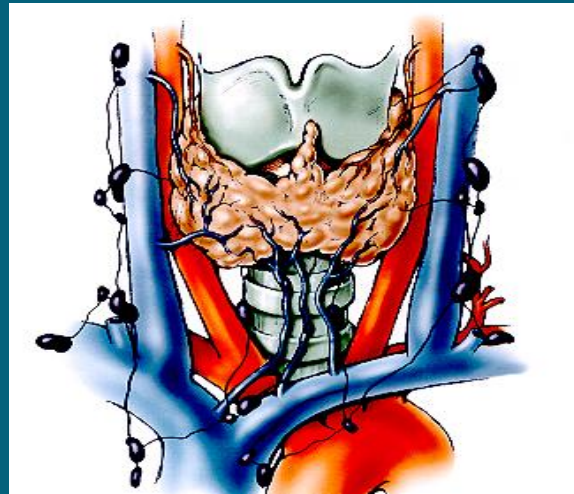


Recent Developments and Future Challenges in Thyroidology: Surgical Review 2013



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Surgery Review

- Trends in Thyroid Surgery
- Prevention of Complications
- Significance of Nodal Metastasis
- Elective/Prophylactic Central Neck Dissection
- BRAF and Extent of Surgery

Trends in Thyroid Surgery

Surgery. 2012 Dec;152(6):1133-41.

Same-day thyroidectomy program: eligibility and safety evaluation.

Mazeh H, Khan Q, Schneider DF, Schaefer S, Sippel RS, Chen H.

Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, WI 53792, USA.

608 patients, 49% same day thyroidectomy

No difference in complication rates

Postop PTH allowed same day total thyroidectomy

Trends in Thyroid Surgery

Thyroid. 2013 Jun;23(6):727-33. Epub 2013 May 28.

Epidemiological and economic trends in inpatient and outpatient thyroidectomy in the United States, 1996-2006.

Sun GH, DeMonner S, Davis MM.

Robert Wood Johnson Foundation Clinical Scholars, University of Michigan, Ann Arbor, Michigan 48109-2800, USA.

Outpatient thyroidectomy increased 61%

Inpatient thyroidectomy increased 30%

Inpatient charges > outpatient

\$22,537 vs. \$7,222

Trends in Thyroid Surgery

Otolaryngol Head Neck Surg. 2013 May;148(5):740-5. Epub 2013 Feb 11.

Outpatient thyroid surgery data from the University Health System (UHC) Consortium.

Stack BC Jr, Moore E, Spencer H, Medvedev S, Bodenner DL.

Department of Otolaryngology-Head and Neck Surgery, University of Arkansas for Medical Sciences (UAMS), Little Rock, Arkansas, USA

64% outpatient thyroidectomy

Charges lower for outpatient vs. inpatient

Trends in Thyroid Surgery

Laryngoscope. 2013 Aug;123(8):2056-63. Epub 2013 Jun 4.

National trends in thyroid surgery and the effect of volume on short-term outcomes.

Loyo M, Tufano RP, Gourin CG.

Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University, Baltimore, Maryland 21287, USA.

Nationwide Inpatient Sample 871,644 patients 1993-2008

High volume surgeons' cases increased 12% to 25%

Low volume surgeons' cases decreased 51% to 34%

High volume surgeons had lower complication rates

RLN, OR 0.7, p=0.02

HypoCa, OR 0.7, p=0.002

Death, OR 0.3, p=0.004

Trends in Thyroid Surgery

Thyroid. 2013 Oct;23(10):1193-202. Epub 2013 Sep 14.

American thyroid association statement on outpatient thyroidectomy.

Terris DJ, Snyder S, Carneiro-Pla D, Inabnet WB 3rd, Kandil E, Orloff L, Shindo M, Tufano RP, Tuttle RM, Urken M, Yeh For The American Thyroid Association Surgical Affairs Committee Writing Task Force MW.

GRU Thyroid Center, Department of Otolaryngology, Georgia Regents University , Augusta, Georgia

Outpatient thyroidectomy is safe in selected patients

Trends in Thyroid FNA and Surgery

Surgery. 2013 Oct 2.[Epub ahead of print]

Increases in thyroid nodule fine-needle aspirations, operations, and diagnoses of thyroid cancer in the United States.

