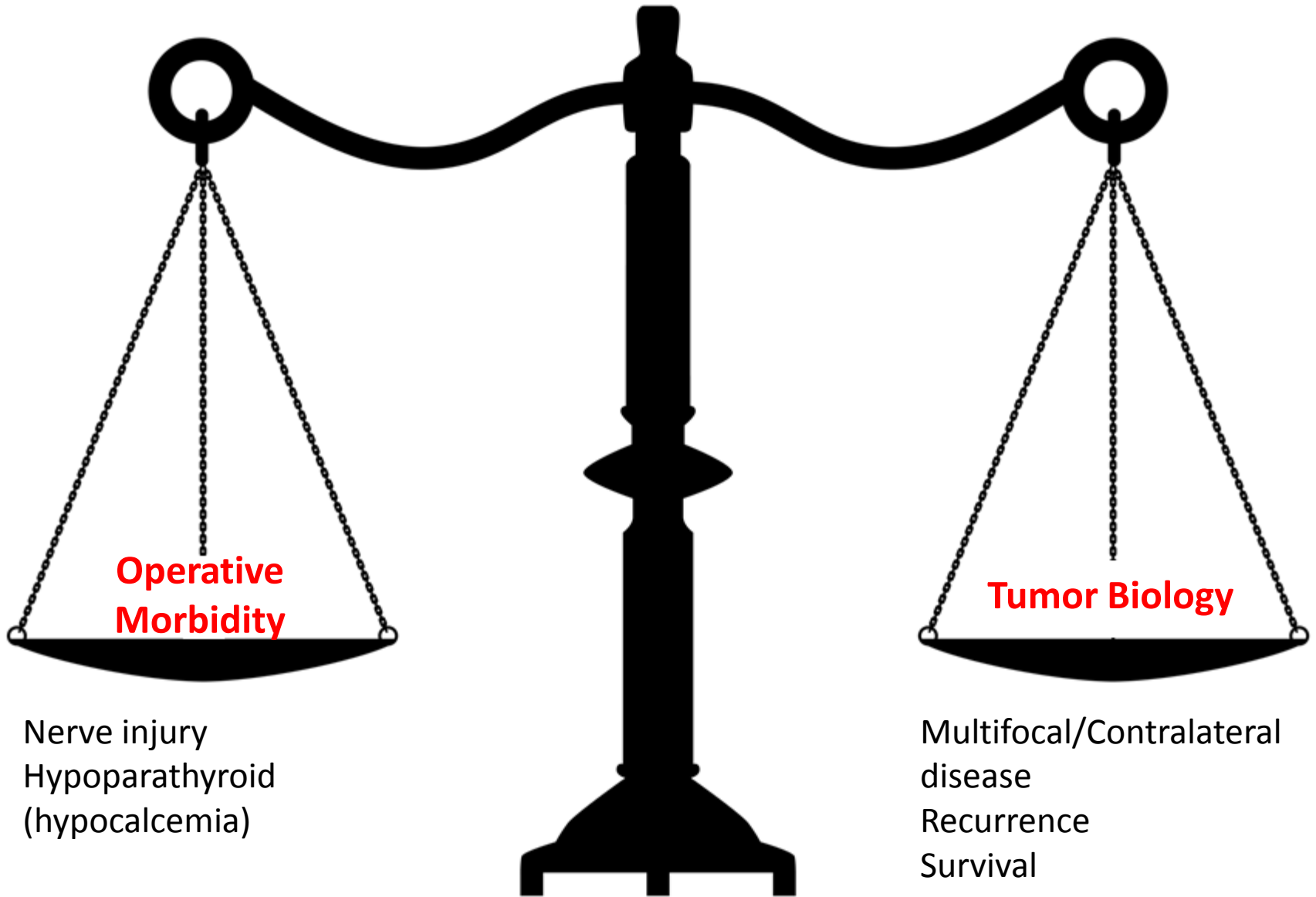
There are NO prospective randomized control trials on the management of well-differentiated thyroid carcinoma

