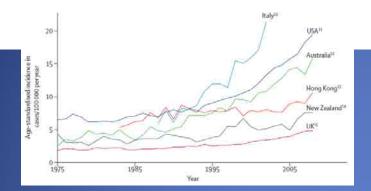
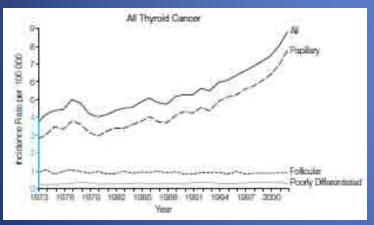


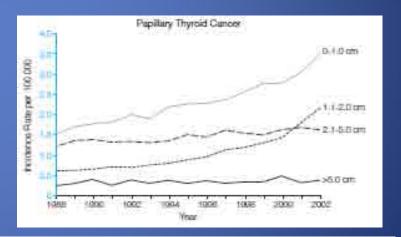
**3^ Divisione Chirurgia Generale** Spedali Civili di Brescia

There is an increasing incidence (3-fold) of DTC over recent decades. The entire increase is attributable to Papillary Thyroid Cancer. 87% of the increase is attributable to tumors measuring less than 2 cm.



Davies L., et al., Arch. Otolaryngol. Head Neck Surg. 2010 Davies L., et al. JAMA 2006



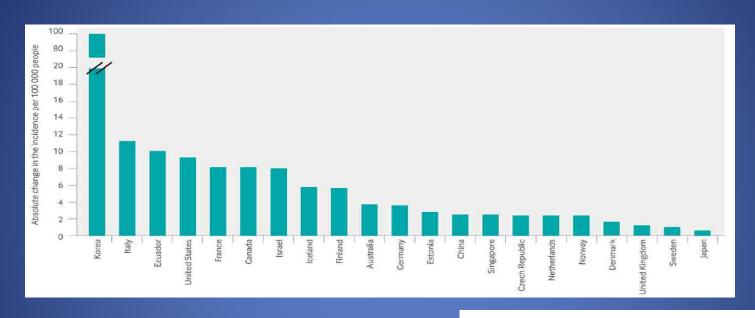


Epidemic of diagnosis: opportunistic screening, diagnostic cascade, serendipitous detection

Davies L., et al. JAMA Otolaryngol. Head Neck Surg. 2014

... a low share of public health expenditure is associated with a high incidence of thyroid cancer.

Lee T.J., et al. JKMS, 2012



Curado M.P., et al. Intern. Ag. Res. Cancer, 2007

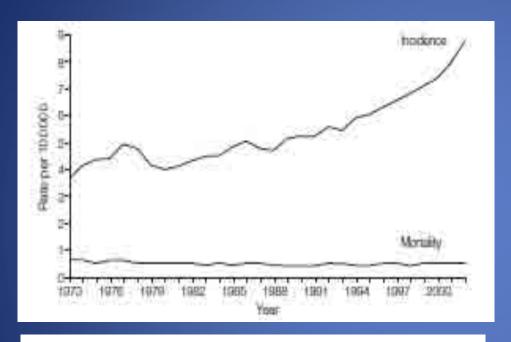
DTC is pojected to surpass rectal cancer in 2019 and colon cancer in 2039

Lang B.H.-H., et al. EJSO, 2015

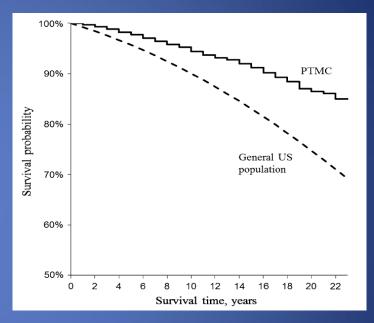
The total costs in 2013: \$1.6 bilion dollars, in 2030: \$3.55 billion dollars

Lubitz C.C., et al. Cancer 2014

# Despite its high prevalence DTC is an uncommon cause of death. Most patients with these lesions have an excellent prognosis.



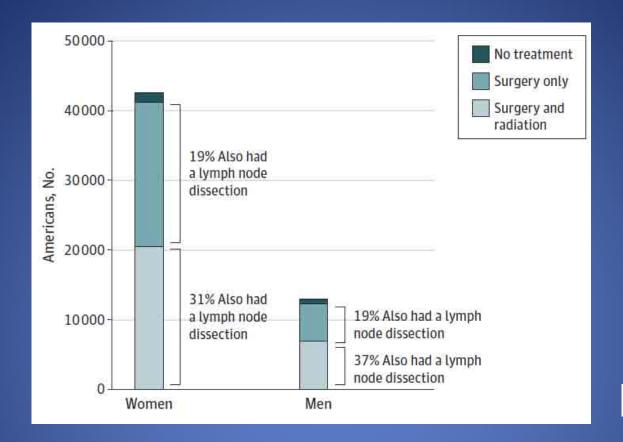
Davies L., et al. JAMA Otolaryngol. Head Neck Surg. 2014



Wang T.S., et al., WJS, 2014

DTC is common among people who die from non-thyroid related cause

Harach H.R., et al. Cancer, 1985 Martinez-Tello F.J., et al. Cancer, 1983



**SEER 9, april 2013** 

Many patients with LOW RISK DTC receive similar care to that for more aggressive disease and worse prognosis: total thyroidectomy is performed for 85% of people diagnosed as having DTC. Many also undergo a lymph node dissection. Half of patients received radiation treatment.