Sosa JA, Hanna JW, Robinson KA, Lanman RB.

Section of Endocrine Surgery, Department of Surgery, Duke University, Durham, NC.

Private and public insurance claims database study 2006-2011

Thyroid FNA doubled

Thyroid surgery increased 31%, mostly total

Outpatient thyroidectomy 62% of cases

Trends in Thyroid Cancer

Thyroid. 2013 Jul;23(7):885-91. Epub 2013 Apr 18.

The increasing incidence of thyroid cancer: the influence of access to care.

Morris LG, Sikora AG, Tosteson TD, Davies L.

Head and Neck Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA. morrisl@mskcc.org

SEER database study

Thyroid cancer rates increasing

9% annually age > 65yrs

6% annually age < 65yrs

Increased rates correlated to higher SES

Education, insured, income

Trends in Ultrasound and Cancer

Thyroid. 2013 Aug 12. [Epub ahead of print]

The Epidemic of Thyroid Cancer in the United States: The Role of Endocrinologists and Ultrasounds.

Udelsman R, Zhang Y.

Yale School of Medicine, Department of Surgery, New Haven, Connecticut, United States

National Program of Cancer Registries by State

Thyroid cancer incidence

Higher in Northeast than South

Significantly correlated with

Endocrinologists, $r=0.6$ $p<0.001$

Ultrasound use, $r=0.4$ $p<0.001$

Prevention of Complications

JAMA Otolaryngol Head Neck Surg. 2013 May;139(5):471-8.

Dexamethasone for the prevention of recurrent laryngeal nerve palsy and other complications after thyroid surgery: a randomized double-blind placebo-controlled trial.

Schietroma M, Cecilia EM, Carlei F, Sista F, De Santis G, Lancione L, Amicucci G.

Department of Surgery, University of L'Aquila, Abruzzo, Italy.

RCT DB 328 pts IV Dexamethasone 8mg vs. Placebo

Temp RLN 4.9% steroid vs. 8.4% placebo, p=0.04

Temp HypoPTH 13% vs. 37%, p<0.05

Reduced pain and N/V, p<0.05

Laryngeal Nerve Integrity Monitoring

Surgery. 2013 Oct;154(4):704-13. Epub 2013 Sep 3.

The long-term impact of routine intraoperative nerve monitoring during thyroid and parathyroid surgery.

Snyder SK, Sigmond BR, Lairmore TC, Govednik-Horny CM, Janicek AK, Jupiter DC.

Scott & White Clinic, Texas A&M Health Science Center, Temple, TX

1936 pts with 3435 RLN at risk using NIM over 7yrs

Reduced RLN injury after 20mths, p=0.04

Aided RLN identification 10% of time

Laryngeal Nerve Integrity Monitoring

World J Surg Oncol. 2013 Apr 23;11:94.

Protective effect of intraoperative nerve monitoring against recurrent laryngeal nerve injury during re-exploration of the thyroid.

Chuang YC, Huang SM.

Department of Surgery, National Cheng Kung University Hospital,
Tainan 704, Taiwan.

**71 patients undergoing revision thyroid/parathyroid
RLN injury 1.4% NIM vs. 20% without, p=0.02**

Laryngeal Nerve Integrity Monitoring

World J Surg. 2013 Oct 1. [Epub ahead of print]

Intraoperative Nerve Monitoring Can Reduce Prevalence of Recurrent Laryngeal Nerve Injury in Thyroid Reoperations: Results of a Retrospective Cohort Study.

Barczyński M, Konturek A, Pragacz K, Papier A, Stopa M, Nowak W.

Department of Endocrine Surgery, Jagiellonian University Medical College, Kraków, Poland

854 pts undergoing reoperation (1326 RLN at risk)
Transient RLN 2.6% NIM vs. 6.3%, p=0.003
Permanent RLN 1.4% NIM vs. 2.4%, p=0.2

Laryngeal Nerve Integrity Monitoring

Laryngoscope. 2013 Sep;123 Suppl 4:S1-S14.

