



16th Biennial Congress of Asian Association of Endocrine Surgeons

Oral Presentations

8th to 10th March, 2018

New Delhi, India

Website: www.asianaes.org

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Fujimoto Award

Sentinel Lymph Node Biopsy in Medullary Thyroid Microcarcinomas after Methylene Blue Dye Mapping: A Single Institution Experience

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INTRODUCTION

Management of lymph nodes (LN) in medullary thyroid carcinoma (MTC) is an ongoing debate. The aim was to analyze usefulness of sentinel lymph node biopsy (SLNB) of jugulo-carotid regions after methylene blue dye (MBD) mapping for detecting true positive patients in cN0 group of micro-MTCs, providing them one-time lateral neck dissection (LND).

MATERIALS AND METHODS

In a 10-year period, 15 cN0 patients were operated in our institution due to micro-MTCs (≤ 10 mm), with serum calcitonin levels < 1000 pg/mL. In all patients, standard treatment was total thyroidectomy, central neck dissection, and sentinel-LN mapping by injecting 1% MBD subcapsularly in both lobes. After exploration of levels II–III bilaterally, sentinel-LNs were extirpated and examined by frozen section. If sentinel-LNs were benign, additional surrounding non-sentinel-LNs were extirpated and sent to standard pathohistology (sPH). If sentinel-LNs were malignant, one-time LND was performed.

RESULTS

One patient with calcitonin level of 221 pg/mL had hereditary, bilateral micro-MTC, central-LN metastases, and positive sentinel-LNs on both sides, thus bilateral LNDs were performed. Sentinel-LNs were predictive for non-sentinel-LNs status (metastases were found in non-sentinel-LNs, as well). Remaining 14 patients had sporadic, unilateral micro-MTCs, without central or sentinel-LN metastases. Frozen section and sPH were 100% match.

CONCLUSION

This study is the first reported experience with SLNB of jugulo-carotid regions in MTCs using MBD, focusing on the subgroup of microcarcinomas. This method can be precisely used for intraoperative assessment of lateral-LNs. It optimizes surgery of micro-MTCs, selecting cN0 patients with sentinel-LN metastases on frozen section, for one-time LND.

***BRAF*^{V600E} Mutation induces Genomic and Epigenomic Changes in Thyroid Cells**

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AIM

BRAF^{V600E} mutation is a major driver mutation in papillary thyroid cancer that initiates carcinogenic cascades. Gene expression regulation followed by upstream deoxyribonucleic acid methylation has been widely studied in cancers. However, few studies

were performed in thyroid cancer, especially focused on *BRAF*^{V600E} mutation. Furthermore, previous thyroid cancer studies did not determine the epigenomic and genomic consequence from initial *BRAF*^{V600E} mutation. Our aim of study was to reveal the association between methylation and gene expression pattern induced by *BRAF*^{V600E} mutation.

MATERIALS AND METHODS

We used Nthy/*BRAF* cell lines, which was originally developed by our laboratory. We compared Nthy/WT (wild-type *BRAF* thyroid cell) and Nthy/V600E (mutant type *BRAF* thyroid cell) by methylation array (three cells per each group) and gene expression microarray (two cells per each group). Infinium methylation EPIC BeadChip (850 K) was used for methylation and Illumina Human HT-12 v4 Expression BeadChip was used for gene expression study.

RESULTS

In the methylation analysis, 199,821 probes were hypermethylated in Nthy/V600E cells. Among them, 14,546 probes were located on the CpG island in promoter region (TSS 1500, TSS 200, 5'UTR, and first exon). In the gene expression analysis, 2,724 probes were downregulated in Nthy/V600E cells. Inverse correlation (hypermethylation–downregulation) in Nthy/V600E cells was observed in 697 genes. In the gene ontology analysis, 10 tumor suppressor genes (*RASSF4*, *PRR5*, *PLA2G16*, *CADMI*, *EFNA1*, *PYCARD*, *BIN1*, *MNI*, *PTEN*, *MTUS1*) and 34 apoptosis-related genes are included in hypermethylated–downregulated genes.

On the contrary, 66,446 probes were hypomethylated in Nthy/V600E cells and 3,022 probes were located on CpG island in promoter area. Number of upregulated probes in Nthy/V600E cells was 2,441. Two hundred twenty-seven genes showed inverse correlation (hypomethylation–upregulation) in Nthy/V600E cells. Ten proto-oncogenes (*EGFR*, *FGF5*, *CCND1*, *FLI1*, *MAFB*, *BCL2*, *ETV1*, *FOXO1*, *MECOM*, *CBFB*) and 22 developmental protein coding genes were included in hypomethylated–overexpressed genes.

CONCLUSION

Induction of *BRAF*^{V600E} mutation leads to frequent hypermethylation in thyroid cells than wild-type *BRAF* cells. Anticancer effect genes, such as tumor suppression or apoptosis were downregulated by upstream hypermethylation, whereas carcinogenic genes, such as proto-oncogenes are upregulated by hypomethylation. This result suggests that *BRAF*^{V600E} mutation in thyroid cell can alter cancer-related gene expression by the epigenomic regulation.

Impact of Autofluorescence-based Identification of Parathyroids during Total Thyroidectomy on Postoperative Hypocalcemia: A before and after Controlled Study

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INTRODUCTION

The clinical impact of intraoperative autofluorescence-based identification of parathyroids using a near-infrared (NIR) camera remains unknown.

MATERIALS AND METHODS

In a before and after controlled study, we compared all patients who underwent total thyroidectomy, by the same surgeon, during Period 1 (January 2015–January 2016) without NIR (NIR– group) and those operated on during Period 2 (February 2016–September 2016) using an NIR camera (NIR+ group). In parallel, we also compared all patients who underwent surgery without NIR during those same periods by another surgeon in the same unit (control groups). Main outcomes included postoperative hypocalcemia (PH), parathyroid identification, autotransplantation, and inadvertent resection.

RESULTS

The NIR+ group displayed significantly lower PH rates (5.2%) than the NIR– group (20.9%) ($p < 0.001$). Compared with the NIR– patients, the NIR+ group exhibited an increased rate of identified parathyroids (76.3 vs 65.7% of the theoretically present parathyroids respectively, Dunn's test $p < 0.05$) and reduced parathyroid autotransplantation rates (2.1 vs 15.0%), although no difference was observed in inadvertent resection rates (1.1 vs 7%). Parathyroids were identified via NIR before they were visualized by the surgeon in 68% patients. In the control groups, parathyroid identification improved significantly from Period 1 to Period 2 (62.6 vs 71.3% respectively, Dunn's test $p < 0.05$), although autotransplantation (16.7 vs 16.1%), inadvertent resection (8 vs 6.9%), and PH rates (16.1 vs 19.5%) did not differ.

CONCLUSION

Near-infrared use during total thyroidectomy significantly reduced postoperative hypocalcemia, improved parathyroid(s) identification, and reduced their autotransplantation rate.

The Synergistic Effects of Celecoxib on Trail-induced Apoptosis in Medullary Thyroid Cancer TT Cells

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INTRODUCTION

Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), as a member of the TNF gene superfamily, induces apoptosis preferentially in human cancer cells. However, medullary thyroid cancer is resistant to TRAIL. Celecoxib, a cyclooxygenase-2 inhibitor, has been identified having an apoptosis promoting effect in various cancer cell lines. We aim to investigate the synergistic effects of celecoxib on TRAIL-induced apoptosis in medullary thyroid cancer TT cells.

MATERIALS AND METHODS

All experiments were conducted in TT cell lines. Cell growth inhibition was detected by MTT assay. Propidium iodide staining was used for detection of cell cycle distribution. Apoptosis was evaluated by Hoechst 33258 staining. Gene expression of DR4, DR5, and c-FLIP was measured by real-time polymerase chain reaction. The cell cycle and apoptosis associated proteins were measured by Western blot.

RESULTS

TT cells were insensitive to TRAIL and the treatment of celecoxib could reverse the resistance of TT cells to TRAIL. Downregulation of cyclin A and Cdk2 accompanied G0/G1 arrest caused by celecoxib contributed to the growth inhibition of TT cells induced by TRAIL. Celecoxib synergistically activated the cleavage of caspase-8 and increased the apoptosis level induced by TRAIL through the upregulation of DR5 and downregulation of c-FLIP in TT cells.

CONCLUSION

Our results suggest that celecoxib could help TT cells to overcome the resistance to TRAIL, which may suggest a framework for TRAIL-based combination treatment of TT cell line and provide a novel strategy for MTC therapy.

A Validation Study of a Novel Predictive Scoring System for Difficult Thyroidectomy

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INTRODUCTION

The risks of permanent complications in total thyroidectomy even though low in the hands of expertise, complications do occur in some group of people causing grave and worrisome alteration. There is a great need to have a predictive scoring system to evaluate them in preoperative period.

MATERIALS AND METHODS

Prospective study at Victoria hospital of patients undergoing total thyroidectomy, September 2015–August 2017. A scoring system called “Thyroidectomy difficulty score (TDS),” which defines six clinical parameters in preoperative period, was designed. Patients were divided into two groups: difficult thyroid (DT), if score is more than 3 and no difficult thyroid (NDT), if score is less than equal to 3. An Intraoperative scoring was done to validate the pre-op predictive scoring system.

RESULTS

A total of 314 patients underwent total thyroidectomy. About 276 (88%) were females and 38 (13%) males. They were scored for TDS. About 204(65%) were grouped as NDT and 110 (35%) as DT. Among 110 patients grouped as DT, 90 (82%) patients were found to have difficulty during surgery and 16 (18%) among them developed complications. Among 204 patients grouped as NDT, only 24 (12%) patients were found to have intraoperative difficulty and 4 (2%) developed complications in postoperative period.

CONCLUSION

We conclude that this pilot study of this new scoring system correlates very well with intraoperative difficulty and post-op complications. This scoring system is simple and effective.

BRAF^{wild} Papillary Thyroid Carcinoma has Two Distinct mRNA Expression Patterns which have Different Clinical Behavior

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INTRODUCTION

The BRAF^{V600E} mutation is the most common genetic alteration in papillary thyroid carcinoma (PTC). Several studies reported that the presence of BRAF^{V600E} mutation was associated with extrathyroidal extension, tumor size, and the number of metastatic lymph nodes in PTCs. However, as for PTCs without BRAF^{V600E} mutation (BRAF^{wild}), some tumors show indolent course while some tumors show very aggressive disease progress. Because not all the BRAF^{wild} PTCs show good prognosis, discovery of some prognostic markers in BRAF^{wild} PTCs, which can predict clinical behavior is absolutely needed. In this study, using a large set of The Cancer Genome Atlas genomic data, we tried to classify BRAF^{wild} PTCs into two subtypes, which have distinct molecular pattern and different clinical behavior. Also, we tried to suggest gene signatures (RAS-score), which could predict the molecular subtype and clinical behavior of BRAF^{wild} PTC.

MATERIALS AND METHODS

Integrated genomic analysis was done using all genomic data of PTC in The Cancer Genome Atlas data portal (<https://tcga-data.nci.nih.gov>) and cancer browser (<https://genome-cancer.ucsc.edu>). Gene-level expression data from mRNA-seq (n = 505), copy number variation data (n = 493), somatic mutation data (n = 505), reverse phase protein array data (n = 375), and clinical information (n = 505) were included in analyses. Clinical data included age, gender, unifocal/multifocal, extrathyroid extension, TNM stage, and BRAF mutation state. Using Gene Ontology and logistic regression test, we selected genes signatures (RAS-score) and applied this prediction model to validation cohort (GSE60542).

RESULTS

When we performed unsupervised clustering, BRAF^{wild} PTCs were divided into two molecular subtypes. Each subtype showed distinct molecular pattern (mRNA expression, CPN alteration, mutation profile, and reverse phase protein array analysis). Also, each subtype showed different clinical behavior—cluster 1 showed indolent clinical behavior but cluster 2 showed aggressive clinical behavior. When we made prediction model and applied it to validation cohort (GSE60542), we could confirm the consistency of gene signatures as a predictive score.

CONCLUSION

We found that BRAF^{wild} PTCs were divided into two molecular subtypes and each subtype showed distinct molecular pattern, different activated pathways and different clinical behavior. Also, with gene signatures (RAS-score) we suggested here, we could predict the molecular pattern and clinical behavior of BRAF^{wild} PTCs in clinical setting.

To Identify Differential Metabolic Signatures of Thyroid Pathology using NMR-based Metabolomics Approach

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INTRODUCTION

Metabolomics provides valuable information about metabolism of malignant cells and has a potential in cancer diagnosis, although such studies on thyroid tumors are scarce in the literature.

OBJECTIVE

This study is aimed to explore the potential use of Proton Magnetic Resonance Spectroscopy to identify specific metabolic signatures for various pathological thyroid lesions.

MATERIALS AND METHODS

After obtaining clearance from Institutional Ethics Committee, 32 fresh thyroid tissue samples were obtained from patients operated for various thyroid pathologies at the Department of Endocrine Surgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow (India) from January 2016 to August 2017. Specimens were snap frozen and transported to laboratory in liquid nitrogen cylinder for spectroscopy analysis. Histopathology of the specimens was papillary thyroid carcinomas (n = 9), colloid nodules (n = 9), follicular adenomas (n = 5), and normal thyroid tissue (n = 9). Metabolic profiles were statistically generated based on the spectroscopy results, which were then correlated with histology.

RESULTS

Principal component analysis of the tissue samples revealed statistically significant correlations among principal components. Various potential biomarkers common to all thyroid lesions were identified. Healthy and benign colloid nodules showed completely different metabolic profile from papillary thyroid cancers. Thyroid follicular adenomas were found to display a partial metabolic profile associated with malignancy.

CONCLUSION

The results indicate the potential of proton magnetic resonance spectroscopy as an ancillary molecular marker in diagnosis of cancer and differentiating it from benign conditions of thyroid.

Physical Assessment Technique and Compound Muscle Action Potential for Recurrent Laryngeal Nerve Neuromonitoring during Thyroid Surgery, to predict Vocal Cord Function: A Validation Study

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INTRODUCTION

Injury to the recurrent laryngeal nerve (RLN) is a dreaded complication of thyroid surgery. An anatomically intact nerve does not translate to a functioning nerve. Current techniques for nerve monitoring have high cost and are complex.

AIM

To develop a simple and cost-effective technique using physical examination to monitor the RLN during thyroid surgery, to predict vocal cord function, postoperatively.

MATERIALS AND METHODS

About 44 nerves at risk were analyzed. Recurrent laryngeal nerve was stimulated with an electrode with a 1 to 1.5 mV current. Concurrently twitch was visualized in the cricopharyngeus muscle and twitch was palpated in the posterior cricoarytenoid muscle. Electrodes placed in the cricopharyngeus muscle also recorded the compound muscle action potential generated in the muscle. Postoperatively patients underwent voice assessment to screen for change in voice.

RESULTS

About 44 nerves were analyzed. Twitch in the cricopharyngeus was recorded in all 44 stimulated nerves and was felt in the posterior cricoarytenoids in all 44 nerves. Compound muscle action potential was recorded and the latency was within normal limits. Post-op voice assessment confirmed that the nerve was functionally intact.