Davies L. et al. JAMA Otolaryngol. Head Neck Surg. 2014

	ATA (2006)	BTA (2007)	AACE/AAES (2001)
Extent of thyroidectomy			
Total or near-total	Age≥45	T>1 cm	High-risk cancer
thyroidectomy	T>1-1.5 cm	Ex (+)	Ex (+)
	N (+)	N (+)	N (+)
	M (+)	Multiple lesions	M (+)
	Bilateral nodularity	Radiation history	
	Radiation history	Family history	
	Family history		
Lobectomy	Other than above	T≤1 cm	T≤1 cm
(+isthmusectomy)		N0	Ex0
			N0
			M0
Lymph node dissection			
Central compartment dissection	N.R	N.R	N.R.
Lateral compartment dissection	N.R	N.R	N.R

Because of the indolence and slow growth of DTC, the studies with very large numbers and long follow-up are retrospective, often with some biases or deficiences in recording analysis.

There are not including randomized studies.

Most patients who undergo total thyroidectomy may also undergo RAI ablation therapy, which means that these studies may not have compared total thyroidectomy with limited thyroidectomy

### «...factors that had not influence on survival were lymph node status, <u>CHOICE</u> <u>OF INITIAL SURGICAL TREATMENT</u>, and a hystory of prior irradiation...»

Cunnigham M.P., et al., Am. J. Surg., 1990

...less extensive initial surgery no affect the cause specific survival...

Tsang R.W., et al. Cancer 1998

«...multivariate analysis revealed that the <u>extent of surgical resection</u> does not impact a significant DSS or OS benefit...»

Mendelsohn A.H., et al. JAMA Otoralingol. Head Mneck Surg. 2010

Hindawi Publishing Corporation Journal of Thyroid Research Volume 2013, Article ID 398194, 5 pages http://dx.doi.org/10.1155/2013/398194

#### Clinical Study

Thyroid Lobectomy Is Associated with Excellent Clinical Outcomes in Properly Selected Differentiated Thyroid Cancer Patients with Primary Tumors Greater Than 1 cm

Fernanda Vaisman, <sup>1,2</sup> Denise Momesso, <sup>1</sup> Daniel A. Bulzico, <sup>2</sup> Cencita H. C. N. Pessoa, <sup>2</sup> Manuel Domingos Gonçalves da Cruz, <sup>3</sup> Fernando Dias, <sup>4</sup> Rossana Corbo, <sup>1,2</sup> Mario Vaisman, <sup>1</sup> and R. Michael Tuttle<sup>5</sup> thyroid lobectomy to be an acceptable alternative to total thyroidectomy in properly selected differentiated thyroid cancer patients with primary tumors greater than I cm.

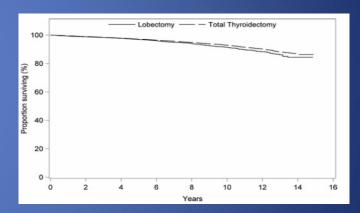
### Extent of Surgery for Papillary Thyroid Cancer Is Not Associated With Survival

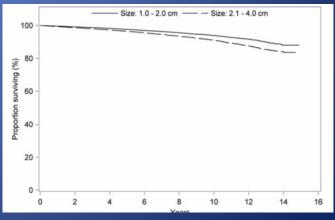
An Analysis of 61,775 Patients

Mohamed Abdelgadir Adam, MD,\* John Pura, MPH,† Lin Gu, MS,† Michaela A. Dinan, PhD,‡ Douglas S. Tyler, MD,\* Shelby D. Reed, PhD,‡ Randall Scheri, MD,\* Sanziana A. Roman, MD,\* and Julie A. Sosa, MD, MA\*‡

Ann. Surg. 2014

Conclusions: Current guidelines suggest total thyroidectomy for PTC tumors > 1 cm. However, we did not observe a survival advantage associated with total thyroidectomy compared with lobectomy. These findings call into question whether tumor size should be an absolute indication for total thyroidectomy.



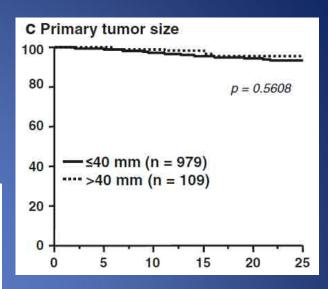




### Thyroid Lobectomy for Papillary Thyroid Cancer: Long-term Follow-up Study of 1,088 Cases

Kenichi Matsuzu · Kiminori Sugino · Katsuhiko Masudo · Mitsuji Nagahama · Wataru Kitagawa · Hiroshi Shibuya · Keiko Ohkuwa · Takashi Uruno · Akifumi Suzuki · Syunsuke Magoshi · Junko Akaishi · Chie Masaki · Michikazu Kawano · Nobuyasu Suganuma · Yasushi Rino · Munetaka Masuda · Kaori Kameyama · Hiroshi Takami · Koichi Ito

Conclusions The long-term clinical outcome of the PTC patients who had been treated by lobectomy without RAI ablation was excellent. Based on the above results, we concluded that lobectomy is a valid alternative to total thyroidectomy for the treatment of PTC patients who are younger than aged 45 years, whose tumor diameter is 40 mm or less, and who do not have clinical lymph node metastasis or extrathyroidal invasion.