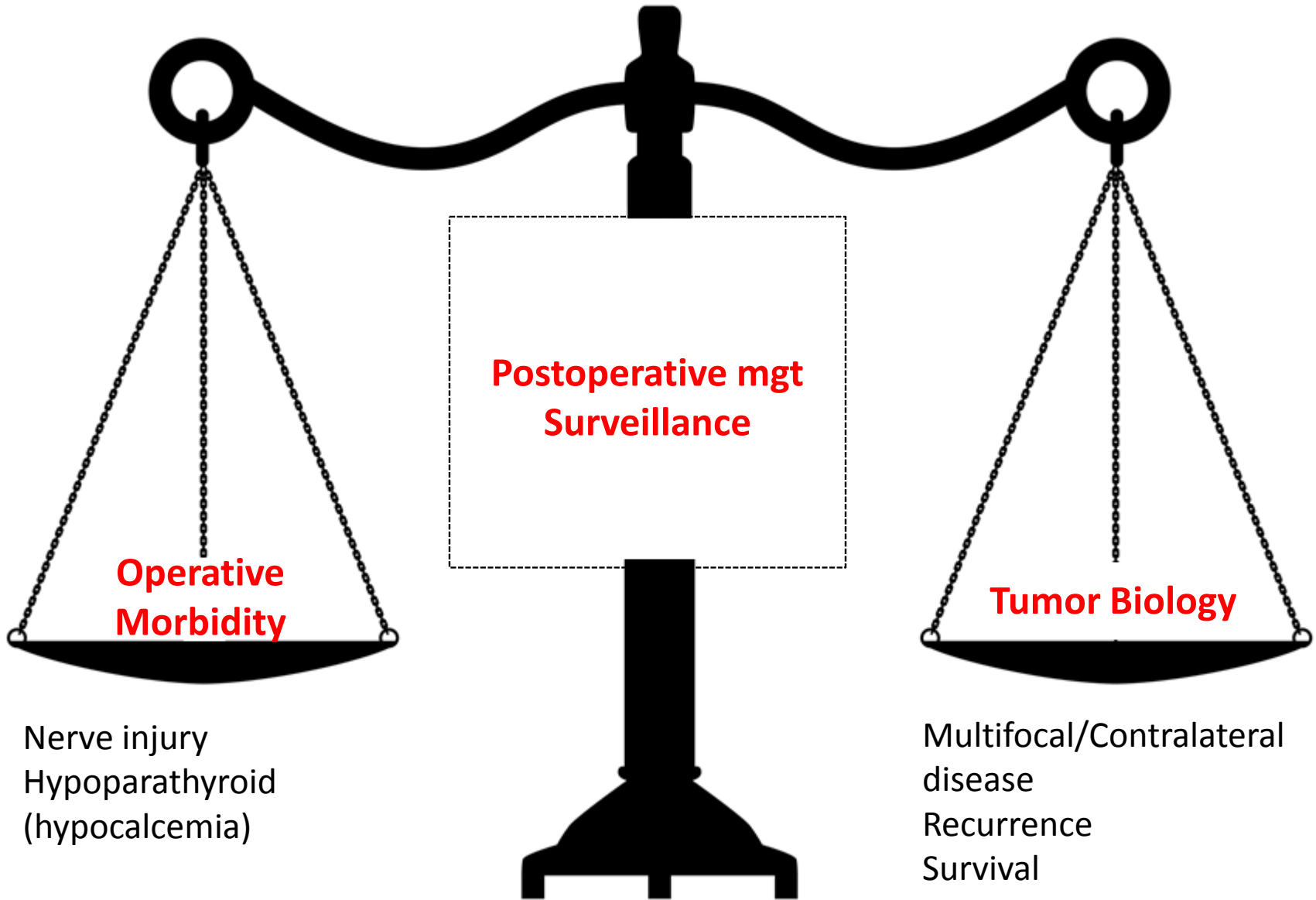


**Operative
Morbidity**

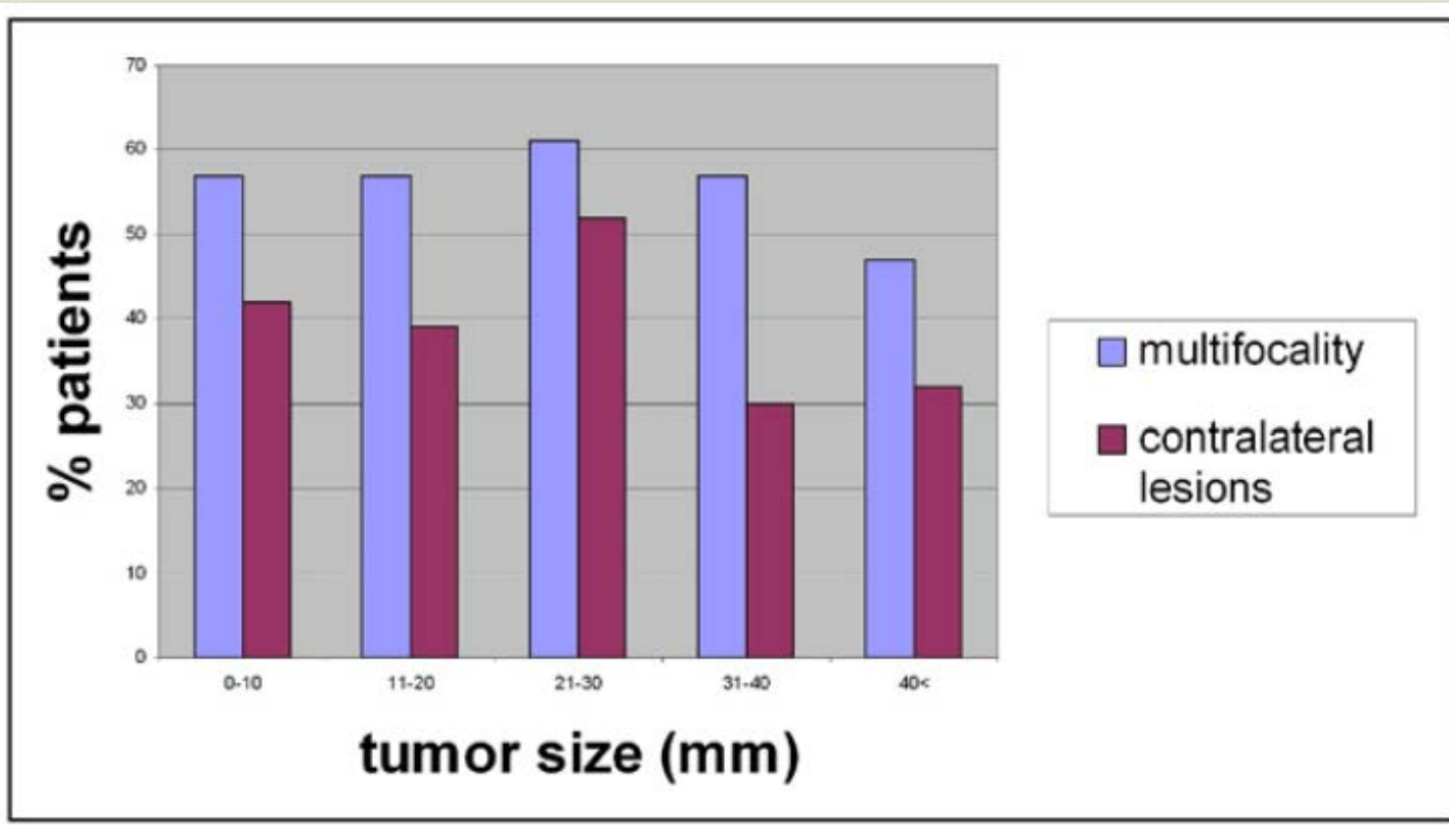
Tumor Biology







Incidence of Multifocality and Contralateral Lesions



Haggi et al. Multifocality in well-differentiated thyroid carcinomas call for total thyroidectomy. The American Journal of Surgery 2011; 201:770-775