DISCUSSION

Recurrent laryngeal nerve supplies the ipsilateral cricopharyngeus muscle. Nerve monitoring provides objective evidence of functional integrity of the RLN. Physical examination of neuromonitoring provides an alternative to the currently used neuromonitoring devices with reduced cost and complexity.

CONCLUSION

Physical examination of neuromonitoring is a reliable technique for confirming anatomical and functional integrity of the RLN.

Thyroid Elastography as a Complement to Conventional Thyroid Ultrasound in the Diagnosis of Malignant Thyroid Nodules: A Prospective Study

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INTRODUCTION

Conventional ultrasound, which has been used for decades to assess thyroid nodules, offers good specificity but low sensitivity. Ultrasound elastography has emerged as a new instrument that has been reported to improve the detection of thyroid malignancy, but it has also received mixed responses. We aimed to determine the efficacy of ultrasound elastography in detecting malignant thyroid nodules and to examine its use alongside conventional ultrasound.

MATERIALS AND METHODS

This prospective study assessed patients with thyroid nodules using conventional ultrasound and strain elastography, as represented by the elasticity contrast index (ECI). The results were compared against the nodule's cytology and/or histopathology before statistical analysis.

RESULTS

Of the 156 nodules included, 12 (7.7%) were malignant, and 144 (88.8%) were benign. Elastography showed a significant but weak positive correlation with thyroid cancer ($r_s = 0.2$, $p < 0.01$) and was an independent predictor of malignancy [odds ratio (OR) = 10.35, 95% confidence interval (CI) = [1.31, 81.6], $p = 0.03$]. The other independent predictors were elongated shape and a central Doppler pattern. The cutoff value for the ECI was 2.04, which resulted in 58.3% sensitivity (95% CI = [27.7, 83.8]), 80.6% specificity (95% CI = [73.1, 86.7%]), 20.0% positive predictive value (95% CI = [12.3, 30.9%]), 95.9% negative predictive value (NPV) (95% CI = [92.2, 97.85]), and 78.85% accuracy (95% CI = [71.6, 85.0]). A proposed score of ≥ 4 combining the ECI, shape, and Doppler pattern improved the sensitivity of malignant thyroid nodule detection to 100% (95% CI = [73.5, 100]) with an NPV of 100%.

CONCLUSION

Thyroid elastography is an independent predictor of thyroid malignancy. Its performance is comparable to that of conventional ultrasound when used alone but improves when used in combination with conventional ultrasound. Elastography is, therefore, a valuable screening tool for thyroid nodules.

LOC

The Malignancy Rates in the Bethesda System for Reporting Thyroid Cytopathology: A Single Center Experience

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INTRODUCTION

Bethesda system for reporting thyroid cytopathology (BSRTC) was introduced to standardize report thus to improve management. A few studies showed a good diagnostic correlation between BSRTC and the final histopathological (HP) result. However, limited studies are done in Asian countries.

OBJECTIVES

To evaluate the accuracy of BSRTC with final histopathology result at Hospital Putrajaya and to provide recommendations to improve the management of thyroid nodules.

MATERIALS AND METHODS

A retrospective study of patients who underwent fine needle aspiration cytology (FNAC) of thyroid gland at Hospital Putrajaya, Malaysia from 2008 to 2017. The FNAC results were compared with final HP result after surgical excision.

RESULTS

A total of 854 patients with thyroid nodule underwent FNAC at our center (729 female and 125 male) with the median age and thyroid nodule size of 42 years and 30 mm respectively. Fine needle aspiration cytology was reported according to Bethesda criteria, showed: 71 (8%) nondiagnostic or unsatisfactory, 528 (62%) benign, 204 (24%) atypia of unknown significant/follicular lesion of undetermined significance (AUS/FLUS), 16 (2%) follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), 10 (1%) suspicious for malignancy (SM), and 25 (3%) malignant cases. Among them, 439 (51%) patients subsequently underwent excision of thyroid gland and the malignancy rate for each BSRTC category based on final HP report are as follows: 41% in non-diagnostic or unsatisfactory, 14% in benign, 27% in AUS/FLUS, 75% in FN/SFN, 75% in SM, and 100% in malignant groups.

CONCLUSION

Bethesda system for reporting thyroid cytopathology underestimated malignancy rates in our center in the first four diagnostic categories. Management of thyroid nodule at our center should be revisited. Ultrasound guided FNAC may improve the diagnostic accuracy.

A New Surgical Concept of *in situ* Preservation of the Inferior Parathyroid Gland during Central Neck Dissection for Papillary Thyroid Carcinoma: A Clinical Study of 591 Cases

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INTRODUCTION

Postoperative hypocalcemia due to dysfunction of the parathyroid glands is the most common complication after total thyroidectomy plus central neck dissection (CND). There is a lack of surgical techniques described to help preserve the inferior parathyroid gland (IPTG) *in situ* during CND. The objective of this study was to introduce the "TBP layer" (layer of thymus–blood vessel–inferior parathyroid gland) concept for preserving the IPTG *in situ* during CND, and to evaluate its effectiveness.

MATERIALS AND METHODS

A total of 591 patients with primary parathyroid carcinoma (PTC) who underwent total thyroidectomy with CND using the new surgical concept "TBP layer" were enrolled in this study, between January 2014 and June 2017. The proportion of IPTGs preserved *in situ* and postoperative hypoparathyroidism rates was investigated.

RESULTS

About 240 patients underwent total thyroidectomy with ipsilateral CND, while 351 patients received total thyroidectomy with bilateral CND. Simultaneous lateral neck dissection was performed in 127 of 591 patients. The median number of received and metastatic lymph nodes in the central compartment were 13.0 (2.0–65.0) and 1.0 (0.0–47.0) respectively. The rate of IPTG preservation *in situ* on the left side was 83.0%, and on the right side was 84.0%. The incidence of transient hypoparathyroidism of 591 PTC patients was 12.4%, and no patient developed permanent hypoparathyroidism.

CONCLUSION

The proposed surgical concept "TBP layer" could greatly improve the rate of IPTG preservation *in situ*, efficiently decrease the incidence of postoperative hypoparathyroidism, and ensure the completeness of CND.

Progression of Adenomatous Nodule through Hyperplasia to Thyroid Carcinoma in Subjects with Concurrent Thyroiditis

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INTRODUCTION

The association between thyroiditis and papillary carcinoma thyroid (PTC) is a subject of debate. We prospectively evaluated the prevalence of thyroiditis in benign and malignant nodules in cytology and histopathological examination (HPE) after total thyroidectomy (TT).

MATERIALS AND METHODS

Subjects with thyroid nodule undergoing TT (n = 235; age = mean \pm standard deviation; 42.1 \pm 13.1 years; M:F= 21:214) in a single institution from August 2014 to July 2017 were studied. Demographic and clinicopathological data were analyzed; p < 0.05 was considered significant.

RESULTS

Histopathological examination comprised of 125 colloid nodule, 29 follicular adenoma, 14 adenomatous nodule, 21 adenomatous hyperplasia, 22 nodular hyperplasia, and 24 PTC. Out of 235 subjects, 29.8% (n = 70) had thyroiditis and 10.2% (n = 24; age = 44.3 \pm 14.1 years; M: F= 5: 19) had PTC in HPE. The incidence of thyroiditis was 11.2% in colloid goiter, 32.5% in adenomatous nodule, 73.8% in nodular, and adenomatous hyperplasia and 54.2% in PTC. Fine needle aspiration cytology correlated well with HPE reports. Thyroiditis was significantly associated with PTC (p < 0.001; 95% CI = 1.19 to 6.51). Age, gender, tumor size, and stage of PTC did not correlate with the presence of thyroiditis.

CONCLUSION

Subjects with thyroiditis had >twofold increased risk of PTC. We observed stepwise progression of adenomatous nodule through hyperplasia to PTC in association with thyroiditis.

Surgeon Performed Transcutaneous Laryngeal Ultrasound vs Video Laryngoscopy for the assessment of Vocal Cords in Postthyroidectomy Patients

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INTRODUCTION

Ultrasonography is a noninvasive tool that is essential for evaluation of all goiters, a potential application of this tool can be extended for the assessment of vocal cord movement. This study intends to assess the reliability of surgeon performed transcutaneous laryngeal ultrasound (SPU) as a substitute to video laryngoscopy (VDL) in the postoperative scrutiny of vocal cord palsy after thyroidectomy.

MATERIALS AND METHODS

A prospective study done on patients who underwent thyroidectomy between September 2016 and August 2017 at endocrine surgery unit in a tertiary care institute (South India), SPU and VDL were performed before and after elective thyroidectomy.

RESULTS

A total of 155 patients who consented were categorized in the study, two of the patients included in the study had preoperative vocal cord palsy and 12 of them had unilateral postoperative vocal cord palsy detected using VDL. In general the postoperative vocal cord palsy rate was 7.74%. Postoperative SPU was ineffective in assessing vocal cords in 16 (10.32%) of patients. The SPU had a sensitivity of 92.3% and negative predictive value of 99.1%, for the visualization of vocal cords in the postoperative period.

CONCLUSION

The SPU is a convenient and noninvasive tool for the assessment of vocal cords in the postoperative period, which can potentially decrease the requirement of cumbersome and discomforting VDL.

Clinical Features of Tall Cell Variant Papillary Thyroid Carcinoma with Tumor Size Smaller than 2 cm and Without Lymph Node Metastasis

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INTRODUCTION

The poor prognostic factors of tall cell variant papillary thyroid carcinoma (TCPTC) include older age, large tumor size, extrathyroidal extension. However, the influence of lymph node metastasis (LNM) on prognosis of TCPTC is controversial. The aim of

the study is to verify the clinical characteristics related to the recurrence of tumor in TCPTC and assess the prognostic behavior of TCPTC without LNM.

MATERIALS AND METHODS

From February 2003 to November 2015, patients underwent thyroidectomy with central lymph node dissection and diagnosed of TCPTC have been enrolled. The definition of TCPTC enclosed PTC harboring over 50% of tall cells. Retrospectively, patients' clinicopathological characteristics, complications, and long-term results have been reviewed.

RESULTS

Out of 154 patients diagnosed with TCPTC within the study period, a total of 97 patients had involved LNM, and 9 patients experienced relapse or remnant of tumor (62.6 and 5.8% respectively). Patients experienced recurrence or remnant tend to present tumors with size over 2 cm, lymphatic invasion, and LNM ($p = 0.003$, 0.011 , and 0.027 respectively). The odds ratio of tumor size over 2 cm was 8.82 [confidence interval (CI) 2.07–37.49], and LNM was 1.10 (CI 1.03–1.18). Disease-free survival period of recurrent patients on both tumor size over 2 cm and LNM were significantly shorter ($p = 0.001$ and $p = 0.017$ respectively).

CONCLUSION

Poor prognosis of TCPTC is closely related to larger tumor size, lymphatic invasion, and LNM. For TCPTC patients with these features can be recommended for aggressive treatments, such as total thyroidectomy with through lymph node dissection, and radioactive iodine ablation therapy.

Impact of lymph Node Volume and Ratio on Recurrence in Clinically N0 and N1 Micropapillary Thyroid Cancer

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INTRODUCTION

The ratio of the number of positive metastatic nodes to the total number retrieved and the volume of lymph nodes in the neck have been proposed as risk factors for recurrence in papillary thyroid carcinoma (PTC). However, its relevance in papillary microcarcinoma is less well studied.

MATERIALS AND METHODS

This is a retrospective study of 87 papillary microcarcinomas of the thyroid treated between January 2000 and December 2015 at a tertiary referral center. Demographic and clinicopathological details including those of tumour size, extrathyroidal extension (ETE), number of metastatic central lymph nodes, and the lymph node ratio were investigated. Patients with lobectomy and a follow-up period of less than 2 years, recurrent cancer, and other malignancies were excluded.

RESULTS

The cohort comprised of 68 F:19 M with a median age of 48 (18–77) years. About 58 (67%) mPTCs were diagnosed incidentally following surgery for benign thyroid disease. Lymph node (LN) metastasis was seen in 29 (33%) patients with 19 (22%) involving the central compartment and 10 (11%) involving both the central and lateral compartments. After a median follow-up period of 79 months, recurrence occurred in 8 patients (9%). On multivariate analysis male gender, extrathyroidal extension, large volume of metastatic nodes (more than 2), and lymph node ratio of more than 0.3 were significantly associated with recurrence.

CONCLUSION

Lymph node ratio and volume of metastatic LNs are independent prognostic risk factors for recurrence in patients with micropapillary thyroid cancer and should be used to guide postoperative treatment and surveillance.

Predictive Factors for Non-small-volume Central Lymph Node Metastases (More than 5 or ≥ 2 mm) in Clinically Node-negative Papillary Thyroid Carcinoma

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INTRODUCTION

The value of prophylactic central neck dissection (pCND) for papillary thyroid carcinoma (PTC) is unclear. However, lymph node metastasis is correlated with local recurrence, especially for more than 5 or ≥ 2 mm. This study aimed to determine the incidence and risk factors of metastatic lymph node in the central compartment with more than 5 or ≥ 2 mm, defined as non-small-volume central lymph node metastases (NSVCLNM).

MATERIALS AND METHODS

A total of 611 patients with clinically node-negative (cN0) PTC were retrospectively analyzed. Cervical lymph nodes were harvested and the size of metastatic lymph nodes was microscopically measured.

RESULTS

Non-small-volume central lymph node metastases were detected in 67 (11.0%) patients. Male gender, age ≤ 36 years, multifocal lesions, extrathyroidal extension, and tumor size >0.85 cm were independent risk factors of NSVCLNM in cN0 PTC. The sensitivity and specificity of having ≥ 3 risk factors for predicting NSVCLNM were 46.3% and 86.8% respectively. After 30 to 54 months follow-up, six patients with NSVCLNM had lymph node recurrence, while recurrence was not detected in patients without NSVCLNM.

CONCLUSION

These findings suggest pCND as suitable procedure for cN0 PTC patients with ≥ 3 risk factors of NSVCLNM.

Changing Profile of Primary Hyperparathyroidism over Two and Half Decades: A Retrospective Study in a Tertiary Care Center of North India

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INTRODUCTION

Most of the cases of primary hyperparathyroidism (PHPT) in developing countries present in symptomatic stage, some even in very advanced stage but in recent years, the trend seems to be changing. This has been corroborated from few recently published literature from developing countries. The scope of this study is to further carry out an in-depth analysis of various clinical and biochemical parameters of PHPT patients at a tertiary care center of northern India.

MATERIALS AND METHODS

In this retrospective analysis, a total of 333 patients with PHPT from the year 1990 to 2016 were studied. The study population was divided into three subgroups based on the time span; 1990 to 1999 (n = 34), 2000 to 2009 (n = 112), 2010 to 2016 (n = 187), and clinical and biochemical parameters were compared.