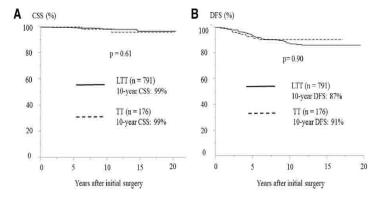


Risk-adapted management of papillary thyroid carcinoma according to our own risk group classification system: Is thyroid lobectomy the treatment of choice for low-risk patients?

Aya Ebina, MD, \* Iwao Sugitani, MD, PhD, \* b Yoshihide Fujimoto, MD, PhD, \* and Keiko Yamada, MD, PhD, \* Tokyo, Japan

Surgery, 2014

Diameter 1 - > 3 cm



**Fig 2.** (*A*) Cause-specific survival (CSS) curves for low-risk group patients who underwent less-than-total thyroidectomy (LTT) or total or near-total thyroidectomy (TT). (*B*) Disease-free survival (DFS) curves for low-risk group patients who underwent less-than-total thyroidectomy (LTT) or total or near-total thyroidectomy (TT).

References	No. of patients	Mean follow-up in months (range)	10-year OS total thyroidectomy	10-year O5 lobectomy	P	DFS total thyroidectomy	DFS lobectomy	p
Momesso 2014 [42]	176 DTC ≤2cm low-risk	169 (115-223)	98.2%	100%	0.2	80.9%	89.4%	0.2
Ebina 2014 [44*]	967 PTC low-risk	99 (36-240)	99%	99%	0.61	91%	87%	0.9
Adam 2014 [50¶]	61775 PTC 1-4 cm	82 (60–179)	Unadjusted OS 92.9% Adjusted OS -	Unadjusted OS 91.4% Adjusted OS HR 0.96 (0.84-1.09)	<0.001 P= 0.54	a(	¥	Ψ
Nixon 2012 [64]	889 DTC T1T2N0	99 (13-291)	92%	93%	0.64	98.5%	100%	0.246
Ito 2010 [39]	2638 T1N0M0	91 [6-240]		¥	÷	98.4%	97.2%	0.017
Bilimoria 2007 [30]	≤1 cm 52 173; All size	69.7	98.4%	HR1.02 (0.74-1.41) 97.1%	0.83	92.3%	HR1.01 (0.77=1.32) 90.2%	0.24
Hay 2008 [71]	900 PTM	206 (1-648)		#		95.5%	94.3%	0.54
Hoigh 2005 [41]	PTC 4402 low risk PTC 1030 high risk	88 (1–144)	89% 72%	91% 78%	<0.07 0.14	#1 3	E	8

It is difficult to show benefit of any intervention when the risk of mortality is close to 1-2% after 20 years of follow-up.

Brito J.P., et al. BMJ 2014

Thyroid lobectomy and isthmusectomy is a definitive treatment for patients with a benign follicular adenoma and patients with minimally invasive follicular cancer

McHenry C.R., et al. The Oncologist, 2011

Hemithyroidectomy was adequate definitive treatment in 87% of patients with follicular neoplasms

Chiu C.G, et al. Can. J. Surg. 2012

Hemithyroidectomy was considered adequate for treatment in 96% of patients (with cytological diagnosis of follicular neoplasms), and no further operation was required

Wiseman S.M., et al. Ann. Surg. Oncol. 2006

Hemithyroidectomy seems to be the preferable initial surgical approach (in 89.48% of patients) for indeterminate follicular lesions

Dobrinja C., et al. Ann. Ital. Chir. 2010

### Intrathyroidal metastases in controlateral lobe, because bilateral cancers have been reported in 30-85% of PTC

Russel W.O., et al., Cancer 1996 Samaan N.A., J. Clin. Endocrinol. Metab. 1983 Clark R.L., et al., Ann. Surg. 1959

The recurrence rate in the remanant thyroid gland at 25 years is just 6.5%

Matsuzu K. Et al., WJS, 2014 Hay I.D. et al., Surgery 1993 Grant C.S., et al., Surgery 1988

Discrepancies between the clinical recurrence rate and the potential recurrence rate

The possibility of intrathyroidal metastasis in controlateral lobe is <u>not alone a</u> <u>sufficient reason to justify routine total thyroidectomy in all cases</u>

#### **RAI** ablation:

- -indication in PTC patients have not yet been clearly defined
- -its therapeutic use has recently been revised (increased risk of secondary cancers)
- -in USA only 56% of the patients who had undergone TT underwent postoperative RAI ablation

Billimoria K.Y., et al. Ann. Surg. 2007 Sawla A.M., et al. Thyroid, 2009 Schvartz C., et al. J. Clin. Endocrinol. Metab. 2012 Gepalakrishna n., et al. Cancer 2011

Use of radioiodine after thyroid lobectomy in patients with differentiated thyroid cancer: does it change outcome?