External branch of the superior laryngeal nerve monitoring during thyroid and parathyroid surgery: International Neural Monitoring Study Group standards guideline statement.

Barczyński M, Randolph GW, Cernea CR, Dralle H, Dionigi G, Alesina PF, Mihai R, Finck C, Lombardi D, Hartl DM, Miyauchi A, Serpell J, Snyder S, Volpi E, Woodson G, Kraimps JL, Hisham AN; International Neural Monitoring Study Group.

Department of Endocrine Surgery, Jagiellonian University Medical College, Kraków, Poland.

EBSLN NIM feasible

Lymph Node Prognostication

Thyroid. 2012 Nov;22(11):1144-52. Epub 2012 Oct 19.

The prognostic significance of nodal metastases from papillary thyroid carcinoma can be stratified based on the size and number of metastatic lymph nodes, as well as the presence of extranodal extension.

Randolph GW, Duh QY, Heller KS, LiVolsi VA, Mandel SJ, Steward DL, Tufano RP, Tuttle RM; American Thyroid Association Surgical Affairs Committee's Taskforce on Thyroid Cancer Nodal Surgery.

Department of Otolaryngology, Harvard Medical School, Boston, Massachusetts 02114, USA. gregory_randolph@meei.harvard.edu

Recurrence rates proportional to clinical node status

cN0 2% vs. cN1 24%

Recurrence proportional to number positive nodes

pN1 < 5 nodes 4% vs. > 5 nodes 19%

Recurrence related to extranodal extension

pN1 with ENE 24%

Patterns of Nodal Metastasis

Head Neck. 2013 Jun 4. [Epub ahead of print]

Tumor location-dependent skip lateral cervical lymph node metastasis in papillary thyroid cancer.

Lee YS, Shin SC, Lim YS, Lee JC, Wang SG, Son SM, Kim IJ, Lee BJ.

Department of Otorhinolaryngology-Head and Neck Surgery, Pusan National University School of Medicine and Medical Research Institute, Busan, Republic of Korea; Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

**Superior pole PTC metastasizes to lateral nodes
Level III LN most common**

Prophylactic Central Neck Dissection

Br J Surg. 2013 Feb;100(3):410-8. Epub 2012 Nov 27.

Prophylactic central neck dissection for papillary thyroid cancer.

Barczyński M, Konturek A, Stopa M, Nowak W.

Third Department of General Surgery, Jagiellonian University Medical College, Kraków, Poland. marbar@mp.pl

640 Patients retrospective study with historic control

282 pts 1993-97 Total thyroidectomy

358 pts 1998-02 Total + bilateral prophylactic CND

10 yr disease specific survival

TT 92.5% vs. TT+CND 98%, p=0.03

10 yr locoregional control

TT 87.6% vs. 94.5%, P<0.01

Multivariate analysis

Extrathyroidal extension (OR 12.5, p<0.001)

CND (OR 0.2, p<0.001)

Prophylactic Central Neck Dissection

World J Surg. 2013 Aug;37(8):1951-8.

Influence of prophylactic neck dissection on rate of retreatment for papillary thyroid carcinoma.

Hartl DM, Mamelle E, Borget I, Leboulleux S, Mirghani H, Schlumberger M.

Department of Head and Neck Oncology, Thyroid Surgery Unit, Institut Gustave Roussy and Paris-Sud University, 114, rue Edouard Vaillant, 94805 Villejuif Cedex, France. dana.hartl@igr.fr

Retrospective case control study 246 pts (26% TT)

Reoperation rate 12% TT vs. 2% TT+CND, $p < 0.001$

RAI Rx number 1.2 TT vs. 1.1 TT+CND, $p = 0.08$

5yr retreatment KM 15% TT vs. 7% TT+CND, $P = 0.01$

Permanent RLN 2% TT vs. 1% TT+CND, $p = 0.9$

Permanent HypoPTH 7% TT vs 3% TT+CND, $p = 0.1$

Prophylactic Central Neck Dissection

Ann Surg Oncol. 2013 Oct;20(11):3477-83. Epub 2013 Jul 12.