RESULTS

The clinical presentation has evolved progressively with increase in older age group (35 vs 39 vs 43.85, $p < 0.001$), less patients with musculoskeletal symptoms (85.3 vs 76.8 vs 61%, $p = 0.309$), and less patients with severe bone disease (29.4 vs 10.7 vs 10.7%, $p = 0.088$). Biochemical parameters also showed a changing trend with significant decrease in mean serum alkaline phosphatase (1,393 vs 965 vs 414.8 IU/L, $p < 0.001$) and serum intact parathyroid hormone (837.52 vs 812.89 vs 635.74 pg/mL, $p = 0.02$). Vitamin D nutrition status showed more patients are insufficient as compared with previous deficient state (mean serum Vit D—10.31 vs 16.16 vs 25.30 ng/mL, $p < 0.001$).

CONCLUSION

Our study reveals a change in trend in PHPT, which is similar to evolution of this disease in Western population and positively corroborated with observations from China, Hong Kong, and Turkey.

***In situ* Preservation of Parathyroid Glands in Thyroid Surgery for Prevention of Hypoparathyroidism**

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INTRODUCTION

Hypoparathyroidism (HPT) is one of the most frequent and severe complications of thyroid surgery. It is caused by intraoperative damage, devascularization, or accidental removal of the parathyroid glands (PTG). The incidence of postoperative HPT is directly proportional to surgery extent and surgeon's experience. The authors present original technique of *in situ* preservation of PTGs during thyroid surgery and 40-years-experience results in postoperative HPT.

MATERIALS AND METHODS

Our surgical technique focuses on meticulous capsular dissection and ligation of blood vessels close to thyroid capsule. The key step is preservation of the middle thyroid, Kocher's, vein trunk, as well as vein branches that accompany posterior branch of superior thyroid artery and inferior thyroid artery trunk. The use of methylene blue dye for sentinel lymph nodes biopsy facilitates identification of PTGs during central neck dissection, since PTGs are not colored in blue, unlike central lymph nodes.

RESULTS

After 40 years of experience in thyroid surgery and several thousands of preserved PTGs, a total prevalence of permanent HPT in the first author's series is less than 0.5%.

CONCLUSION

This original technique of venous trunk's preservation, along with so far known surgical steps for *in situ* preservation of PTGs on arterial pedicle, provides good outcome for patients after total thyroidectomy, with or without central neck dissection, regarding HPT as one of the most severe complications of thyroid surgery. We find methylene blue dye useful, not only for sentinel lymph nodes biopsy, but also for avoiding accidental removal of PTGs.

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Sentinel Lymph Node Biopsy in Papillary and Medullary Thyroid Carcinomas and Microcarcinomas in Decision for Selective Modified Lateral Neck Dissection

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INTRODUCTION

Surgical management of cN0 patients with thyroid carcinomas remains debatable due to frequency of lymph node metastases (LNMs). Preoperative ultrasound identifies only half of LNMs found at surgery. Our aim was to investigate if sentinel lymph node biopsy (SLNB) using methylene blue dye (MBD) is accurate in the detection of LNMs in lateral neck compartments, selecting cN0 patients with papillary and medullary thyroid carcinomas and microcarcinomas for selective modified lateral neck dissection (sMLND).

MATERIALS AND METHODS

We present three studies that analyzed SLNB method: the first with 153 cN0 papillary thyroid carcinomas (PTC), the second with 111 cN0 papillary thyroid microcarcinomas (PTMCs), and the third with 15 cN0 medullary microcarcinomas (micro-MTC) with serum calcitonin levels <1,000 pg/mL. All patients underwent total thyroidectomy with prophylactic central neck dissection and SLNB of lateral neck compartments using MBD. One-time sMLND was performed in all cases with metastases in sentinel lymph nodes on frozen section.

RESULTS

Lymph node metastases were histologically verified in 40.9% of cN0 PTCs and 25% of cN0 PTMCs. Only one patient with hereditary micro-MTC had LNMs in central and both lateral regions. Sentinel lymph node biopsy method enabled detection of

LNMs in lateral neck compartments in 21% of patients. Skip metastases were detected in about 4%. Overall accuracy was high in all studies, but highest in study with micro-MTCs (100%).

CONCLUSION

Sentinel lymph node biopsy method with MBD is accurate in detection of LNMs in lateral neck compartments and may help in decision for sMLND in cN0, but true positive patients with papillary and medullary thyroid carcinomas and microcarcinomas.

To Study the Relationship of Preoperative Serum Thyroglobulin Levels in Benign and Malignant Thyroid Disorders

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INTRODUCTION

Thyroglobulin (TG) is secreted exclusively from thyroid follicular cells. We aim to study the relationship if any on the preoperative serum TG levels in benign and malignant thyroid disorders. Thyroglobulin is currently used as a tumor marker in the postoperative surveillance of differentiated thyroid cancer.

MATERIALS AND METHODS

Our study was done in the Department of Endocrine Surgery, Madras Medical College, where a sample of 50 patients with either benign or malignant thyroid disorders were selected over a period of 6 months. All patients had serum TG levels and antithyroglobulin (ATG) antibody levels estimated preoperatively. Ultrasonography neck measurements of the thyroid lobes were recorded. All the thyroidectomy specimens were measured to assess the volume of the specimen. Only patients with negligible levels of ATG antibodies and absence of thyroiditis were included in the study. Relationship between serum triglyceride levels, volume of thyroid gland, cytology, and histopathology were analyzed using Statistical Package for the Social Sciences version 22 software. Chi-square test was used as test of significance and p-value of <0.05 was considered as statistically significant.

RESULTS

All 50 patients underwent total thyroidectomy, 39 were diagnosed with benign thyroid disease and the rest were malignant. Majority were female patients. Mean preoperative serum TG was proportionately higher in patients with larger thyroid volume. There was a significant association between the preoperative TG levels and the volume of the thyroid gland. There was no significant correlation between the levels of serum TG levels and the pathology of the thyroid gland.

CONCLUSION

By estimating preoperative TG we hope that it can be used as a tool to assess the burden of tumor tissue present at presentation and during post-op surveillance for recurrence.

Predictors for Central Lymph Node Metastases in CN0 Papillary Thyroid Microcarcinoma: A Retrospect Analysis of 1304 Cases

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INTRODUCTION

Presence of lymph node metastases (LNMs) increases the risk of recurrence, but whether to perform prophylactic central neck node dissection for patients with papillary thyroid microcarcinoma (mPTC) is controversial. We aim to find the clinical predictors of central lymph node metastases (CLNM) in CN0 mPTC patients.

MATERIALS AND METHODS

We retrospectively reviewed the clinicopathological and genetic characteristics of 1,304 patients with CN0 mPTC operated at the First Hospital of Jilin University between January 2013 and May 2016, all of whom underwent thyroid lobectomy or total thyroidectomy with uni/bilateral prophylactic central neck dissection. Univariate and multivariate analyses were used to identify the predictors of CLNM in CN0 mPTC patients.

RESULTS

About 30.7% of CN0 mPTC patients had CLNM. Univariate analysis found CLNM to be associated with age (≤ 45), gender (male), tumor size (>0.5 cm), multifocality, bilaterality, capsular invasion, lymphovascular invasion, and extrathyroidal infiltration, but not associated with BRAF mutation, tumor location, preoperative thyroid-stimulating hormone (TSH), and antithyroglobulin level. Multivariate logistic regression showed age ≤ 45 years [$p < 0.001$, odds ratio (OR) = 2.05], male gender ($p < 0.001$, OR = 1.94), tumor size >0.5 cm ($p < 0.001$, OR = 1.87), bilaterality ($p = 0.003$, OR = 1.86), and capsular invasion ($p = 0.013$, OR = 1.49) to be independent predictors for CLNM in CN0 mPTC patients.

CONCLUSION

Prophylactic central neck dissection has higher yield for CN0 mPTC patients with age ≤ 45 years, male gender, tumor size >0.5 cm, bilaterality, and capsular invasion. BRAF mutation is not a predictor for CLNM in CN0 mPTC patients.

Table 1: Comparison of clinical characteristics for patients of CN0 mPTC with CLNM and those without CLNM

	LN(-) (n = 904)	LN(+) (n = 400)		p-value
<i>Gender</i>				
Female (0)	800 (88.5)	317 (79.3)	$X^2 = 19.272$	<0.01
Male (1)	104 (11.5)	83 (20.8)		
<i>Age</i>				
≤ 45 (0)	441 (48.8)	264 (66.0)	T = 7.087	<0.01
>45 (1)	463 (51.2)	136 (34.0)	$X^2 = 33.098$	<0.01
<i>Tumor size</i>				
≤ 0.5 cm (0)	0.512 \pm 0.207	0.608 \pm 0.195	t = -7.830	0.522
>0.5 cm (1)	362 (40.0)	83 (20.8)	$X^2 = 45.921$	<0.01
<i>Location</i>				
Upper (0)	234	101	$X^2 = 0.997$	0.607
Middle (1)	202	81		
Lower (2)	468	218		
<i>Multifocality</i>				
Unifocus (0)	421 (46.6)	98 (24.5)	$X^2 = 56.377$	<0.01
Multi foci (1)	483 (53.4)	302 (75.5)		
<i>Bilaterality</i>				
Unilateral (0)	541 (59.8)	140 (35.0)	$X^2 = 68.605$	<0.01
Bilateral	363 (40.2)	260 (65.0)		
<i>Capsular invasion</i>				
No (0)	343 (36.4)	82 (20.5)	$X^2 = 38.401$	<0.01
Yes (1)	561 (62.1)	318 (79.5)		
<i>Extrathyroidal infiltration</i>				
No (0)	821 (90.8)	341 (85.3)	$X^2 = 8.861$	<0.01 (0.003)
Yes (1)	83 (9.2)	59 (14.8)		
<i>Lymphovascular invasion</i>				
No (0)	904	393 (98.3)	$X^2 = 15.905$	<0.01
Yes (1)	0	7 (1.8)		
<i>Hashimoto</i>				
No (0)	600 (66.4)	269 (67.3)	$X^2 = 0.096$	0.756
Yes (1)	304 (33.6)	131 (32.8)		
<i>BRAF mutation</i>				
No (0)	51 (5.6)	22 (5.5)	$X^2 = 1.936$	0.380
Yes (1)	255 (28.2)	128 (32)		
Unknown (2)	598 (66.2)	250 (62.5)		
<i>TSH (pre-O)</i>				
No increased (0)	2.82 \pm 3.955	2.64 \pm 1.625	t = 0.876	0.381
Increased (1)	775 (85.7)	343 (85.8)	$X^2 < 0.01$	0.992
<i>Anti-Tg (pre-O)</i>				
Normal (0)	129 (14.3)	57 (14.2)	$X^2 = 0.106$	0.745
Increased (1)	684 (75.7)	306 (76.5)		
<i>Variables</i>				
	Odds ratio	95% CI		p-value
1. Age (≤ 45 years)	2.050	1.583	2.654	<0.01
2. Gender (male)	1.935	1.376	2.722	<0.01
3. Size (>0.5)	1.873	1.381	2.539	<0.01
4. Bilaterality (bilateral)	1.857	1.243	4.564	<0.01
5. Capsular invasion (positive)	1.493	1.087	2.050	0.013

CI: Confidence interval

Circumferential Laryngotracheal Resection in Thyroid Cancer: Experience in a Single Center

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INTRODUCTION

Locally advanced thyroid cancer, one that has breached the capsule with invasion of surrounding vital structures, poses a management challenge both to the surgeon and to the patient. The aim of this study was to report our experience with the management of such advanced thyroid cancers.

MATERIALS AND METHODS

This is a retrospective review of prospectively entered data of thyroid cancer invading the airway, managed with circumferential resection at our institute (January 2000–December 2015). Clinicopathologic, management details and outcome were noted.

RESULTS

Ten patients (4 men and 6 women) were identified. Mean age of patients was 49.6 ± 08.3 years (32–58 years). About 70% of patients were symptomatic with hemoptysis, dyspnea; voice change was present in 2, 5, and 3 patients, respectively, while 30% had TENIS. About 40% patients present as new and 60% with recurrent disease. All patients underwent bronchoscopy and contrast-enhanced computed tomography neck. Distant metastases were present in 40%. Total laryngectomy, tracheal resection with end-to-end anastomosis, and laryngotracheal resection were done in 3, 5, and 2 patients respectively. Thrombectomy was performed in three patients. Partial sternotomy was required in four patients. Salivary fistula and neck hematoma were seen in two and one patient respectively. Histology revealed PTC, FTC, HCC, and PDTC in 50, 10, 10, and 20% patients respectively. One margin involvement was seen in three patients. Radioactive iodine therapy and radiotherapy were given to 60 and 40% patients in adjuvant setting respectively. Median follow-up was 33 (12–65) months. Five years overall survival was 83%.

CONCLUSION

Circumferential resection for airway invasive differentiated thyroid cancer, although technically demanding procedure provides excellent disease control and long-term disease control with minimal morbidity especially at a referral center.

Bone Mineral Density in Thyroid Cancer Patients: Data from Korea National Health and Nutrition Examination Survey

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AIMS

There are conflicting results about bone mineral density after thyroid-stimulating hormone suppression in thyroid cancer treatment. The aim of this study is to investigate osteopenia and osteoporosis in Korean thyroid cancer patients using Korea National Health and Nutrition Examination Survey (KNHANES).

MATERIALS AND METHODS

Data were collected from 2008 to 2011 of KNHANES IV-V. Among total 37,753 participants, 18,618 subjects were included. Osteopenia and osteoporosis were evaluated according to the thyroid cancer history. Subgroup of women and postmenopausal women were analyzed by the same method.

RESULTS

Among the 18,618 subjects, 80 thyroid cancers were observed. There was no significant difference in osteopenia and osteoporosis with or without thyroid cancer history ($p = 0.091$). In the subgroup analysis of women and postmenopausal women, no difference was observed in bone mineral density according to thyroid cancer history ($p = 0.233, 0.101$).

CONCLUSION

This study showed that bone mineral density was not decreased in thyroid cancer patients. The result was the same in the subgroup of women and postmenopausal women.

Evaluation of Radioiodine Avidity in Patients with Metastatic Papillary Thyroid Cancer

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INTRODUCTION

Patients with radioiodine avid lesions are more likely to benefit from radioiodine therapy (RIT). The aim of this study is to define characteristics of patients who will benefit from RIT for distant metastasis of papillary thyroid cancer (PTC) by using avidity rates (ARs) of the metastatic lesions.

MATERIALS AND METHODS

From January 2007 to December 2016, 136 adult cases of initial RIT for distant metastasis of PTC were performed. The total group had 27 male, 109 female, average age of initial surgery (IS) was 52.9. The total group was divided into three groups by age of IS: 21 to 40, 41 to 60, and over 61 and were also divided by the interval of 24 months for initial RIT. The ARs were compared.

RESULTS

The total group had only 23.5% in AR, but the group that had RIT within 24 months had AR of 39.6% and was significant compared with those after 24 months (AR 13.3%, $p < 0.01$). In each age group, the ARs were 21 to 40: 46.3%, 41 to 60: 15.8%, and over 61: 12.3%. With each age group divided by interval of 24 months, ARs were higher when treated earlier (21–40: 62.5 vs 36.0%, 41–60: 55.6 vs 3.4%, over 61: 21.4 vs 3.4%). Significance in AR was only seen in the eldest group compared with the youngest group when RIT was given within 24 months ($p < 0.05$).