Kiernan C.M., et al. J. Am. Coll. Surg. 2015

I-131: its diagnostic use is increasingly being supplanted by US and MR, which are more reliable than I-131 in patients with advanced disease

Molver B. Oral Oncol. 2013

Tg assay after conservative surgery: looking at the trend of values

Vaisman F., et al. J. Thyroid Res. 2013

### Recurrence can occur in 3 forms:

- -Distant metastasis
- -«true» local recurrence
- -Disease within lymph nodes (LNM)

90% of recurrence is LNM (most likely represent disease persistence)

Recurrence rates of 4-10% in patients with low-risk after conservative treatment 6.9% in the cervical LNM, 1.6% in the remnant thyroid and 1.3% in distant sites In high-risk patients recurence rates are as high as 20-40%

Sugitani I. et al., Surgery 2004 Haigh P.I., et al., Ann. Surg. Oncol., 2005

Cervical recurrence are reported to have little to no effect on survival: 8% of patients die of locoregional recurrence

Saha A.R., et al. Laryngoscope 2004 Mazzaferri E.L., et al. Am. J. Med. 1994 Schlumberger M.J., et al. J. Endocrinol. Invest. 1999

Guo K., et al., Int. J. Ex. Pathol., 2014

Reference	Country	Study of year	Rec/Total patients (%)	Follow-up durations	Mean Rec time	DFS	DSS
Albuja-Cruz [11]	America	2012	9/117 (8%)	25 (1-256) M	35 m	5-(1)	-
Baek [12]	Korea	2010	33/189 (17.5%)	81 (48-386) M	=	LNM (+) 77.8% LNM (-) 57.9% (P < 0.05)	_
Grogan [13]	America	2013	75/269 (28%)	11-27 у	8.1 y	10-year 81.0% 20-year 75.1% 30-year 73.2% 40-year 72.1%	10-year 94.8% 20-year 92.6% 30-year 92.2% 40-year 91.1%
Kim 2012 [14]	Korea	2012	36/416 (8.7%)	120.79 M	87 m	10-year 90.4%	10-year 91.6% 100% (one) 83.1% (multiple)
Kim 2013 [15]	Korea	2013	138/2095 (6.6%)	84 (1-188) M	43 (11-130) m	<u>1-01</u>	-
Kruijiff [16]	Australia	2014	94/1183 (7.9%)	-	31 (6-407) m	5-year 95% 10-year 92%	10-year 98.9%
Leboulleux [17]	France	2005	8/148 (7%)	8 (0.1-6 y)	4.7 (1-7) y	5-year 96% 10-year 91%	10-year 99%
Ma [18]	China	2013	18/206 (8.7%)	4.1 (3-5) y	30.4 (3-42) m	===	-
Ryu [19]	Korea	2014	17/295 (5.8%)	78 (63-137) M		5-year 94.6% 10-year 92.8% LNR ≤ 0.65 98.6% LNR > 0.65 75.4% (P < 0.001)	10-year 100%
Shah [20]	America	2012	27/444 (6.1%)	27.5 M	21 m	10-year 93.9%	10-year 100%
Tanaka [21]	Japan	2004	39/386 (10.1%)	125 m	3	20-year 87%	10-year 97.8% 20-year 96%
Toniato [22]	Italy	2008	79/950 (7.8%)	7.8 (2-17) y	=	<del>50</del>	10-year 91.38% 15-year 88.69%
Zhao [23]	China	2013	109/459 (23.7%)	> 5 y	40 (1.5-108) m		-

Risk factors influencing recurrence: male, extrathyroid extension, LNM, tumor size more than 2 cm, distance metastases, subtotal thyroidectomy

Dan Decurrence DEC	Disposa Fron Curvival- DCC	Disease-Specific Survival: LNM	Lumnic Mada Matactacie: I MD	Lumnii Made Datin

Table 1. Characteristics of studies included in the meta-analysis

	subtotal dessect	Rec(+)	total dessect /	Rec(+)		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Baek 2010	0	11	33	178	6.2%	0.19 [0.01, 3.28]	•
Grogan 2013	32	72	39	167	20.1%	2.63 [1.46, 4.72]	
Kim 2012	7	84	29	332	16.5%	0.95 [0.40, 2.25]	<del>-</del>
Ma Zhenhai 2013	11	56	7	150	4.7%	4.99 [1.83, 13.64]	<del></del> (
Tanaka 2004	7	154	14	88	26.2%	0.25 [0.10, 0.65]	
Toniato 2008	10	53	69	897	9.6%	2.79 [1.34, 5.79]	
Zhao Cui 2013	81	188	19	186	16.7%	6.65 [3.82, 11.60]	-
Total (95% CI)		618		1998	100.0%	2.38 [1.81, 3.12]	•
Total events	148		210				
Heterogeneity: Chi2=	44.44, df = 6 (P < 0.	00001); [7:	= 86%				100
Test for overall effect						F	0.01 0.1 1 10 100 Favours [experimental] Favours [control]