A Meta-analysis of the Effect of Prophylactic Central Compartment Neck Dissection on Locoregional Recurrence Rates in Patients with Papillary Thyroid Cancer.

Wang TS, Cheung K, Farrokhyar F, Roman SA, Sosa JA.

Department of Surgery, Medical College of Wisconsin, Milwaukee, WI

6 comparative studies of 1,740 patients (60% TT)

Recurrence 8% TT vs. 5% TT+CND

RR=0.6 (0.3-1.1), NNT = 31

Prophylactic Central Neck Dissection

Thyroid. 2013 Sep;23(9):1087-98. Epub 2013 Aug 28.

A systematic review and meta-analysis of prophylactic central neck dissection on short-term locoregional recurrence in papillary thyroid carcinoma after total thyroidectomy.

Lang BH, Ng SH, Lau LL, Cowling BJ, Wong KP, Wan KY.

Department of Surgery, The University of Hong Kong , Hong Kong, China

14 studies including 3331 patients (48% TT+CND)

RAI 72% TT+CND vs. 53% TT

Temp hypoCa 26% TT+CND vs. 11% TT

LRR 4.7% TT+CND vs. 8.6% TT

NNT LRR = 31, NNH Temp HypoCa = 7

Prophylactic Central Neck Dissection

Ann Surg Oncol. 2013 Aug 24. [Epub ahead of print]

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

Lang BH, Wong CK.

Division of Endocrine Surgery, Department of Surgery, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China,

Cost model of TT vs. TT+CND

Initial : TT \$6,702 vs. TT+CND \$10,062

20 year: TT \$19,888 vs. TT+CND \$22,761

BRAF Prognostication

World J Surg. 2013 Sep 20. [Epub ahead of print]

BRAFV600E Mutation Analysis in Papillary Thyroid Carcinoma: Is it Useful for all Patients?

Ito Y, Yoshida H, Kihara M, Kobayashi K, Miya A, Miyauchi A.

Department of Surgery, Kuma Hospital, 8-2-35, Shimoyamate-dori, Chuo-ku, Kobe, 650-0011, Japan, ito01@kuma-h.or.jp.

766 pts PTC without distant mets

BRAF+ no significant association with recurrence or survival overall

BRAF+ was associated with worse disease specific survival for UICC Stage IVa patients

BRAF Prognostication and CND

Endocr Relat Cancer. 2013 Jan 21;20(1):13-22. Print 2013 Feb.

Impact of lymph node metastases identified on central neck dissection (CND) on the recurrence of papillary thyroid cancer: potential role of BRAFV600E mutation in defining CND.

Alzahrani AS, Xing M.

Division of Endocrinology and Metabolism, Laboratory for Cellular and Molecular Thyroid Research, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA

379 patients with PTC

Recurrence proportional to extent of CND

5% vs. 16% vs. 41%

Recurrence related to BRAF and CND

BRAF to Determine Prophylactic Central Neck Dissection

Thyroid. 2012 Nov 27. [Epub ahead of print]

BRAF, A TOOL IN THE DECISION TO PERFORM ELECTIVE NECK DISSECTION?

Dutenhefner SE, Marui S, Santos AB, Lima EU, Inoue M, Neto JD, Shiang C, Fukushima J, Cernea CR, Friguglietti C.

HC FMUSP, Head and Neck Surgery, Av Dr Eneas de Carvalho Aguiar, 255 8andar sala 8124, Cerqueira Cesar , São Paulo, São Paulo, Brazil

51 patients total + prophylactic CND

BRAF+ did not predict central node metastasis

BRAF in Indeterminate Nodules

J Clin Endocrinol Metab. 2013 Apr;98(4):E761-8. Epub 2013 Mar 8.

Does addition of BRAF V600E mutation testing modify sensitivity or specificity of the Afirma Gene Expression Classifier in cytologically indeterminate thyroid nodules?

Kloos RT, Reynolds JD, Walsh PS, Wilde JJ, Tom EY, Pagan M, Barbacioru C, Chudova DI, Wong M, Friedman L, LiVolsi VA, Rosai J, Lanman RB, Kennedy GC.