CONCLUSION

Radioiodine therapy can have benefits for patients with distant metastasis of PTC, especially when RIT is performed within 24 months of IS and younger than 60 years of age when IS.

Validation of Radioactive Iodine Scanning vs Ultrasonography and Computed Tomography in the Detection of Residual Thyroid Tissue

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INTRODUCTION

Differentiated thyroid carcinomas (DTCs) are among the most curable cancers. However, some patients are at high risk for recurrent disease. Most of these patients can be identified at the time of diagnosis by using well-established prognostic indicators. The aim of this work was to study the validity of radioactive iodine scanning (RAIS) vs ultrasonography (USG) and computed tomography (CT) in the detection of residual thyroid tissue after total thyroidectomy for patients with DTC.

MATERIALS AND METHODS

This is a prospective study conducted in Alexandria Main University Hospital and it comprised 30 patients with DTC who were treated by total thyroidectomy and the appropriate type of neck dissection. One month postoperatively, they were adjuvantly treated with radioactive iodine. Patients were followed up by the following:

- RAIS, CT, and USG within 2 weeks.
- Serum thyroglobulin (Tg) after radioactive iodine ablation after 1 month.
- RAIS, CT, and USG after 2 months.

RESULTS

Two weeks postoperatively, serum Tg was detectable in five patients. The RAIS gave false-positive results in four patients; CT gave two false-positive results, while USG didn't give any. So USG was 90% accurate followed by RAIS 86.60% and then CT 83.33%. After 2 months, USG accuracy reached 100%, CT 96.6%, and RAIS 90%.

CONCLUSION

Neck (USG) is highly specific for detection of residual tumors compared with RAIS, although it is an operator-dependent technique. Computed tomography follows USG as regards specificity for detection of residual tumor but it is less sensitive.

Low-risk Well-differentiated Papillary Thyroid Cancer—To Ablate or Not to Ablate?

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INTRODUCTION

Radioactive iodine therapy (RAI) remnant ablation postthyroid surgery for low-risk well-differentiated thyroid cancer is still controversial. The aim of the study was to assess any difference in outcomes in patients with or without ablation in low-risk disease.

MATERIALS AND METHODS

Retrospective analysis of patients treated for papillary thyroid cancer from 2000 to 2015 at a tertiary institution. Demographic, clinicopathological profiles, and treatment details were collected and divided into two cohorts: patients with and without RAI ablation. Outcomes analyzed were overall survival, disease-free survival, and recurrence of thyroid cancer at last follow-up.

RESULTS

A total of 408 patients (294 F and 114 M) were treated for papillary thyroid cancer, of whom 155 (38%) patients were classified as being American Thyroid Association low risk. The mean age in both the cohorts was similar (45 years) with similar gender distribution. Patients who did not receive RAI had smaller tumors (T1 more than T2), whereas in the ablation group the sizes were similar. There were no significant differences between the two cohorts on any other parameters assessed. Recurrences were similar in both groups (1 vs 1%) in the regional lymph nodes but disease-specific survival was 100% in both groups.

CONCLUSION

The RAI ablation is of proven benefit in low-risk differentiated papillary thyroid cancer.

Prognostic Factors for Intrathyroidal Papillary Thyroid Carcinomas

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INTRODUCTION

The aim of this study was to examine prognostic significance of patient-related, tumor-related, and treatment-related factors for intrathyroidal papillary thyroid carcinomas (PTCs) via multivariate analysis.

MATERIALS AND METHODS

This study included 153 patients with intrathyroidal PTC (pT1/pT2/pT3) surgically treated in our institution during two-decade period. Patients with locally invasive tumors (pT4) and initial distant metastases (M1) were excluded. Parameters of interest were: gender (male; female), age (≤ 45 ; >45 years), tumor size (pTNM classification, WHO 1984), multifocality (no; yes), histological type of PTC ("pure"; microcarcinoma; follicular; low-differentiated), presence of lymphonodal metastases (pN1a; ipsilateral-pN1b; contralateral-pN1b; total), surgery extent (total thyroidectomy; total thyroidectomy with lymphonodal dissections). Univariate and multivariate analyses of all parameters were performed in order to distinguish factors of significance for disease-free (DFS) and cancer-specific overall survival (cs-OS).

RESULTS

In the follow-up, 10% of patients had locoregional or distant relapse, while 5.2% died due to PTC. Univariate analysis distinguished older age ($p = 0.0001$), male gender ($p = 0.042$), tumors over 4 cm in diameter ($p = 0.006$), multifocality ($p = 0.0004$), and poorly differentiated PTC types ($p = 0.0001$) as unfavorable prognostic factors for cs-OS. The DFS was significantly shorter in males *vs* females (log rank = 6.64; $p = 0.01$), as well as in patients with multifocal *vs* solitary PTC (log rank = 6.72; $p = 0.0095$). Tumor multifocality was unfavorable prognostic factor on both DFS and cs-OS ($p = 0.0095$ and $p = 0.0004$ respectively). Independent prognostic factors for intrathyroidal PTC, based on Cox multivariate analysis, were multifocality and gender for DFS, and multifocality and age at diagnosis for cs-OS.

CONCLUSION

Prognostic factors define risk groups within population of differentiated PTCs providing adequate, timely treatment, and opportunity for longer and quality life of patients with PTCs.

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Increasing Incidence of Differentiated Thyroid Cancer in Sri Lanka, 2001–2010

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INTRODUCTION

An increasing incidence of thyroid cancer is observed in many countries. While better diagnostic scrutiny and reporting might have contributed to this increase, an inherent increase is also a likely reason. We conducted this study to examine trends in thyroid cancer incidence and histological patterns in Sri Lanka.

MATERIALS AND METHODS

A retrospective cohort evaluation of patients with thyroid cancer during 2001 to 2010 was performed using population-based data published from the Sri Lanka National Cancer Registry. Trends in incidence and histological patterns were analyzed by age and gender.

RESULTS

The age-standardized incidence of thyroid cancer increased from 2.44 per 100,000 in 2001 (95% confidence interval [95% CI]: 2.21–2.67) to 5.16 per 100,000 in 2010 (95% CI: 4.85–5.47) ($p < 0.05$ for trend). A greater part of this increase is attributable to increase in incidence of papillary thyroid cancer, which increased from 1.64 to 3.61 per 100,000 ($p < 0.05$ for trend). Follicular cancer showed lesser, yet a significant increase from 0.56 to 0.95 per 100,000 ($p < 0.05$). Other varieties of thyroid cancer showed no significant increases in incidence. Highest incidence of papillary cancer was observed in 30- to 39-year age group, which has increased from 5.56 to 12.9 per 100,000, a 2.32-fold increase ($p < 0.001$).

CONCLUSION

The increasing incidence of thyroid cancer in Sri Lanka is predominantly due to the increasing incidence of papillary cancers. These trends may reflect increased detection and better reporting, although an inherent increase in the incidence cannot be excluded. Further studies including tumor stage and mortality may help answer these questions.

Detection of Serum Glycans in Benign and Malignant Thyroid Nodules— A Proof of Concept Study

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INTRODUCTION

Glycosylation of proteins is one of the most common forms of posttranslational modification and alterations in glycans can lead to disease states including cancer (Adamczyk et al. *Biochim Biophys Acta* 2012;1820:1347–1353, Ruhaaket al. *Mol Cell Proteomics* 2013;12:846–855). The structural changes in the glycan of serum proteins are associated with some diseases rheumatoid arthritis and hepatocellular carcinoma, where they have suggested to be useful as clinical markers. However, little research has been performed on the glycans in the serum glycoprotein of patients with benign and malignant thyroid disease.

MATERIALS AND METHODS

This study was approved by the Ethics Committee at the National University Hospital of Singapore. The blood samples were prospectively collected from 10 patients undergoing thyroid surgery for benign (five patients) and malignant disease (five patients) and snap frozen in liquid nitrogen. The serum samples underwent preparation and derivatization of the N-linked oligosaccharide moiety. Quantitative glycan analysis was performed by UPLC-MS. Glycan structures were proposed by referencing the experimental glycan database (GlycoBase V3.1) and verified by accurate mass with additional exoglycosidase digestion. Glycan abundance is presented as means \pm standard deviation of the replicates, relative to the total glycan pool.

RESULTS

The following glycans were identified from the serum: sialylated, fucosylated, mannosylated, antennary, and bisecting glycans. In order of quantity, antennary two glycans were the most common glycan seen followed by sialylated glycans, fucosylated, and then di-sialylated glycans. There was no statistical difference in the serum levels of the various glycans between the benign and malignant state (antennary glycans benign *vs* malignant: 76.30+2.02 *vs* 78.51+1.43; sialylated glycans: 55.95 + 11.99 *vs* 56.90 + 9.58; fucosylated glycans: 49.74 + 7.56 *vs* 49.52 + 10.54; di-sialylated glycans 34.54 + 6.85 *vs* 35.13 + 6.51).

CONCLUSION

This proof of concept study shows that it is feasible to extract serum-based glycans in thyroid disease in both benign and malignant state. However, more work needs to be done to assess if the expressed glycans can be used as potential serum-based biomarkers.

Synergistic Anticancer Activity of Tyrosine Kinase Inhibitors and Paclitaxel with Radiation on Anaplastic Thyroid Cancer *in vitro* and *in vivo*

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INTRODUCTION

Anaplastic thyroid carcinoma (ATC) although rare is the most deadly form of thyroid cancer. The goal of this study was to investigate the antitumor activities of paclitaxel with radiation in combination with tyrosine kinase inhibitors (TKIs) in anaplastic thyroid cancer cells *in vitro* and *in vivo*.

MATERIALS AND METHODS

Three ATC cell lines were exposed to TKI in the presence or absence of paclitaxel with radiation and cell viability was determined by MTT assay. Effects of combined treatment on cell cycle and intracellular signaling pathways were assessed by flow cytometry and Western blot analysis. The ATC cell line xenograft model was used to examine the antitumor activity *in vivo*.

RESULTS

Our data showed that paclitaxel with radiation and TKIs synergistically decreased cell viability in ATC cells and also significantly increased apoptotic cell death in these cells, as proved by the cleavage of caspase-3 and deoxyribonucleic acid fragmentation. Paclitaxel and TKI with radiation combination reduced antiapoptotic factor in ATC. Thus, TKI that targeted the vascular endothelial growth factor receptor family (VEGFR-2 and -3) and platelet-derived growth factor receptor family (PDGFR-beta and Kit) plays key roles in tumor progression and angiogenesis. Combination therapy with paclitaxel and TKI with radiation significantly decreased vessel density, and most significantly reduced tumor volume and increased survival in ATC xenografts.

CONCLUSION

These results propose that paclitaxel and TKI with radiation have significant anticancer activity in preclinical models, potentially suggesting a new clinical approach for patients of advanced thyroid cancer type.

Utility of Frozen Section Plus Immunohistochemical Staining for determining the Extent of Thyroidectomy in Patients with Follicular Neoplasm

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INTRODUCTION

The purpose of this study was to evaluate the role of frozen section plus immunohistochemical (IHC) staining for determining the extent of thyroidectomy in patients with preoperative fine-needle aspiration cytology result of follicular neoplasm.

MATERIALS AND METHODS

Between January 2010 and December 2015, 194 patients who underwent thyroidectomy for follicular neoplasm were enrolled. All lesions diagnosed by follicular neoplasm in preoperative cytology were examined by intraoperative frozen section. According

to performing the IHC staining, patients were divided in two groups: group I, conventional frozen section examination without IHC (n = 129) and group II, frozen section plus IHC staining (n = 65).

RESULTS

Clinicopathologic characteristics between two groups were similar. In group I, 53 patients (41.1%) were diagnosed as defer in frozen section, and 16 patients (24.6%) were diagnosed as defer in group II. Reoperation rate was decreased in group II (1.5%) rather than group I (9.3%).

CONCLUSION

Frozen section plus IHC staining is of value for determining the extent of thyroidectomy in patients with follicular neoplasm.

Clinical Significance of BRAF V600E Mutation Analysis in AUS/FLUS Thyroid Nodules

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AIM

The treatment plan of patients with cytology of atypia or follicular lesion of undetermined significance (AUS/FLUS) is a complex clinical problem. To overcome this problem, novel diagnostic procedures have developed to generate clinically actionable information in fine needle aspirations (FNAs) with indeterminate cytology in USA. Several studies have reported the potential diagnostic utility of deoxyribonucleic acid, messenger RNA, and microRNA (miRNA) in preoperative thyroid nodules FNAs. However, the BRAF V600E mutation is only used in Korean insurance. The aim of this study is to evaluate the clinical significance of BRAF V600E mutation analysis in AUS/FLUS thyroid nodules and to verify the value of its utilization as a diagnostic tool.

MATERIALS AND METHODS

Between March 2010 and August 2017, a retrospective analysis was performed on all patients who underwent thyroid surgery for thyroid nodule with AUS/FLUS cytology. Diagnostic accuracy of FNAB with/without BRAF V600E mutation analysis was compared between the three groups: preoperative BRAF V600E mutation-positive, preoperative BRAF V600E mutation-negative, without preoperative BRAF V600E mutation analysis.

RESULTS

Of the 94 patients, 27 patients (28.7%) underwent preoperative BRAF V600E mutation analysis and 67 patients (71.3%) did not. Of the 27 patients who underwent preoperative BRAF V600E mutation analysis, 15 patients (55.6%) were BRAF V600E mutation-positive and 12 patients (44.4%) were BRAF V600E mutation-negative. Preoperative BRAF V600E mutation-positive group had 14 patients with thyroid carcinoma (93.3%). Preoperative BRAF V600E mutation-negative group had seven patients with thyroid carcinoma (58.3%). Without preoperative BRAF V600E mutation analysis group had 34 patients with thyroid carcinoma (50.7%).

CONCLUSION

Preoperative BRAF V600E mutation analysis should be recommended in patients with cytology of AUS/FLUS. And insurance application for an additional genetic diagnostic tool that can complement the BRAF V600E mutation analysis is required.

Sorafenib Lenvatinib Alternating Treatment SoLAT: A New Treatment Protocol using Sorafenib and Lenvatinib Alternatively on Refractory Thyroid Cancer

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INTRODUCTION

Several tyrosine kinase inhibitors (TKIs), which disrupt pathways involved in proliferation and tumorigenesis of thyroid cancer, have been extensively studied. The duration of TKI response is not durable and resistance will arrive sooner or later. The goal of this study was to investigate a new treatment protocol SoLAT using sorafenib and lenvatinib alternatively.

MATERIALS AND METHODS

Patient-derived aggressive papillary thyroid cancer cell lines from patients with proven aggressive radioactive iodine-refractory papillary thyroid cancer (PTC) were exposed to sorafenib and lenvatinib alternatively. Human thyroid cancer cell xenograft was obtained by injecting patient-derived aggressive PTC cell lines into the flank of female BALB/c nude mice. Mice were treated with sorafenib and lenvatinib alternatively. Cell viability assay, immunofluorescence analysis, confocal imaging, immunoblot analysis, flow cytometry analysis of cell cycle, and tube formation assay were performed.