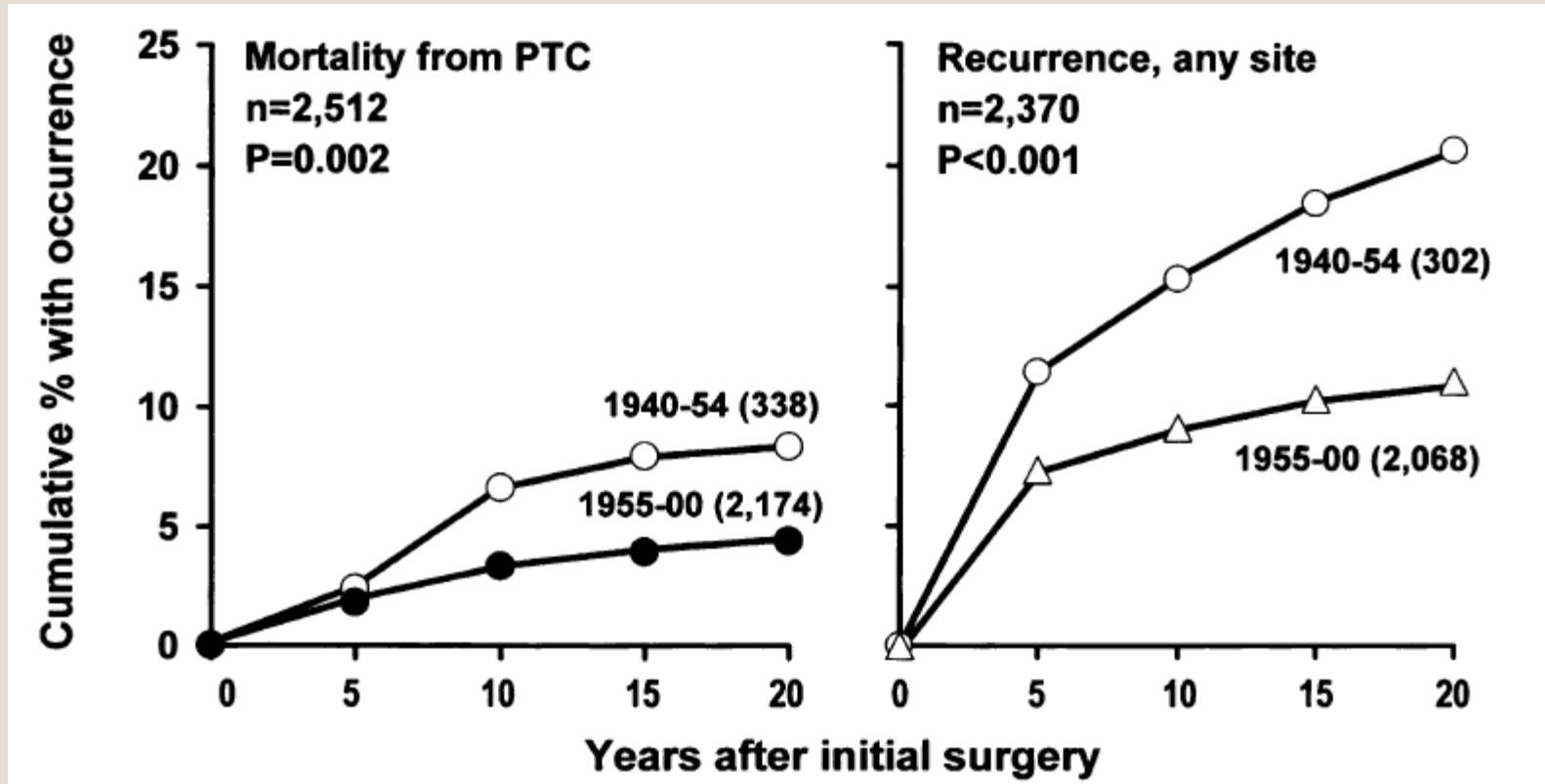
Multifocality as a risk factor for Contralateral disease



	Second surgery negative	Second surgery positive	
No. of patients ($n = 81$)	52	29	
Age (years)	40.2 ± 12.2	41.7 ± 12.0	ns
Histopathologic diagnosis			ns
Follicular carcinoma	36	17	
Papillary carcinoma	13	11	
Initial tumour size (cm)	3.9 ± 2.1	3.3 ± 1.4	ns
Cancer multifocality (%)	14 (26.9)	20 (69.0)	$P < 0.001$
Coexistent benign nodule	8	5	ns
Nodes positive at first operation	1/52	2/29	ns
Extrathyroidal extension	4/52	2/29	ns