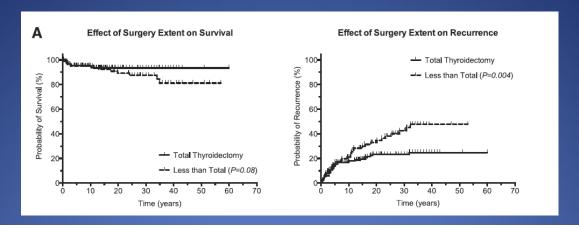
TABLE 4 Summary of recent studies that examined the recurrence rate of papillary thyroid cancer Median ORR Disease Surgical extent RAI Primary endpoint Study (year) patients F/U (%) ablation Recurrence Thyroid (%) Level Level Cancer-(years) II-V VI specific mortality Matsuzu et al. 1088 17.6 CPTC Size, ETE CELNM 9.4 LTT Age, size. 201422 ETE Kruiff et al. 1183 26 7.9 PTC TT Age, sex, size, LN, vascular NA 201325 invasion, ETE Barczyński et al. 760 5 PTC LN, LN ratio NA 201424 27 28.0 PTC TT (66)/LTT (31)/ Rogan et al. 269 Age, FVPTC, TNM stage Age, TNM 2013<sup>25</sup> unknown (3) stage Schneider et al. 217 NA 23.2 PTC LN ratio NA 201326 Durante et al. 1020 10.4 PTC TT ATA risk NA 1.4 201317 Kim et al. 201327 2095 2.1 PTC Size, LN, distant metastasis, NA multifocality, cLNDb Ito et al. 201228 5768 Ю 7.0 PTC TT (51)/LTT (49) Age, sex, ETE, size, CELNM NA Shah et al. 2012 2.3 29.0 PTC NA CELNM NA Tuttle et al. 7 1.4 TC TT NA. ATA risk, response to therapy NA 201031 Back et al. 189 6.8 17.5 PTC TT (94.2)/LTT (5.8) N stage NA 2010 Lin et al. 200932 1682 7.7 14.4 PTC TT (58.9)/LTT (41.1) Multifocality<sup>h</sup> Multifocality Kim et al. 20083 PTMC 5.4 5.0 TT (56.4)/LTT (43.6) Sex. N stage NA PTC Bilimoria et al. 52,173 TT (82.9)/LTT (17.1) NA Size, surgical extent Size, surgicul 200734 extent

F/U follow-up, ORR overall recurrence rate, cPTC conventional papillary thyroid carcinoma, PTC papillary thyroid carcinoma, TC thyroid carcinoma, TC conventional papillary thyroid microcarcinoma. FVPTC follicular variant papillary thyroid carcinoma, LTT less than total, TT total thyroidectomy. ETE extrathyroidal extension, CELNM clinically evident lymph node metastasis, LN lymph node, cLND central lymph node dissection, NA not available, RAI radioactive iodine, ATA American Thyroid Association, + indicates performed in all patients, - indicates performed in no patients, ± indicates performed in some patients

Conclusions. Tumor size, bilaterality, gross ETE, lymph node metastasis, and vascular invasion were associated with locoregional recurrence. Evaluation of these prognostic factors appears to help identify patients who require close monitoring.

a Only 84 patients received RAI ablation in this study

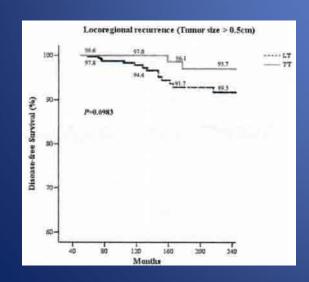
b Persistence was considered in addition to recurrence

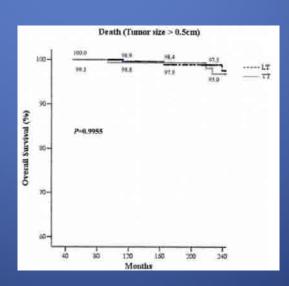


11% of recurrences and 17% of deaths occurred after 20 years, furthermore 4% of recurrences and 13% of deaths occurred more than 30 years after the diagnosis of thyroid cancer.

Risk factors for recurrence were older age, FVPTC, T4 tumors, cervical limph node involvement, metastases, and stage > 4°

Grogan R.H., et al., Surgery 2013

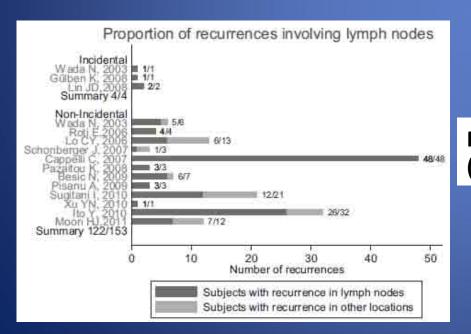




Clinical-pathological features of mPTC incidental or not incidental in different series.