RESULTS

SoLAT was more efficient on advanced PTC cell line than individual treatment. Immunoblot analysis showed that SoLAT markedly increased levels of inhibitors of cell cycle, proapoptotic factors, and decreased levels of positive regulators of cell cycle and antiapoptotic factor. Increased sub-G₀/G₁ population was observed in the SoLAT group, leading to apoptosis, cell cycle arrest, and strong inhibition of advanced PTC viability. SoLAT reduced the level of epithelial-to-mesenchymal transition (EMT) markers such as vimentin, E-cadherin, Snail, and Zeb1 by FGFR inhibition.

CONCLUSION

SoLAT was more efficient than individual treatment with sorafenib or lenvatinib in inhibiting tumor progression by inducing cell cycle arrest. We suggest that these effects may be due to reduced EMT-mediated drug resistance in the aggressive PTC model.

Predicting Outcomes in Papillary Thyroid Cancer using Ratios Derived from Standard Hematological Indices

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INTRODUCTION

Ratios derived from standard hematological indices, such as the neutrophil lymphocyte ratio (NLR) or platelet lymphocyte ratio (PLR), have been studied and used to predict clinical outcomes in various conditions, such as peripheral vascular disease or malignancies. In this study, we aim to correlate these derived ratios with histopathological and clinical outcomes in patients with papillary thyroid cancer.

MATERIALS AND METHODS

Patients who were diagnosed with papillary thyroid cancer and underwent curative surgery in our institution from the period of January 2000 to June 2011 were included in this study. Patient demographic and clinicopathological data were collected retrospectively from electronic medical records. Neutrophil to lymphocyte ratios, neutrophil to monocyte ratios, PLR, and red cell distribution width to platelet ratios were calculated from each patient's preoperative full blood count. Data analysis was performed using Statistical Package for the Social Sciences version 23.

RESULTS

A total of 222 patients were included in this study. There were no significant differences in all derived ratios in various outcomes such as capsular extension, multifocality, lymphovascular invasion, lymph node positivity, presence of thyroiditis, and local recurrence. However, PLR was significantly elevated in patients with extra-thyroidal extension (204.79 ± 167.51 vs 155.53 ± 63.96 , $p = 0.049$). Receiver operating characteristics curve analysis demonstrated an area under curve of 0.596.

CONCLUSION

Preoperative PLR may be able to predict the presence of extrathyroidal extension in patients with papillary thyroid cancer. Larger studies are needed.

Expression and Clinical Significance of BRAF V600E and Ki-67 in Thyroid Papillary Carcinoma

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INTRODUCTION

It is known that many genes are closely related to thyroid carcinoma. BRAF V600E mutation is the most common in papillary thyroid carcinoma (PTC). Ki-67 is a gene that is related to cell proliferation and is expressed in a variety of malignant tumors. This study was designed to investigate the expression of BRAF V600E and Ki-67 in PTC and its clinical significance.

MATERIALS AND METHODS

Clinical data of 162 cases of PTC treated in the Department of Thyroid Surgery, No.1 Hospital of Jilin University from October 2015 to September 2016 were collected. The inclusion criteria were: the operation was done by the same surgeon and the pathologic diagnosis was made by the same pathologist. BRAF V600E mutation was detected by qRT-PCR, and Ki-67 was detected by immunohistochemistry.

RESULTS

The rate of BRAF V600E mutation in PTC was 84.6% and the average value of Ki-67 expression level (Ki-67 (%)) was 3.64%. There was no significant difference between both BRAF V600E mutation and Ki-67 with gender, age, capsule invasion, number of lesions, nodular goiter, and clinical stage ($p > 0.05$). However, they were both correlated with tumor diameter ($p < 0.05$) and Ki-67 was also related to lymph node metastasis, nerve and vascular invasion, and Hashimoto's thyroiditis ($p < 0.05$). And we also found that Ki-67 was highly expressed in BRAF V600E positive patients ($p < 0.05$).

CONCLUSION

There is a correlation between BRAF V600E mutation and Ki-67 protein in PTC, which is related to the development of PTC.

Predictive Role of High-Density Lipoprotein and Body Mass Index in Differentiated Thyroid Carcinoma

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OBJECTIVE

High-density lipoprotein (HDL) and body mass index (BMI) have been implicated in carcinogenesis. However, the significance of HDL and BMI in differentiated thyroid carcinoma (DTC) has not been elucidated. The aim of this study was to assess the roles of HDL and BMI in the carcinogenesis and prognosis of DTC.

MATERIALS AND METHODS

High-density lipoprotein concentrations and BMI values were measured in 155 male patients with DTC and 65 male patients with benign thyroid nodules. Multivariate logistic regression and Cox regression analyses were performed to evaluate the correlation between variables. Receiver operating characteristic (ROC) curves were constructed to assess the performance of HDL and BMI in the diagnosis of DTC and the prediction of 4-year recurrence.

RESULTS

High-density lipoprotein [odds ratio (OR), 0.581; 95% confidence interval (CI), 0.371–0.909; $p = 0.018$] and BMI (OR, 1.174; 95% CI, 1.051–1.130, $p = 0.004$) were both independent risk factors of DTC. The HDL was negatively correlated with distant metastasis (OR, 0.006; 95% CI, 0.000–0.517; $p = 0.025$), while BMI was significantly correlated with capsule invasion (OR, 1.193; 95% CI, 1.057–1.347; $p = 0.004$) and multifocality (OR, 1.208; 95% CI, 1.079–1.353; $p = 0.001$). An ROC analysis indicated that HDL could be a good marker for the diagnosis of DTC (area under curve (AUC), 0.857; 95% CI, 0.805–0.910; $p = 0.006$) at a cutoff value of 1.37 mmol/L and the prediction of 4-year recurrence (AUC, 0.730; 95% CI, 0.585–0.875; $p = 0.006$) at a cutoff value of 1.14 mmol/L. Multivariate Cox regression analysis showed that a low HDL level (≤ 1.14 mmol/L) was able to predict 4-year recurrence (heart rate, 0.199; 95% CI, 0.059–0.667; $p = 0.009$) and a worse outcome.

CONCLUSION

A low HDL level incurs an increased risk of DTC and 4-year recurrence, while a high BMI is associated with capsule invasion and multifocality. However, more advanced research is needed in the future to confirm these results.

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Pitfalls in Cytology of Thyroid Nodules and Its Corelation to Histology in Patients coming from Iodine-deficient Areas

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OBJECTIVE

The aims of the study were to evaluate the diagnostic application of Bethesda System of reporting thyroid cytopathology, to review the cytomorphological spectrum, histologic–cytologic correlation, and detailed discussion on various pitfalls in cytological diagnosis.

MATERIALS AND METHODS

This study included patients who underwent fine needle aspiration cytology and/or histopathological (HP) evaluation, between June 2016 and September 2017.

RESULTS

There were a total of 207 cases where HP specimens were received either as resection specimen or core needle biopsy. M:F = 1:4. The age ranged from 2 to 80 years (mean age 41 years). The adequacy rate of cytology smears: 95.8%. Majority of the lesions (60.5%) fall under Bethesda category (BC) II with colloid goiter being the commonest. There were 4.2% cases, which came in BC III. The lesions suspicious for malignancy (BC V) included 2.3% cases, while in 15.6% cases the diagnosis was given as a malignancy (BC VI). The most common malignancy was papillary carcinoma (50%) was followed by anaplastic carcinoma (25%). Histo-cyto correlation was seen in 90% of the cases. The most common category misdiagnosed on cytology was follicular neoplasm/suspicious of follicular neoplasm (FN/SNF), i.e., there were eight cases, which were categorized as FN/SNF (BC IV) on cytology but turned out to be follicular variant of papillary carcinoma thyroid (FV-PTC) (four cases), adenomatous goiter (three cases), and Grave's disease on histopathology. There were four cases, which was categorized as ASUS, of which two turned out to be adenomatous goiter on histology, while other two cases were finally diagnosed as papillary carcinoma thyroid. Other entities, which were cytologically misdiagnosed, included (one case each of) non-Hodgkin's lymphoma diagnosed as lymphocytic thyroiditis, Hashimoto's thyroiditis as Hurthle cell neoplasm (HCN), minimally invasive FC as hyperplastic/adenomatous colloid nodule, and cystic variant of papillary carcinoma as colloid nodule. The malignancy rates in category I, II, III, IV, V and VI were 57.1, 4, 28.6, 33.3, 100, and 100% respectively. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for malignant thyroid lesions were 88.9, 100, 100, 96, and 96.9% respectively.

CONCLUSION

Fine needle aspiration is a sensitive and specific method in diagnosing thyroid swelling. Increasing Bethesda correlates well with increased risk of malignancies. Atypia of undetermined significance should not be used as a wastebasket. The most commonly misdiagnosed BC is FN, hence such smears should be reported with extra caution.

To Admit or Not to Admit: Experience with Outpatient Thyroidectomy for Graves' Disease in a High-volume Tertiary Care Center

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INTRODUCTION

Total thyroidectomy has been increasingly performed in the outpatient setting in the United States, with proponents citing enhanced patient comfort and reduced hospital costs as major benefits. The Graves' patient is a unique member of this cohort,

with the generally more-challenging nature of this pathology amplifying the potential for perioperative complications. However, we offer that even these patients can be successfully managed with ambulatory surgery.

MATERIALS AND METHODS

The experience of a single high-volume endocrine surgeon at a tertiary referral center with thyroidectomy for Graves' disease was examined from January 2016 to November 2017. Forty-nine patients were identified. Patients were excluded if inpatient consultations (6) or planned admissions (2). The remainder were routinely scheduled as outpatient procedures. Patient demographics, American Society of Anesthesiologists (ASA) score, perioperative parameters, and postoperative outcomes including emergency room utilization and readmission were collected.

RESULTS

The mean age was 32.7 ± 17.5 years, 82% were female, and average body mass index was 27.2 kg/m^2 . The mode ASA score was 3, and median operative time was 1 to 2 hours. Average blood loss was 57.7 mL. Two patients were ultimately admitted for non-medical reasons. Complications included transient and permanent clinical hypocalcaemia in 17.0% and 2.4% respectively, and transient recurrent laryngeal nerve palsies in 9.7%. There were no permanent recurrent laryngeal nerve injuries. Hematoma requiring evacuation was reported in 4.9%. Emergency room visits were noted in 9.7%, and 30-day readmission rate was 7%.

CONCLUSION

Outpatient thyroidectomy is safe and cost-effective with acceptable morbidity in the Graves' patient.

Use of Serum Parathyroid Hormone and Ionized Calcium Trend as a Predictor of Early Next-day Discharge after Total Thyroidectomy

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INTRODUCTION

Traditionally patients undergoing total thyroidectomy in our country are hospitalized for 48 to 72 hours to watch for symptoms of hypocalcemia. Increasing demand for hospital beds requires reducing hospitalization stay after elective surgery. We studied the predictive value of serum intact parathyroid hormone (iPTH) and ionized calcium (iCa) levels taken immediately postoperatively and on postoperative day one (POD1) to determine early discharge after total thyroidectomy.

MATERIALS AND METHODS

The prospective study (December 2016–March 2017) included subjects undergoing total or completion total thyroidectomy for benign or malignant thyroid pathology. Cases involving cervical nodal dissection and redo thyroid surgery were excluded. Samples of iPTH and iCa immediate post surgery and on day 1 were evaluated along with symptoms of hypocalcemia. Discharge criteria were asymptomatic patients with iPTH or iCa levels above 0.9 pmol/L and 0.9 mmol/L respectively. All patients were reviewed early on day 3 in the outpatient clinic to remove drains and review hypocalcemia symptoms.

RESULTS

Among the 30 eligible patients, mean immediate and POD1 iPTH levels were 3.29 pmol/L and 3.25 pmol/L respectively. Mean immediate and POD1 iCa were 1.10 mmol/L and 1.01 mmol/L respectively. There was a significant downward trend between iCa levels in immediate post-op levels and POD1 ($\beta = -0.76$, $p\text{-value} < 0.001$); however, none of the patients experienced any symptoms of hypocalcemia above the cut-off point of 0.9 mmol/L. Mean length of hospitalization was 1.2 days. About 24 of 30 patients (80%) were discharged next morning as they fulfilled the discharge criteria. The remainder six patients (16.6%) went home on day 2 due to social and caregiver issues despite meeting the discharge criteria. One patient (3.4%) refused to go home until the neck drain was removed. There were no unscheduled readmissions or A&E visits after early discharge.

CONCLUSION

Majority of patients who undergo total thyroidectomy can be safely discharged on POD1 if discharge criteria are met with no unscheduled readmissions.

Long-term Efficacy of Parathyroid Allograft Transplantation in Alleviating Permanent Surgical Hypoparathyroidism: A Feasibility Study

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INTRODUCTION

Post-thyroidectomy permanent hypoparathyroidism is a serious health ailment and patients suffer from both regular hypocalcemia symptoms and long-term sequelae (cardiac dysfunction, basal ganglia calcification, poor quality of life). There is no permanent cure for this condition. In this context, we analyzed the efficacy of parathyroid allograft transplantation in offering a cure in this condition.

MATERIALS AND METHODS

This is a prospective study conducted in Endocrine Surgery department of a tertiary care hospital. In all, five patients with post-thyroidectomy permanent hypoparathyroidism were included in this study. With proper consent and HLA cross-matching, two healthy parathyroid glands were harvested from donors (mostly parents, siblings) and implanted in left brachioradialis muscle of patients in the same setting. All relevant data are collected and statistical analysis was done with Statistical Package for the Social Sciences version 18.0. Mean follow-up period was 14.5 ± 3.2 months (14–24). No immunosuppression was used.

RESULTS

Preoperative serum intact parathyroid hormone (PTH) level was 1.4 ± 0.6 pg/mL (0–3.5), serum calcium was 6.2 ± 1.5 mg/dL (4.2–7.9), and postoperative PTH level was 14.5 ± 7 pg/mL (12–36), serum calcium was 8.1 ± 1.2 mg/dL (7.5–9.0) at 1 year. Preoperative daily calcium dose was 3.0 ± 1.2 (2.5–7) gm and postoperative dose was 0.9 ± 0.8 (0.5–2.5) gm. No episodes of severe tetany or carpo-pedal spasms were recorded at follow-up. The preoperative–postoperative comparisons of PTH, serum calcium, and calcium dose are statistically significant with p-value of 0.009, 0.01, and 0.03 respectively.

CONCLUSION

Parathyroid allograft transplantation from HLA compatible first-degree relative appears to be an optimal option for curing post-thyroidectomy permanent hypoparathyroidism. Long-term impact and routine application needs active research.

Clinical Utility of Intraoperative Parathyroid Scores System in Thyroidectomy

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AIM

To establish the intraoperative parathyroid scores system (IPSS) for thyroidectomy and to study the clinical value of IPSS for thyroidectomy.

MATERIALS AND METHODS

Intraoperative parathyroid scores system include transplantation parathyroid scores and *in situ* parathyroid scores, from 2014. Totally 266 cases of thyroid tumor patients received bilateral thyroidectomy in Fujian Medical University Union Hospital. The IPSS were recorded, parathyroid hormone and calcium were tested in d0, d1, d14, d60 postoperation. The correlation between intraoperative parathyroid scores and parathyroid hormone (PTH) calcium was calculated. A receiver operating characteristic curve and logistic regression were tested for the prediction value.