Veracyte, Inc, South San Francisco, CA 94080, USA

296 nodules

Cyto benign BRAF+ 2/40 (5%)

Cyto malignant BRAF+ 36/48 (75%)

Cyto indeterminate BRAF +10%

AUS/FLUS 2%

FN 1%

Susp for malignant 42%

BRAF for Indeterminate Nodules

Cancer. 2013 Apr 15;119(8):1495-502. Epub 2012 Dec 21.

Preoperative BRAF(V600E) mutation screening is unlikely to alter initial surgical treatment of patients with indeterminate thyroid nodules: a prospective case series of 960 patients.

Kleiman DA, Sporn MJ, Beninato T, Crowley MJ, Nguyen A, Uccelli A, Scognamiglio T, Zarnegar R, Fahey TJ 3rd.

Department of Surgery, New York Presbyterian Hospital-Weill Cornell Medical College, New York, New York, USA.

310 pts cyto indeterminate undergoing surgery

13 pts (4%) BRAF+

1 pt (0.3%) AUS/FLUS or FN

12 pts (3%) Suspicious for malignancy

Sensitivity for malignancy

Cytology 73%, BRAF+ 15%, Combined 76%

Summary

- Trends in Thyroid Surgery
 - Increasingly outpatient thyroidectomy
 - Increasingly high volume surgeons
 - Increasingly performed
 - Possible consequence of increased US and FNA
- Prevention of Complications
 - High volume surgeons
 - IV Dexamethasone
 - Laryngeal Nerve Integrity Monitoring
- Significant Nodal Metastasis
 - Clinically detectable, > 5, extranodal extension
- Elective/Prophylactic Central Node Dissection
 - Possible reduced recurrence rates (NNT 31)
- BRAF more hype than help?

BRAF Prognostication

JAMA Otolaryngol Head Neck Surg. 2013 Sep 12. [Epub ahead of print]

Lack of Association of BRAF Mutation With Negative Prognostic Indicators in Papillary Thyroid Carcinoma: The University of California, San Francisco, Experience.

Gouveia C, Can NT, Bostrom A, Grenert JP, van Zante A, Orloff LA.

Department of Otolaryngology-Head and Neck Surgery, University of California, San Francisco, San Francisco²Department of Otolaryngology-Head and Neck Surgery, Northwestern University, Chicago, Illinois

429 pts with PTC (73% BRAF+)

BRAF+ not significant on multivariate analysis

BRAF Prognostication

World J Surg Oncol. 2013 May 20;11:99.

Clinical implication of the BRAFV600E mutation in papillary thyroid carcinoma.

Kim YS, Kim JS, Bae JS, Park WC.

Department of Surgery, College of Medicine, The Catholic University of Korea, Seoul, Korea.

241 patients

No significant association of BRAF+ in multivariate analysis

BRAF Prognostication

J Clin Endocrinol Metab. 2013 Sep;98(9):3702-12. Epub 2013 Aug 22.

Does BRAF V600E Mutation Predict Aggressive Features in Papillary Thyroid Cancer? Results From Four Endocrine Surgery Centers.

Li C, Aragon Han P, Lee KC, Lee LC, Fox AC, Beninato T, Thiess M, Dy BM, Sebo TJ, Thompson GB, Grant CS, Giordano TJ, Gauger PG, Doherty GM, Fahey TJ 3rd, Bishop J, Eshleman JR, Umbricht CB, Schneider EB, Zeiger MA.

Johns Hopkins Hospital, Department of Surgery, Baltimore, Maryland

**BRAF+, age, and T stage associated with central node metastasis in PTC
but BRAF+ not significant for classical PTC**

BRAF Prognostication

J Clin Endocrinol Metab. 2012 Dec;97(12):4559-70. Epub 2012 Oct 9.

BRAF V600E mutation and its association with clinicopathological features of papillary thyroid cancer: a meta-analysis.

Li C, Lee KC, Schneider EB, Zeiger MA.

Endocrine Surgery Section, Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA.

32 studies, 6372 patients

BRAF associated with

T stage

N Stage

Classic and Tall Cell PTC