Author (ref)	Diagnosis	Patients	Multicentric	Bilateral	Invasive	Lymph node metastases	Distant metastases
Baudin et al <sup>46</sup>	Incidental	189	56 (30%)	25 (13%)	21 (11%)	41 (22%)	0 (0%)
	Not incidental	92	56 (61%) <sup>a</sup>	$21(23\%)^{a}$	21 (23%) <sup>a</sup>	89 (91%) <sup>a</sup>	$8(8.6\%)^{a}$
Pellegriti et al <sup>66</sup>	Incidental	151	37 (24.5%)	22 (14.6%)	16 (10%)	24 (15.9%)	1 (0.7%)
	Not incidental	148	58 (39.2%) <sup>a</sup>	33 (22.3%)	38 (25%) <sup>a</sup>	66 (44.6%) <sup>a</sup>	7 (4.7%)
Roti et al <sup>48</sup>	Incidental	52	10 (19%)	6 (11%)	8 (15%)	2 (4%)	0 (0%)
	Not incidental	191	68 (36%)	39 (20%)	34 (18%)	30 (16%)	4 (2%)
Chung-Yau et al <sup>67</sup>	Incidental	75	9 (12%)	n.d	0 (0%)	0 (0%)	0 (0%)
5	Not incidental	110	35 (32%) <sup>a</sup>	n.d	21 (19%) <sup>a</sup>	43 (39%) <sup>a</sup>	3 (2.7%)

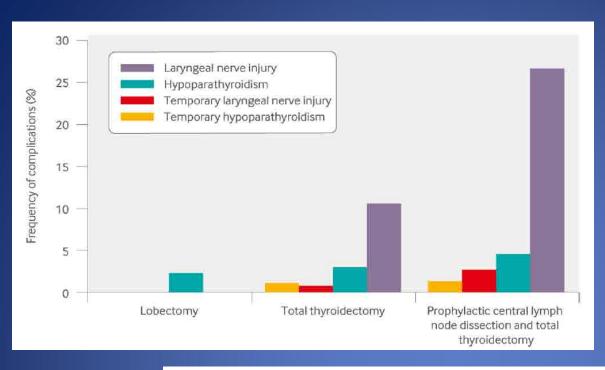
<sup>&</sup>lt;sup>a</sup> Significantly different.



Pacini F. Best & Res. Clin. Endocrinol. & Metabol. 2012

Mortality: no significant differences was found (p=0.2)

Mehanna H., et al. J. Clin. Endocrinol. Metab. 2014



Sywak M., et al., Surgery, 2006 Roh J.L., et al., Ann. Surg., 2007

**Table III.** Postoperative complications in patients with low-risk papillary thyroid carcinoma according to the extent of thyroidectomy

			LTT, n/N (%)		TT, n		
Complication	<i>Total</i> (n = 967)	Isthmusectomy (n = 22)	Lobectomy (n = 674)	Subtotal thyroidectomy (n = 95)	Near-total thyroidectomy (n = 62)	Total thyroidectomy (n = 114)	P value (LTT vs TT)
Overt hypothy	roidism (exclud	ing patients as	signed to underg	go TSH-suppre	ession therapy	)	
270	234/775 (30)	2/16 (13)	72/558 (13)	25/66 (38)	39/39 (100)	96/96 (100)	<.0001
Hypoparathyre	oidism						
Transient	83/967 (9)	0/22(0)	3/674 (0.4)	7/95(7)	11/62 (18)	62/114 (54)	<.0001
Permanent	16/967(2)	0/22(0)	0/674(0)	3/95(3)	3/62(5)	10/114 (9)	<.0001
Recurrent lary	ngeal nerve pal	sy per nerve at	risk (excluding	patients with l	Ex2 or Ex3 to	the recurrent n	ierve)
Transient	98/1,832 (5)	1/44 (2)	66/1,288 (5)	8/172 (5)	7/118 (6)	16/210(8)	.14
Permanent	33/1,832 (2)	0/44(0)	20/1,288 (2)	3/172(2)	3/118(3)	7/210(3)	.061

#### ORIGINAL ARTICLE - ENDOCRINE TUMORS

### Oncologic Outcomes After Completion Thyroidectomy for Patients with Well-Differentiated Thyroid Carcinoma

Brian R. Untch, MD<sup>1</sup>, Frank L. Palmer, BA<sup>2</sup>, Ian Ganly, MD<sup>2</sup>, Snehal G. Patel, MD<sup>2</sup>, R. Michael Tuttle, MD<sup>3</sup>, Jatin P. Shah, MD<sup>2</sup>, and Ashok A. Shaha, MD<sup>2</sup>

"...completion thyroidectomy is not necessary in all patients with WDTC.
...it should be used in cases of large tumors, bulky nodal disease, and
concerning histologic features.
Risk group stratification and postoperative risk-adapted evaluation is
very important..."

### Currently available data on the prognostic influence of PCND during initial surgery are controversial

Ito Y., et al. WJS 2010
Pereira J.A., et al. Surgery 2005
Wada N., et al. Ann. Surg. 2003
Carling T., et al Thyroid 2012
Shah N.D., et al. Laryngoscope 2003

LNM are common in patients with PTC.