RESULTS

Transplantation parathyroid scores were positively correlated with transplanted PTH; the Pearson's relation value is 0.563 and $p = 0.00$. Intraoperative parathyroid scores and *in situ* parathyroid scores were positively correlated with PTH postoperative; the correlation values are 0.404 and 0.301. Intraoperative parathyroid scores is a predicted factor for long-term PTH function, the sensitivity was 49.0% and specificity was 81.0%.

CONCLUSION

Intraoperative parathyroid scores system can clear record every state and the function of the parathyroid glands. Intraoperative parathyroid scores system is a predicted factor for long-term PTH function and it can reduce hospital stay and make a dissection making in patients with recurrent surgery, this system has great clinical significance and social benefits. It can be easily promoted in thyroid surgery.

Comparison of Intraoperative Vital Sign Changes during Total Thyroidectomy Between Controlled and Intractable Graves' Disease

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INTRODUCTION

Intractable Graves' disease is known to cause dangerous conditions, such as sudden changes in blood pressure and heart rate during thyroid surgery. However, most of the data reported so far are case reports and no clinical studies have been reported. We would like to report a comparison of intraoperative vital sign changes during total thyroidectomy between controlled and intractable Graves' diseases.

MATERIALS AND METHODS

Patients who underwent thyroidectomy for Graves' disease at Seoul National University Bundang Hospital from 2013 to 2016 were retrospectively reviewed. The definition of controlled Graves' disease and intractable Graves' disease was defined as the case of normalization of thyroxine (T4) values and continuously high T4 levels by taking preoperative antithyroid drugs respectively.

RESULTS

Twenty-seven Graves' patients were divided into eight controlled Graves' group (CG group) and 19 intractable Graves' group (IG group). The mean age of CG and IG was 39.3 and 37.4 years respectively ($p = 0.699$). Preoperative free T4 levels were 1.14 ng/dL for CG and 2.43 ng/dL for IG ($p < 0.001$). Preoperative thyroid stimulating hormone is 0.83 U/mL for CG and 0.07 U/mL for IG ($p = 0.031$). The mean highest systolic blood pressure (SBP) was 138.3 mm Hg in CG and 133.2 mm Hg in IG ($p = 0.392$). In SBP, the average number of times higher than 140 was 0.50 in CG and 0.89 in IG ($p = 0.550$). Mean heart rate was 85.8 in CG and 96.8 in IG ($p = 0.246$).

CONCLUSION

There is no statistically significant difference in the change of vital signs during thyroid surgery between controlled and intractable Graves' disease.

A National Survey in Turkey; Thyroid Hormone Replacement Therapy after Total Thyroidectomy for Benign Thyroid Disease

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INTRODUCTION

This survey depicts the current approach and management of thyroid replacement therapy by general surgeons in Turkey.

MATERIALS AND METHODS

General surgeons were invited to participate in an 11-item survey via online Internet forms and announcement of the Turkish Association of Endocrine Surgery. Surgeons were asked for demographic information and different options regarding thyroid replacement therapy.

RESULTS

A total of 200 surgeons completed the survey. When asked for the most commonly preferred time to start postoperative thyroid replacement, most surgeons choose to wait for the definitive pathology result. Nearly 40% of surgeons expressed to take action immediately after surgery in each patient. Moreover, 101 (51%) surgeons preferred to initiate the L-thyroxine (LT4) treatment at a daily dose of 100 µg and 45 (23%) surgeons initiated it as 1.6 µg/kg/day, comparable to global rates. On the contrary, only a few of them (2.5%) preferred the patients to refer to the endocrinologist for the adjustment of LT4 dosage. Nearly half of the surgeons used free thyroxine in addition to serum thyroid-stimulating hormone (TSH) for monitoring LT4 therapy. A vast majority of surgeons (96%) started LT4 dose as once a day in the morning on a fasting state. There was a significant difference between surgeon's experience and follow-up frequency after reaching target TSH levels ($p < 0.0001$). There was also a significant difference between the surgeon's affiliation and start of replacement therapy ($p = 0.001$).

CONCLUSION

Although most of the surgeons in Turkey have a near standard approach to replacement therapy after thyroidectomy, with this survey it has been understood that replacement therapy has not been fully standardized yet.

The Evaluation of Significance of the Prophylactic Modified Neck Dissection for Unaffected Lateral Side of Medullary Thyroid Carcinoma

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INTRODUCTION

Therapeutic ipsilateral modified neck dissection (MND) for unilateral cN1 patients with medullary thyroid carcinoma (MTC) is standard of care. However, significance of prophylactic MND for unaffected side is unclear. We reviewed our experience with MTC and evaluated the significance of the prophylactic MND for unaffected side.

MATERIALS AND METHODS

Of 47 cases with MTC who underwent initial radical surgery in our hospital between 1981 and 2016, 67 unaffected lateral compartments were analyzed. While prophylactic dissection was performed before 2000 (group I; $n = 27$), we took active surveillance policy for unaffected compartments after 2000 (group II; $n = 40$) basically. Postoperative surveillance was performed by cervical ultrasonography, calcitonin, and CEA levels at interval of 6 months or 1 year.

RESULTS

Biochemical cure during follow-up period has been achieved in both groups. In group I, pathological lymph node metastases were observed in four cases. In group II, lymph node recurrence developed in three undissected compartments during follow-up period. However, there were no cases with cause-specific death in both groups.

CONCLUSION

According to our results, active surveillance for unaffected compartment could be allowed as postoperative follow-up if prudent postoperative surveillance is warranted.

Clinicopathological Features of Needle Tract Recurrence following Thyroid Fine Needle Aspiration Cytology

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INTRODUCTION

Thyroid fine needle aspiration cytology (FNAC) is a reliable, safe, and cost-effective test. However, FNAC is rarely followed by complications like needle tract recurrence (NTR). The clinicopathological features of NTR have not been sufficiently studied so far. The present study is designed to investigate the clinicopathological characteristics of thyroid NTR.

MATERIALS AND METHODS

Patients who underwent FNAC for thyroid nodules and its lymph nodes metastases at Kuma Hospital between 2006 and 2017 were retrospectively evaluated. Needle tract recurrence was defined as macroscopic recurrent tumor at the previous insertion site of FNAC. Needle tract recurrence was identified in 66 patients, including 137 nodules. The clinicopathological features of NTR and its corresponding primary site were compared.

RESULTS

The histological types found in the NTR were as follows: papillary thyroid carcinoma (PTC; classic, n = 36; tall cell, n = 7; hobnail, n = 2; follicular variant, n = 5, interval between aspiration and NTR (IAN) 6–309 months, median 83.7), follicular carcinoma (n = 7; IAN 36–169 months, median 71.1), poorly differentiated carcinoma (PDC; n = 7; IAN 36–256 months, median 103.8), and anaplastic carcinoma (n = 2; IAN 6 months). Needle tract recurrence was confined in the skin in 16 out of 137 nodules (11.7%), subcutaneous tissue in 87 out of 137 nodules (63.5%), and muscle in 34 out of 137 nodules (24.8%). The histological findings of NTR were similarly identical to those of primary tumors except for 12 cases that exhibited more aggressive variants or carcinomas in NTR. The incidence (n = 32, 48.5%) of patients with high Ki-67 labeling index (>10%) in NTR was significantly higher than those (n = 6, 14.6%) in primary carcinomas (p < 0.05). Needle tract recurrence was solitary in 38 (57.6%) patients and multiple in 28 (42.4%) patients respectively. Out of patients with NTR, seven (10.6%) cases died from the disease and six (9.1%) had distant metastases.

CONCLUSION

We demonstrated that any type of thyroid carcinomas except medullary carcinomas can develop NTR. The microscopic findings of NTR may change to more aggressive histological variant and show higher Ki-67 labeling index than its corresponding primary site. This is the first study presenting the largest series of thyroid NTR with histopathological and clinical correlation.

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Fast Track Hemithyroidectomy

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INTRODUCTION

Hemithyroidectomy is a procedure that is conventionally done under general anesthesia (GA). General anesthesia especially endotracheal intubation is not devoid of complications and warrants admission for at least 1 day. Superficial cervical plexus block (SCPB), which has been previously used for anterior neck surgeries, was found to provide adequate analgesia for hemithyroidectomy.

AIM

To study the effectiveness and complications of unilateral SCPB in hemithyroidectomy.

INCLUSION CRITERIA

Solitary thyroid nodule (STN) or multinodular goiter (MNG) sizing less than 4 cm.

MATERIALS AND METHODS

We recruited a total of 50 patients with indications for hemithyroidectomy to undergo the procedure under unilateral SCPB. About 10 mL of 0.5% bupivacaine was injected (Erb's point) midway between the mastoid and clavicular head of sternocleidomastoid on the posterior border. The incision line was infiltrated with 5 mL of 1% lignocaine with adrenaline. The surgery was then performed using Fentanyl up to 50 µg iv to supplement the analgesia when needed.

RESULTS

Mean age of the patients was 36 ± 10 years with male to female ratio of 3.16:1. Strap muscles were divided in three (6%) patients. None of the patient required drain. All the patients were discharged within 2 hours.

CONCLUSION

Hemithyroidectomy can be effectively performed under SCPB avoiding complications related to GA and intubation. Patients can be safely discharged within few hours of surgery saving lot of time and resources.

Which is the Ideal Technique of Endoscopic Thyroidectomy? A Comparative Study Between Trans-oral and Trans-axillary Techniques

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INTRODUCTION

For endoscopic thyroidectomy (ET), various technical approaches such as chest wall, trans-orificial, postauricular, assisted, axillo-mammary routes have been reported, but trans-axillary route remains the commonest route. Of late, trans-oral route is being done with increasing frequency especially in South Asia including our center. In this context, we analyzed our experience in morbid, technical, cosmetic, and feasibility aspects of both these techniques by comparing each other.

MATERIALS AND METHODS

In this retrospective study spanning 18 months conducted at tertiary care hospital, only benign nontoxic nodular goiters were included. Individuals undergoing trans-oral ET were placed in group I and trans-axillary ET in group II. Statistical analysis was done with Statistical Package for the Social Sciences 18.0 version.

RESULTS

Out of 176 eligible individuals, groups I and II included 92 and 84 respectively. Female:male was 76:16 and 81:3 in groups I and II respectively. Mean age of groups I is 30.5 ± 4.5 (16–43) and II is 29.6 ± 5.7 (18–47). Mean operative time was 107.3 ± 24.8 (72–190) and 138.8 ± 27 (98–205) in groups I and II respectively. Subcutaneous ecchymosis occurred in 9 and sternomastoid muscle stiffness in 8 cases of group II. Subcutaneous emphysema occurred in four cases of group II. Prolonged wound drainage and operative time were longer in group II than in group I, reaching statistical significance (p -value < 0.05).

CONCLUSION

(1) Trans-axillary technique appears to be ergonomically more cumbersome, takes longer operative time and cosmetically less gratifying than trans-oral ET. (2) But, as both the techniques are feasible, cases should be judiciously chosen based on institutional logistics along with patient's choice.

A Novel Modified Transoral Approach for Endoscopic Thyroidectomy

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INTRODUCTION

The relative delay in the inception of endoscopic thyroidectomy could be explained by narrow operative field and numerous vital structures. The first endoscopic thyroidectomy was done in 1997 by Huscher et al, in Italy. Wilhem and Metzger developed a total transoral endoscopic thyroidectomy, by using a three-point access sublingually.

MATERIALS AND METHODS

Inclusion criteria were benign solitary nodule thyroid or multinodular goiter less than 5 cm in size. The exclusion criteria were nodules larger than 5 cm, malignant features on fine needle aspiration biopsy, and patients who did not consent to the surgery. A novel modified transoral thyroidectomy was performed.

RESULTS

A total of 28 patients underwent the modified transoral endoscopic thyroidectomy. Nineteen patients were female and nine were male. Sixteen patients with multinodular goiter underwent total thyroidectomy. One patient underwent isthmectomy for solitary nodule over the isthmus. Twelve of these patients had solitary nodule successfully underwent hemithyroidectomies. The mean operating time was 118.75 minutes with a standard deviation of 15.52. Blood loss was less than 3 mL in each case. No patient developed recurrent or superior laryngeal nerve injury. No patient developed postoperative hypocalcemia. Two patients developed an abscess over the anterior aspect of the neck in the midline, which was drained and treated with antibiotics

CONCLUSION

This novel modified transoral approach is an effective and practical approach to treating solitary thyroid nodules and multinodular goiters. It provides the advantage of triangulation of instruments, while not compromising on cosmetic outcome.

Initial 50 Experiences of Transoral Endoscopic Thyroid Surgery Vestibular Approach for Thyroid Cancer by Single Surgeon

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AIM

Transoral endoscopic thyroid surgery vestibular approach (TOETVA) is a promising thyroid surgery technique that does not leave a neck scar. Since 2015 when the first 60 human report was released, various hospitals actively adopted TOETVA but there is little report for TOETVA in thyroid cancer surgery. We herein report our single surgeon experience of TOETVA in patients with thyroid cancer.

MATERIALS AND METHODS

This case series consisted of 50 consecutive patients who underwent TOETVA in our institution between August 2016 and November 2017. All cases were performed by a single endocrine surgeon (JW Yi). Indications for TOETVA for thyroid malignancy were as follows: Fine-needle aspiration-proven tumors with Bethesda category IV, V, and VI, maximal diameter less than 2 cm in suspicious papillary thyroid carcinoma (PTC) or less than 8 cm in suspicious follicular neoplasm, not located tracheoesophageal groove, and no radiologic evidence for lateral lymph node metastasis.

RESULTS

Twelve total thyroidectomies, 37 lobectomies, and 1 wide isthmusectomy have been performed. Forty-one were classic PTC, 5 were follicular variant PTC, and 4 were noninvasive follicular neoplasm. Forty-six patients were female and mean age was 45.8 years (21–71). Mean operation time was 123.8 minutes (50–250). Tumor size ranged from 0.2 to 5 cm and mean number of harvested central lymph nodes was 3.1 (0–10). Transient vocal cord palsy occurred in two patients. Among 12 total thyroidectomy patients, mean PTH level in postoperative 1 day was 27.2 (11.9–55.7). Two patients received radioiodine therapy (RAI) and their stimulated triglyceride level at the first RAI was 3.42 and 1.13. Mental nerve injury or surgical site infection was not observed.

CONCLUSION

TOETVA could be an alternative surgical option for selected thyroid cancer patients. Large prospective cohort study will be needed to prove oncologic outcome of TOETVA.

Endoscopic Hemithyroidectomy: Experience at a Single Center

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INTRODUCTION

Endoscopic or minimally invasive surgery (MIS) is becoming more and more popular. Since the introduction of laparoscopic cholecystectomy in the early 1980s, endoscopic procedures have become standard in nearly all fields of surgery. Minimally invasive video-assisted hemithyroidectomy is the next step in the evolution of thyroid surgery. It has become a commonly accepted and used surgery for thyroid disorders worldwide, as it combines the advantages associated with endoscopic magnification with those due with traditional surgery. In selected patients, it is considered as safe and valid alternative.