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Recurrence and Mortality



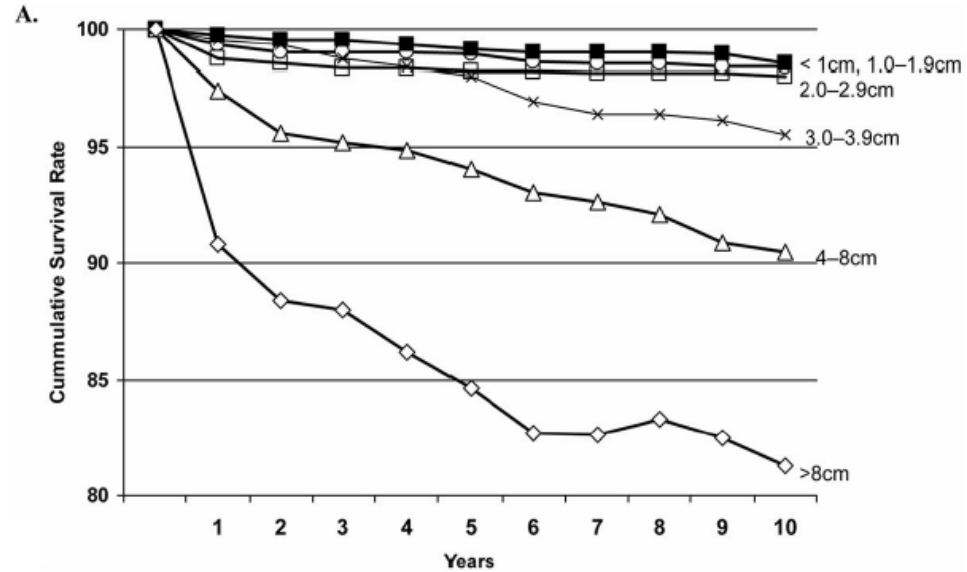
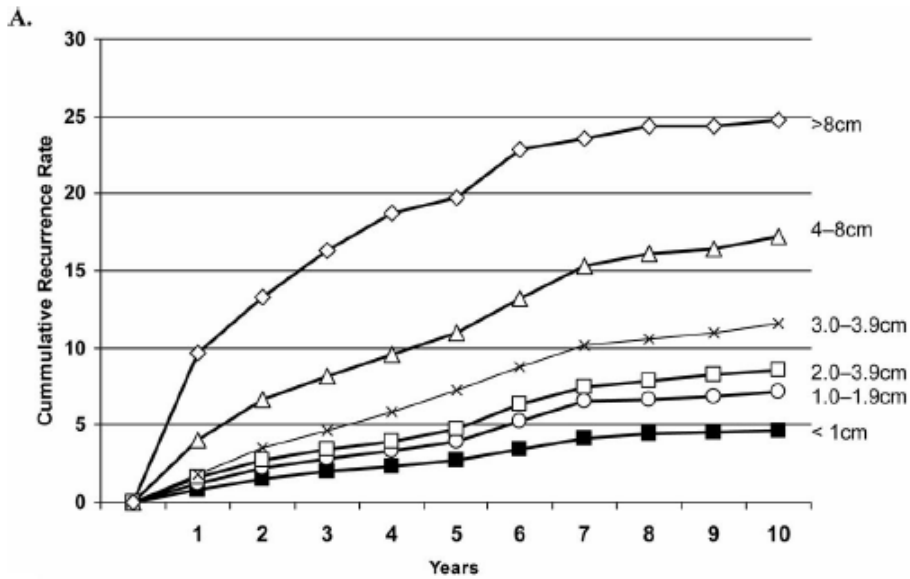
Hay et al. Managing Patients with Papillary Thyroid Carcinoma: Insights Gained from the Mayo Clinic's Experience of Treating 2512 Consecutive Patients During 1940 Through 2000. Transactions of the American Clinical and Climatological Association 2002; 113:241-261.

Tumor Size



Recurrence Rate

Survival Rate



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Recurrence and Survival Risk



TABLE 2. Cox Proportional Hazards Analysis Stratified by Tumor Size Demonstrating the Risk of Recurrence and Death for Patients Who Underwent Lobectomy Compared to Total Thyroidectomy for PTC

	Hazard Ratio (95% Confidence Interval)				
	All Patients	< 1.0 cm	≥ 1.0 cm	1.0–2.0 cm	2.1–4.0 cm
No. patients	42,952	10,247	32,705	12,778	16,365
Recurrence					
Total thyroidectomy	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Lobectomy	1.57 (1.20–2.06) <i>P</i> = 0.001	1.01 (0.77–1.32) <i>P</i> = 0.24	1.15 (1.02–1.30) <i>P</i> = 0.04	1.24 (1.01–1.54) <i>P</i> = 0.04	1.26 (1.03–1.42) <i>P</i> = 0.03
Survival					
Total thyroidectomy	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Lobectomy	1.21 (1.02–1.44) <i>P</i> = 0.027	1.02 (0.74–1.41) <i>P</i> = 0.83	1.31 (1.07–1.60) <i>P</i> = 0.009	1.49 (1.02–2.17) <i>P</i> = 0.04	1.31 (1.01–1.69) <i>P</i> = 0.04

Hazard Ratios greater than 1.0 indicate increased risk of recurrence or death.

*Adjusted for gender, age, race, nodal status, distant metastases, socioeconomic factors, RAI administration, year of diagnosis, and hospital volume.

Operative Morbidity



- Hypoparathyroidism
 - Hypocalcemia is usually transient
- Recurrent laryngeal nerve injury

- Sosa et al. (1998) “The importance of surgeon experience for clinical and economic outcomes from thyroidectomy” *Annals of Surgery*

Post-operative management and Surveillance



- Radioiodine Ablation
- Enhances monitoring for recurrence
 - Thyroglobulin level
 - Radioiodine scanning



Summary



- High incidence of multifocal and contralateral disease in well-differentiated thyroid carcinoma
- Total thyroidectomy has a lower incidence of local and region recurrence
- Operative morbidity is comparable in the hands of experienced surgeons
- Allows more effective and lower dose of radioiodine ablation for treatment of metastatic disease
- Most effective use of serum thyroglobulin level and radioiodine scan for detection of recurrent disease

References



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