35% of patients with PTC have macroscopically LNM and 80% have microscopic LNM (clinically non-palpable disease)

Kim W.W., et al. Head Neck 2013 Miao S., et al. ORL J. Otorhinolaryngol. Relat. Spec. 2013 Machens A., et al. WJS 2002

Pereira J.A., et al. Surgery 2005

Lee Y.S., et al. WIS 2007

It is important to recognize that all LNM are not the same in terms of their implications for recurrence and mortality.

Schlumberg M. N. Engl. J. Med. 1998 Noguchi S., et al. Surg. Clin. N. Am. 1987 Cranshaw I.M., et al. Surg. Oncol. 2008 Randolph G.W., et al. Thyroid 2012 The overal rate of positive lymph nodes by cytokeratin immunohistochemistry (all negative for metastasis by H.H. staining) was 53%, with > 90% positive node in the central compartment: all patients were alive, implying that <u>node positivity was not life threating</u>

Qubain s.K., et al. Surgery 2002

PCND no changes the incidence of recurrence or disease specific mortality for patients with low risk PTC

Tisell L.E., et al. WJS 1996 Salvesen H., et al. Eur. J. Surg. 1991 Roh J.L., et al. Ann. Surg. 2007

No difference between the rate of disease-specific mortality in patients with and without lymph node metastases in PTC

Hay i.D., et al. Surgery 1992 Spires J.R., et al. Head Neck 1989

Removal of microscopic lymph node metastases has not been shown to improve survival

McHenry C.R., et al. Surg. Clin. N. Am. 2014

#### Prophylactic Central Compartment Neck Dissection for Papillary Thyroid Cancer

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Surg. Clin. N. Am. 2014

If PCND is not performed recurrence may be rare, even less than 1% Wada N., et al. Ann. Surg. 2003

Two meta- analyses have shown an absence of a clinically significant reduction in disease recurrence from PCND

Shan C.X., et al. Laryngoscope 2012 Zetoune T., et al. Am. Surg. Oncol. 2010

Table 1
Central compartment recurrence of papillary thyroid cancer (PTC) following total thyroidectomy (TT) versus TT with prophylactic central compartment node dissection (pCCND)

Authors, Ref. Year	N	TT Only	TT + pCCND	Recurrence with TT	Recurrence with TT + pCCND
Barczyński et al, <sup>27</sup> 2013	640	282	358	22 (7.8%)	2 (0.6%)
Besic et al, <sup>43</sup> 2009	89	83	6	0 (0.0%)	0 (0.0%)
Costa et al, 31 2009	244	118	126	4 (3.4%)	4 (3.2%)
Gemsenjäger et al, <sup>39</sup> 2003	159	88	71	2 (2.3%)	4 (5.6%)
Hughes et al, 49 2010	143	65	78	2 (3.1%)	2 (2.6%)
Lang et al, <sup>28</sup> 2012	185	103	82	0 (0.0%)	0 (0.0%)
Moo et al, <sup>30</sup> 2010	81	36	45	2 (5.6%)	1 (2.2%)
Moreno et al, <sup>58</sup> 2012	252	133	119	3 (2.3%)	2 (1.7%)
Roh et al, <sup>41</sup> 2009	197	49	148	0 (0.0%)	0 (0.0%)
Roh et al, <sup>40</sup> 2007	113	73	40	3 (4.1%)	1 (2.5%)
Sywak et al, <sup>33</sup> 2006	447	391	56	7 (1.8%)	0 (0.0%)

There is no significant difference in the rate of recurrence whether a PCND is performed or not

Current Treatment Options in Oncology (2012) 13:1-10 DOI 10.1007/s11864-011-0175-z

Endocrine Tumors (O Clark and A Dackiw, Section Editors)

Extent of Surgery for Papillary Thyroid Cancer: Preoperative Imaging and Role of Prophylactic and Therapeutic Neck Dissection

Robin M. Cisco, MD\* Wen T. Shen, MD Jessica E. Gosnell, MD Importantly, the rate of locoregional recurrence requiring reoperation was not significantly different between the two groups (3.6% in LN dissection group, 5.6% in TTX alone group).

There remains no compelling evidence that prophylactic CLND favorably affects survival.

Central compartment observation is safe in N0 cases with Papillary Throid Carcinoma without extrathyroidal extension

(recurrence 3%, reoperation of Central Compartment 4%)

Liu J., et al. Eur. Arch. Otorhinolarigol. 2014

LN features most predictive of neck recurrence appears to be the presence of ExtraNodal Spread (ENS) in the positive central neck

Wang L.Y., et al. Thyroid 2014

#### ORIGINAL ARTICLE - ENDOCRINE TUMORS

### Prophylactic Central Neck Dissection in Differentiated Thyroid Cancer: An Assessment of the Evidence

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2013

TABLE 1 Published series of prophylactic central neck dissection in differentiated thyroid cancer