MATERIALS AND METHODS

Retrospective study at single center was done from 2014 till date with total duration of 4 years.

RESULTS

Twenty patients underwent with endoscopic hemithyroidectomy during 4 years of study with a mean operative time of 60 (± 22) minutes. The median age of the patients was 30 (16–44) years. Average hospital stay was 1.4 days with no major postoperative morbidity.

CONCLUSION

Endoscopic or minimally invasive video-assisted hemithyroidectomy should be considered as safe and valid alternative for thyroid surgeries. It can be performed safely with a low complication profile in a high-volume MAS center. The minimally invasive aspect and cosmetic advantage seem to be the most important factors for the patients.

Recurrent Laryngeal Nerve Injury: The Accuracy of Clinical Assessment compared with Gold Standard Flexible Laryngoscopy Postthyroid and Parathyroid Surgery

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INTRODUCTION

Recurrent laryngeal nerve (RLN) injury is the paramount complication in neck surgery especially in thyroid and parathyroid surgery. The gold standard assessment for RLN injury is by using flexible laryngoscopy (FL). It is a normal practice to assess the vocal cord function via FL prior to thyroid and parathyroid surgery. However, it is not a routine procedure after the surgery. Usually, only patients with clinical evidence of vocal cord injury will be reassessed by FL postoperatively. Hence, the clinical assessment (CA) is the most important measures to recognize vocal cord injury. We prospectively evaluate the accuracy of CA in detecting vocal cord injury compared with FL.

MATERIAL AND METHODS

A prospective controlled, double-blinded, non-randomized study of 40 patients undergoing thyroidectomy and parathyroidectomy for various diagnosis. The CA for vocal cord function was done by a single nurse a day before operation and at day two postoperatively. The parameters of CA are hoarseness of voice, choking on swallowing clear fluid, and production of cough. The FL also was done at the same period of time by the Otolaryngology medical officer. Demographic data were collected and results were compared.

RESULTS

Forty patients underwent thyroid and parathyroid surgery. Abnormal FL was observed in four (10.0%) patients. Seven (17.5%) patients were noted to have hoarseness of voice. Two (28.6%) of them had abnormal FL giving rise to sensitivity of 50% and specificity of 86.1%. One patient (2.5%) had unproductive cough and was found to have abnormal FL give the sensitivity of 25% and specificity of 100%. No patient experience choking in this study.

CONCLUSION

Hoarseness of voice is specific but less sensitive to predict RLN injury. Coughing is very specific but less sensitive test. Meanwhile choking is not a reliable test. Clinical assessment does help in predicting RLN injury; however, post-op FL is still necessary in view of poor sensitivity of clinical assessment.

A Randomized Controlled Trial of Bilateral Superficial Cervical Plexus Block vs Local Wound Infiltration for Pain Control in Thyroid Surgery

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INTRODUCTION

Multiple approaches have been devised for pain control in patients undergoing thyroid surgery. Bilateral superficial cervical plexus block (BSCPb) and local wound infiltration (LWI) of analgesia are among the established methods. However, the results of both have been equivocal. This study is to assess the efficacy of BSCPb as compared with LWI in reducing postoperative pain and the need for additional opioids for the first 24 hours from the time of skin closure.

MATERIALS AND METHODS

A prospective single-blinded randomized controlled trial was performed with two arms: group I—LWI and group I—BSCP. Both arms utilized ropivacaine 0.5%. Local wound infiltration or BSCP, chosen randomly, was performed immediately after intubation. Intra-operative and postoperative analgesia were standardized for both arms. Subcutaneous injection of tramadol was given as per protocol, whenever the pain score reached ≥ 4 on the visual analog scale (VAS) or when requested by patient. Postoperative pain score was assessed at 4, 12, 16, and 24 hours from the time of skin closure using VAS. Total tramadol given was recorded in each patient.

RESULTS

A total of 54 patients were recruited. Both groups showed no significant difference in pain control or the requirement for additional doses of tramadol. One patient in the BSCP group experienced transient left upper limb weakness, which recovered after 10 hours.

CONCLUSION

Our study showed the efficacy of BSCP is equivalent to LWI. Hence, BSCP can be used as an alternative method for postoperative pain control, if expertise is available.

Institution of Complete Assessment of the Recurrent Laryngeal Nerve: Real-world Benefits and Challenges

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INTRODUCTION

There is increased use of intraoperative intermittent or continuous nerve integrity monitors (NIM), which permit real-time recurrent laryngeal nerve (RLN) assessment in neck surgery. However, there is wide variability in RLN injury rates (1–8%) from inadequate perioperative functional vocal cord checks (VCC). Therefore, recommendations for NIM use vary, with data yet to show benefit for RLN injury. Complete assessment ideally requires intraoperative NIM and pre-/postoperative functional VCC via an independent specialist, which is labor intensive. Since 2016, the Northern Hospital (Melbourne, Australia) has instituted policy for routine VCC/NIM for all thyroidectomies. We analyzed policy establishment success and overall clinical outcomes.

MATERIALS AND METHODS

Retrospective analysis of all thyroidectomy cases between January 2014 and July 2017 for NIM usage and VCC adherence pre-/postpolicy introduction.

RESULTS

About 394 thyroidectomies between 2014 and 2017 were analyzed. Since protocol establishment in 2016, 97% of cases had NIM use but only 43% underwent complete VCC. Notably, VCC improved from 14% prior to August 2016 to 95%, attributed to improved referral patterns, clinic access, and nasoendoscope availability. Although suspected RLN injury rates pre-/post-2016 remained unchanged (1%), there was lower permanent RLN injury (0.7 vs 0.1%), attributed to better assessment, treatment, and long-term follow-up.

CONCLUSION

Our data suggest rapid adherence to NIM utilization but delayed perioperative VCC uptake, due to resource constraints. Importantly, improved permanent RLN injury rates were noted. Complete functional VCC should be instituted due to its value in accurate assessment and streamlining treatment should RLN injury be suspected.

Does Intraoperative Nerve Monitoring reduce the Time taken to identify Recurrent Laryngeal Nerve by a Junior Surgeon? A Pilot Study

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INTRODUCTION

Visual identification of the recurrent laryngeal nerve (RLN) is the gold standard in performing thyroidectomy. However, due to anatomical variation of RLN development and its close proximity to the thyroid gland, it can be difficult to be identified especially to inexperienced surgeons. Because of this, a number of inventions were developed to aid surgeons in identifying the

nerve and reducing its injury. One such invention is intraoperative nerve monitoring (IONM). However, recent meta-analysis showed that IONM did not significantly reduce the incidence of permanent RLN injuries. Majority of the center involved in the meta-analysis came from centers that performed large number of thyroidectomy and experienced surgeons. It did not address whether IONM system will help junior surgeon in identifying the RLN.

OBJECTIVES

This study aimed to demonstrate that IONM system does help a junior surgeon in identifying RLN by looking at the ability of the junior surgeon to be able to find RLN within less than 8 minutes compared with visualization alone (VA).

MATERIALS AND METHODS

Total of 40 nerve-at-risks from 25 patients who underwent thyroidectomies were randomized into IONM and VA group. Intraoperatively, the IONM system was set according to the guidelines set by the International Neural Monitoring Study Group, and standard thyroidectomy was performed. When the thyroid was medially rotated, a single junior surgeon will start searching for the RLN with IONM or VA according to the patient's group.

RESULTS

There was no difference in the demographic data (age, gender, ethnicity, and thyroid pathology) within both groups. The junior surgeon was able to find 90% of RLN within less than 8 minutes using IONM compared with 60% in VA group ($p = 0.028$).

CONCLUSION

IONM helps junior surgeons to identify RLN faster compared with VA. This indirectly will reduce the risk of injuring the recurrent laryngeal nerve.

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Mild Hyperparathyroidism, Negative Tumor Localization, and Surgical Cure: Experience from South India

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INTRODUCTION

In India, primary hyperparathyroidism (PHPT) is a symptomatic disease (SPHPT). Localization by ultrasonography (USG) and Sestamibi (MIBI) has been positive in 85 to 90% of SPHPT. Asymptomatic disease (APHPT) is increasingly being picked up.

AIM

To assess the usefulness of localization study (MIBI and USG) in APHPT and surgical cure in nonlocalized disease.

MATERIALS AND METHODS

Retrospective study conducted at two tertiary care centers. Thirty-one patients with asymptomatic PHPT and 82 patients with symptomatic disease SPHPT during the period 2008 to 2017 were included. Asymptomatic was defined as patients who had biochemical evidence of PHPT without bone/renal disease. Patients with single gland disease in the final histopathology were included and those with hyperplasia and double adenoma were excluded. The demographic data, localization studies, and the operative findings between APHPT and SPHPT were compared.

RESULTS

Prevalence of APHPT was 22.43% ($n = 31$). The APHPT occurred in the older patients ($p < 0.05$). Serum calcium and parathyroid hormone were higher in SPHPT ($p < 0.05$). Bone disease, renal disease, and brown tumors in SPHPT were 77, 36, and 42% respectively. Ultrasonography and MIBI scans were positive in 88 and 90% respectively in SPHPT. The APHPT group showed USG and MIBI positivity in only 25 and 17% respectively. Ultrasonography and MIBI in APHPT was false positive in 25 and 40% cases respectively. Intraoperative tumor size in APHPT was smaller than SPHPT ($p < 0.05$). All parathyroid tumors in the nonlocalized group were excised during exploration. Intraoperative parathyroid hormone showed fall in both the groups.

CONCLUSION

Asymptomatic PHPT is associated with nonlocalized tumors. However, they can be successfully removed during surgery.

Real-time Virtual Sonography, a Coordinated Sonography and MRI/CT System, for Localization of Parathyroid Gland in Patients with Hyperparathyroidism: A Pilot Study

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INTRODUCTION

Ultrasound has been shown to have a sensitivity of 69 to 85% for localization of parathyroid hyperplasia/adenoma; however, success of the examination depends largely on the experience of the operator. Recently, we have developed real-time virtual sonography (RVS) that enables simultaneous display of both sonography and magnetic resonance imaging/computed tomography (MRI/CT) of the same site in real time by using a magnetic position tracking system. In this pilot study, RVS was applied as a new diagnostic tool to detect the site of parathyroid lesions.

MATERIALS AND METHODS

Fifteen lesions in eight patients who underwent operation for hyperparathyroidism (HPT; four primary HPT and two secondary HPT) were enrolled in this study. Magnetic resonance imaging/CT and (99m) Technetium-sestamibi scintigraphy were performed in all patients preoperatively. The diagnostic sensitivity of the procedures was analyzed.

RESULTS

Using RVS, 14 (93%) pathologic glands could be detected, compared with 11 (73%) using MRI/CT, 11 (73%) using 11 (73%) Technetium-sestamibi scintigraphy examinations. Using RVS, the two different forms of diagnostic imaging can be integrated in real time, and thereby complement each other. All MRI/CT-detected lesions were localized by RVS. Parathyroidectomy could be performed successfully based on RVS findings. All patients showed normal serum levels of calcium and parathyroid hormone serum levels 3 months after parathyroidectomy.

CONCLUSION

Real-time virtual sonography represents a highly sensitivity for localization of parathyroid glands in patients with hyperparathyroidism. It is suggested that RVS could be useful for sonographic detection of ectopic parathyroid glands, which could only detect MRI/CT alone.

Persistent and Recurrent Primary Hyperparathyroidism: A Retrospective Review

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INTRODUCTION

The morbidity of repeat surgery in patients with persistent and recurrent primary hyperparathyroidism (PHPT) remains a problem in endocrine surgery. Some studies propose bilateral cervical exploration during the initial parathyroid surgery to avoid repeat surgery.

OBJECTIVES

To analyze the causes and outcomes of patients with persistent or recurrent PHPT.

MATERIALS AND METHODS

Retrospective study involving all patients who had recurrent or persistent PHPT at Hospital Putrajaya, Malaysia, from 2002 to 2016.

RESULTS

A total of 24 patients (17 women and 7 men) with a mean age of 60 years had recurrent or persistent PHPT (13 had recurrent PHPT and 11 had persistent PHPT). About 79% were symptomatic. All 21% asymptomatic patients had hypercalcemia after first parathyroidectomy. Majority (88%) only had one previous surgery with a median duration of 4.5 months from previous surgery. The commonest cause for failed first surgery was multiple parathyroid adenoma (58%), followed by parathyroid cancer (21%) and adenoma in normal position missed in previous surgery (8%). We reported two patients (8%) with ectopic positions (intrathymic and intrathyroidal) and one patient (4%) with a regrowth of previously resected tumor as causes of first surgery

failure. Bilateral exploration was performed more during repeat operation (63%) as compared with those undergoing their first surgery (25%). One patient suffered from permanent unilateral recurrent laryngeal nerve injury and 1 patient had temporary hypocalcemia post reoperation.

CONCLUSION

Patient with PHPT should be follow up more than 6 months postoperatively with clinical and biochemical assessment to detect recurrent or persistent PHPT. Bilateral neck exploration may be considered during first parathyroid surgery in view of large number of multiple parathyroid adenoma in our cohort study. Successful first operation can prevent serious complication of multiple parathyroid surgery.

Surgery for Persistent Hyperparathyroidism: Where is the Adenoma?

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INTRODUCTION

Persistent hyperparathyroidism that occurs after failed parathyroidectomy is rare, but it is a challenging problem that has increased risk of complications due to recurrent surgery. In this study we aimed to discuss the clinical management of patients with persistent hyperparathyroidism and to review the localization of missed adenomas.

MATERIALS AND METHODS

Patients with persistent hyperparathyroidism who had surgery in our clinic for primer hyperparathyroidism (pHPT) between January 2011 and December 2016 were analyzed retrospectively.

RESULTS

Out of 258 operated pHPT patients, 16 had persistent hyperparathyroidism. This group consisted of 12 (77%) women and 4 (23%) men with a mean age of 56 (44–72) years. The adenoma site was detected with preoperative localization examinations in 14 patients. In 14 patients (87%), rapid intraoperative parathyroid hormone examination was performed. Parathyroid hormone values decreased to normal range in all patients. Definitive pathology of resected specimen was reported as adenoma in 15 (93%) and hyperplasia in one (7%) patient. Thymus was the site where the adenoma was located in two cases, whereas one adenoma was localized retrosternal, one intrathyroidal, and one retropharyngeal. All other patients had a non-ectopic localized adenoma. In addition, dual adenoma was detected in one patient. There was no persistence or recurrence during follow-up.

CONCLUSION

It is of utmost importance to use preoperative localization examinations with imaging methods during the evaluation of patients with persistent hyperparathyroidism. Patients, where it is not possible to localize the missed adenoma in the preoperative work-up, should undergo bilateral neck exploration.

Small Nonfunctional Parathyroid Cysts: Our Experience

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INTRODUCTION

Parathyroid cysts (PCs) account for less than 1% of all parathyroid lesions and are most commonly located along thyroid lobes, rarely at ectopic sites. Parathyroid cysts are important because they can pose a differential diagnostic challenge against other cystic formations of the neck. Parathyroid cysts can be functional (elevated serum parathyroid hormone level) and nonfunctional.