Study	Year	n pCND	n Control	Ultrasound	Extent of pCND	Node- positive pCND	RAI dose pCND	RAI dose control	Central recurrence pCND (median follow-up)	Central recurrence control (median follow-up)
Moreno <sup>21</sup>	2012	119	133	All patients negative	Not stated	71.4 %			1.8 % (60 mo)	2.4 % (60 mo)
Hughes 19	2010	78	65	All patients negative	Bilateral	62 %	150 mCi	30 mCi	2 % (19.1 mo)	2 % (27.5 mo)
Roh <sup>22</sup>	2007	40	73	No	Bilateral with or without lateral				2.5 %	4 %
Sywak <sup>23</sup>	2006	56	391	All patients negative	Ipsilateral	38 %	5.2 GBq	4.8 GBq	0 % (24.5 mo)	1.7 % (70 mo)
Gemsenjager <sup>18</sup>	2003	29	88	Performed in most	Ipsilateral or bilateral sampling	14 %			4 %	2 %
Moo <sup>20</sup>	2010	45	36	All patients negative	Bilateral	33 %	102.7 mCi	66.3 mCi	0 %	5.6 %
Mean						47.4 %			1.7 %	2.2 %

pCND prophylactic central neck dissection, RAI radioactive iodine

In summary, there is no convincing evidence that pCND leads to an improvement in recurrence rate, overall survival, or any clinically significant variable when applied indiscriminately to all DTC patients. Furthermore, pCND may result in inappropriate upstaging and subsequent overtreatment of patients with RAI. Exposing patients to the additional potential morbidity of pCND, even if minimal, currently appears unwarranted.

One-third of patients who have PCND may be upstaged, and a consequence RAI theraphy is used significantly more frquently in these patients

Barczynski M. et al. BJS 2013 Shindo M., et al. Arch. Otolaryngol. Head Neck surg. 2006

No studies have shown that such upstaging improves long-terms outcomes

McLeod D.S.A., et al. Lancet 2013

### Permanent hypoparathyroidism ranges from 2.7% to 25% after T.T. + PCND, and permanent vocal cord paralysis is 3.4%

Bonnet S., et al. J. Clin. Endocrinol. Metab. 2009 Pattou F., et al. WJS 1998 Goretzki P.E., et al. BJS 1993

Table 2 Defining the morbidity of central neck dissection								
			Recurrent L Nerve Pa		Perma Hypoparath	15 - 20		
Authors, Ref. Year	TT + CCND	TT Only	TT + CCND	TT Only	TT + CCND	TT Only		
Henry et al, <sup>59</sup> 1998	50	50	0	0	2 (4%)	0		
Gemsenjäger et al, <sup>39</sup> 2003	88	71	4 (5.6%)	0	1 (1.4%)	0		
Rosenbaum & McHenry, <sup>42</sup> 2009	22	88	0	1 (1.1%)	1 (4.5%)	0		
Hughes et al, <sup>49</sup> 2010	78	65	0	2 (3.1%)	2 (2.6%)	0		
Giordano et al, <sup>53</sup> 2012	308	394	7 (2.3%)	4 (1%)	50 (16.2%)	25 (6.3%)		
Pereira et al, 60 2005	43	0	0	_	2 (4.6%)	_		

### PCND is not recommended for low-volume thyroid surgeons

Barczynski M., et al. BJS 2013 Carling T., et al Thyroid 2012

**Hemythyroidectomy + unilateral PCND** 

Hyun S.M., et al. Am. Surg. Oncol. 2011

Ann Surg Oncol (2014) 21:416-42:	5
DOI 10.1245/s10434-013-3234-9	



ORIGINAL ARTICLE - ENDOCRINE TUMORS

A Cost-Minimization Analysis Comparing Total Thyroidectomy Alone and Total Thyroidectomy with Prophylactic Central Neck Dissection in Clinically Nodal-Negative Papillary Thyroid Carcinoma

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TT + pCND is more expensive in the medium- and long-term and seems less justified compared with TT alone for cNO PTC

	Average direct medical	Average direct medical cost (in USD) accrued per patient					
Base-case analysis	TT alone	TT + pCND	Incremental cost				
	19888.36	22760.86	2872.5				

Ann Surg Oncol (2014) 21:354-355 DOI 10.1245/s10434-013-3301-2 Annals of SURGICAL ONCOLOGY

EDITORIAL - ENDOCRINE TUMORS

Prophylactic Central Neck Dissection Increases the Cost of Thyroid Cancer Care

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...the higher costs of pCND are mostly attributable to (1) longer operative time and greater complexity of the operation, (2) more initial complications, and (3) higher percentage of postoperative RAI in patients with pCND

# Patient outcome is much more linked to prognostic factors intrinsic to the tumor or to the patient themselves rather than to treatment options



Management of small DTC should be based on tumor size and the presence of clinical, histopathological and <u>molecular</u> risk factors. Based on current clinical data, in patients with small tumors and no additional risk factors a conservative surgical approach without radioiodine therapy might be appropriated.

- Multidisciplinary Team
- Patients wishes

Differentiated thyroid cancer-personalized therapies to prevent overtreatment

Luster M., et al. Nat. Rev. Endocrinol. 2014

## Grazie per l'attenzione