MATERIALS AND METHODS

Seven cases of nonfunctional PCs are presented. All patients underwent physical examination and ultrasonography of the neck with ultrasound-guided fine-needle aspiration biopsy (UG-FNA). The material thus obtained was stained by the standard May-Grünwald-Giemsa method. Parathyroid hormone level was determined in aspirate and serum, along with serum levels of total calcium, inorganic phosphates.

RESULTS

In three asymptomatic patients, remission occurred after initial aspiration biopsy; one patient had compression syndrome with vocal cord paresis that required surgical treatment; two patients had cyst recurrence that was surgically removed, and one patient not operated.

CONCLUSION

Cystic neck masses can pose a major differential diagnostic problem considering different approach, treatment method, and preoperative and postoperative follow up. Surgical treatment is necessary in case of functional and large nonfunctional PCs (due to compression syndrome), whereas individualized therapeutic approach is used in case of small nonfunctional PCs. Ultrasonography with UG-FNA, cytologic analysis of the material obtained, and determination of parathyroid hormone level in aspirate and serum are crucial for making an accurate diagnosis.

Parathyroid Mass and Parathyroid Hormone Level in Chronic Kidney Disease Patients

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INTRODUCTION

Secondary hyperparathyroidism of chronic kidney disease (CKD) is part of a systemic disorder and parathyroid hormone (PTH). Parathyroid hormone is considered as a uremic toxin. The aim of this work was to identify the correlation between the mass of the resected parathyroid gland and the PTH level in CKD patients with secondary hyperparathyroidism.

MATERIALS AND METHODS

From January 2014 to July 2015, 30 patients suffering from secondary hyperparathyroidism due to CKD were admitted to Alexandria Main University Hospital, Egypt. All patients were subjected to either total or subtotal parathyroidectomy. All patients had serum PTH level more than 500 pg/mL, serum phosphorus level >6 mg/dL, and low or normal serum calcium level. Both the size and the weight of the excised parathyroid glands were estimated during the operation.

RESULTS

A total of 123 parathyroid glands were excised. The mean serum PTH level was 1599.0 ± 545.62 pg/mL preoperatively and postoperatively was 79.8 ± 110.62 pg/mL, so the percentage of change was $\downarrow 94.93 \pm 7.15\%$. Both the preoperative PTH and the reduction of PTH were significantly correlated with the size and the weight of parathyroid glands. In those patients with PTH < 1,500 pg/mL, this significant correlation is lost.

CONCLUSION

Higher levels of serum PTH usually indicate that surgical parathyroidectomy might be required. As PTH levels could be influenced by other factors as pharmacotherapy or plasma protein levels, the large size of parathyroid gland might be used as a much more appropriate guide that indicates the need of operative treatment even when considering PTH < 1,500 pg/mL.

Consideration for Renal Hyperparathyroidism Patients receiving Parathyroidectomy: Peritoneal Dialysis vs Hemodialysis

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AIM

Postparathyroidectomy hypocalcemia, a common complication in renal hyperparathyroidism patients, requires intensive postoperative monitoring and calcium supplement. There are some physiologic differences in calcium and phosphate homeostasis between peritoneal dialysis and hemodialysis. However, there are little evidences regarding their individual incidence of hypocalcemia as well as the calcium requirement after parathyroidectomy.

MATERIALS AND METHODS

From August 2010 to August 2016, 218 patients who underwent parathyroidectomy for renal hyperparathyroidism were included. Patients were grouped by peritoneal dialysis (PD) and hemodialysis (HD). The demographic, serum blood test before and after operation (intact PTH, phosphate, calcium, alkaline phosphate), postoperative calcium requirement, and hospital days between groups were analyzed.

RESULTS

The demographics and preoperative blood test were similar between two groups, except for higher phosphate levels in patients with PD. The incidence of hunger bone syndrome (HBS; calcium < 8.5 mg/dL along with phosphate decrease on postoperative day 3) did not differ significantly between the two groups (78.3% in PD vs 64.5% in HD, $p = 0.232$). However, patients with HD had more severe HBS than patients with continuous ambulatory peritoneal dialysis, including significantly lower day-3 calcium level (7.3 vs 7.7 mg/dL, $p = 0.039$) and higher calcium supplement requirement.

CONCLUSION

Peritoneal dialysis patients undergoing parathyroidectomy for renal hyperparathyroidism have a similar incidence of HBS as compared with HD patients, but the hypocalcemia is less severe and easier to handle. This could be explained with different bone turnover rates from the two dialysis approaches.

Practice Patterns in Parathyroid Surgery: A Survey of Asia-Pacific Parathyroid Surgeons

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INTRODUCTION

Practice variations exist among parathyroid surgeons depending on their expertise and resources. Our study aims to elucidate the choice of surgical techniques and adjuncts used in parathyroid surgery by surgeons in the Asia-Pacific region.

MATERIALS AND METHODS

A 25 question online survey was sent to members of the Australia and New Zealand Endocrine Surgeons, Asian Association of Endocrine Surgeons, and General Surgeons Australia in March 2017. The respondents were divided into three distinct regions: Australasia, South/South East Asia, and East Asia.

RESULTS

A total of 85 parathyroid surgeons across Asia-Pacific returned the questionnaire. Most surgeons (96%) routinely perform preoperative imaging with 76% of surgeons preferring dual-imaging modalities namely ^{99m}Tc sestamibi and ultrasound. Four percent of surgeons use parathyroid CT as first-line imaging. Minimally invasive parathyroidectomy (MIP) is still the favored technique of choice (96%) over bilateral neck exploration. However, half of all surgeons use frozen section to confirm the parathyroid gland excised but South/South East Asian surgeons tend to rely on visual judgment. Rapid intraoperative parathyroid hormone was used more sporadically across the three regions but more widely accessible to East Asian surgeons. Routine use of intraoperative neuromonitoring was only favored by 20% of surgeons, mainly the otolaryngologists.

CONCLUSION

Dual localization techniques still are the preferred choice of investigations in preparation for parathyroid surgery, with minimally invasive surgery the preferred approach in Asia-Pacific region. Use of adjuncts to assist in parathyroid surgery was more sporadic and limited to certain centers.

Survival and Prognosis of Anaplastic Thyroid Cancer: A 16 Years Observation at a Single Asian Institute

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INTRODUCTION

Anaplastic thyroid cancer (ATC) is an aggressive tumor. The optimal multimodal therapy for ATC remains elusive.

OBJECTIVES

This study was aimed at reporting the survival and prognostic factors of ATC patients at our center.

MATERIALS AND METHODS

This was a retrospective observational study of all ATC patients (65 patients) who were treated at Putrajaya Hospital, Malaysia, between 2002 and 2017. Kaplan–Meier and log-rank test were used to analyze survival. Cox model was used for multivariate analysis.

RESULTS

The median age was 62 years (33–81 years). Majority of the patients presented with stage IVC (50.8%), while others presented with IVA (3.1%) and IVB (46.2%). Most patients were treated palliatively (36.9%), while 29.2% underwent surgery only, 16.9% underwent radiotherapy only and 16.9% underwent multimodal treatment. The survival rates for 6 months and 1 year was 7.7 and 1.5% respectively. Median survival was 2 months. Of all deaths, four patients (6.2%) did not pass away due to disease progression. Kaplan–Meier and log-rank showed that multimodal treatment (surgery, radiotherapy, and chemotherapy) significantly increased median survival ($p = 0.01$). Univariate analysis showed that multimodal treatment with surgery and radiotherapy improved survival with a hazard ratio (HR) of 0.421, confidence interval (CI) of 0.193–0.92, $p = 0.03$. However, multivariate analysis showed that multimodal treatment with surgery, radiotherapy, and chemotherapy was the only independent factor improving survival (HR 0.035, CI: 0.022–0.619, $p = 0.02$).

CONCLUSION

Our observation concurs with the findings of various other studies that demonstrated multimodal treatment may offer improved survival outcomes. More studies need to be done to ascertain the most optimal multimodal treatment for ATC.

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Rising Incidence of Neuroendocrine Tumors in Singapore: An Epidemiological Study

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INTRODUCTION

The incidence of neuroendocrine tumors (NETs) is increasing worldwide (Hallet et al *Cancer* 2015;121(4): 589–597, Dasari et al *JAMA Oncol* 2017;3(10): 1335–1342). This study looks at the trend of neuroendocrine cancers in Singapore.

MATERIALS AND METHODS

Retrospective population-based study of all neuroendocrine cancers treated during the period 1993 to 2014 in Singapore. The main outcomes studied were trends in incidence, gender and racial variations, histology, and overall survival data.

RESULTS

During the study period, 1,725 cases were identified and the incidence increased from 0.8 to 3 per 100,000 per year. The mean age of diagnosis was 56 (19–82) years, with highest incidence in Chinese race ($n = 1391$) (80 and gender ratio nearly 1:1). Histologically, the tumors were predominantly carcinoid tumor (53%) and neuroendocrine carcinoma (40%), with tumors arising most commonly in the rectum (26%), lung and bronchus (14%), colon (14%), pancreas (9%), small intestine (6%), stomach (7%), and other organs (21%). Majority were G1 (52%) and G3 (37%) tumors, and clinical stage—Stage I (41%) and Stage IV (36%). Treatments offered were surgery only (36%), surgery plus radiotherapy/chemotherapy or combination of RT plus CT (5%), RT or CT only (7%), and others (43%). The 5-year overall survival for the cohort was 40% for all NETs and 10-year survival at 18%. Predictors for poor survival in this cohort include primary tumor site, gender, and advancing age.

CONCLUSION

The incidence of NETs has markedly increased nearly fourfold over the last two decades. The reasons for the increasing trend may be improved detection besides other unevaluated factors but needs further evaluation.

Paragangliomas and Recurrence: A Decade of Clinical Experience in an Endocrine Center

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INTRODUCTION

Paraganglioma (PG) tumor arises from extraadrenal chromaffin cells. Despite comprehensive management, many cases develop recurrence, which require repeated surgeries.

MATERIALS AND METHODS

All PG and recurrent PG cases managed in our center from 2007 to 2017.

RESULTS

Twenty-six patients were analyzed, 16 were female and 10 male. Thirteen (50.0%) of the patients were above 50 years old, 4 (15.4%) cases were < 18 years old and youngest was 16 years. Majority of the patients were Malay (11, 42.3%) and Chinese (11, 42.3%) and other race (4, 15.4%). Two (7.7%) patients had familial history of PG. Majority of tumors were at the retroperitoneal space (9, 34.6%), paraaortic region (9, 34.6%), and less common at the diaphragm (2, 7.7%) and other sites namely carotid, mediastinum, kidney, pelvis, and even lymph nodes. Eighteen (69.2%) cases were functioning tumors presented with uncontrolled hypertension and paroxysmal symptoms. Diagnosis was established by computed tomography scan (22, 84.6%) and magnetic resonance imaging scan (4, 15.4%). Ten (38.5%) cases also had functional imaging, such as positron emission tomography scan, sestamibi, or gallium dotatate scan. Malignancy is defined by the existence of metastasis rather than by histology. Two (7.7%) patients presented lymph node metastasis and one (3.8%) with bone metastases. The mainstay of treatment was surgical removal with 22 (84.0%) patients undergoing surgery. Three (11.5%) patients were inoperable and one patient received radiotherapy. Angiography and embolization were performed in two (7.7%) patients. Recurrence developed in 11 (42.3%) cases requiring multiple surgeries. Risk factors for recurrence include site of disease (5, 45.5%), lymph node involvement (2, 18.2%), and family history (2, 18.2%). Twenty-two (84%) patients are still alive, 12 (54.5%) of them have been disease-free survival (DFS) > 5 years. In recurrent PG, five (45.5%) of operated patients remain DFS > 5 years. Other four cases, two died and two defaulted appointment.

CONCLUSION

Paraganglioma requires aggressive surgical management. Recurrence disease can be successfully operated. Factors for recurrence are site of disease and family history, not the surgical resection margin.

Timing of Surgical Intervention has an Impact on Cure of Endocrine Hypertension: Results from a Tertiary Referral Center in South East Asia

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INTRODUCTION

The prevalence of endocrine hypertension (HT) is reported in 15% of all cases of hypertension. Aim of the study was to investigate outcomes of adrenalectomy for patients who presented with endocrine HT.

MATERIALS AND METHODS

Retrospective analysis of patients with endocrine HT treated with adrenalectomy from 1996 to 2017 at a tertiary referral hospital. Demographic, clinicopathological profiles, and treatment details were collected. Primary outcome studied was cure of hypertension at 12 months postintervention.

RESULTS

A total of 136 patients with endocrine HT (75 F:61 M) with a mean age of 49 years (18–77) underwent resection for adrenal tumors (132 benign and 4 malignant). The mean time from diagnosis of hypertension to adrenalectomy was 9 years. At 12 months postadrenalectomy cure was 87% (21/24) for pheochromocytomas, 78% (70/90) for Conn's, and 95% (21/22) for Cushing's syndrome. Predictors of failure to cure were older age, longer duration of hypertension, higher number of anti-hypertensive agents, and Conn's adenoma. Surgical interventions were 118 laparoscopic and 18 open adrenalectomies, with morbidity in five patients (four conversion to open and one CBD injury), with cohort mortality of 3% due to progressive disease associated with malignancy.

CONCLUSION

Early diagnosis and treatment are essential to achieve cure in endocrine hypertension, especially in Conn's syndrome. Morbidity from surgical interventions is very low in expert centers.

Insulinoma

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INTRODUCTION

Insulinomas are uncommon endocrine tumors with prevalence of around 1/100,000 person-years. However, they represent the most common functioning endocrine tumor of the pancreas and are main cause of hypoglycemia due to endogenous hyperinsulinism. In the presence of significant financial constraints in the patient population pancreatic insulinoma's management is difficult.

MATERIALS AND METHODS

We performed analysis of clinical series in order to study clinical and biological spectrum of presentation, the preoperative imaging and results of surgical approach in a backward and poor infrastructure setup in central India. Between 2002 and 2016, 10 patients with symptoms suggesting insulinoma were hospitalized in our department. All cases presented with neuroglycopenic symptoms and five had history of unconsciousness. Preoperative localization of insulinoma was possible in eight patients. Intraoperative ultrasound was performed in four patients. Enucleation was performed in eight cases, while in one case tumor was not palpable during the time of surgery and patient underwent blind distal pancreatectomy and in one case multiple tumors were present in distal pancreas and distal pancreatectomy was done. The dimensions of the tumor were >2 cm in most patients of enucleation group; one had multiple insulinomas. Nine patients proved to have benign insulinomas on histopathology.

RESULTS

Following surgery, the symptoms disappeared in all patients except one. The most common complication after enucleation was pancreatic fistula, seen in two cases.

CONCLUSION

Presentation of insulinoma in developing country is delayed due to late diagnosis and in most tumor size was >2 cm. Patients are younger and have aggressive neuroglycopenic symptoms.

Giant and Difficult Adrenal Lesion Series: Diagnostic Surprises and Challenges in Management

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INTRODUCTION

Giant adrenal tumors (>10 cm size) pose varied challenges to surgeons in terms of diagnosis, planning surgical approach, and also intraoperative difficulties in resection.

AIM

Aim of our study is to discuss challenges in management of giant and difficult adrenal lesions.

MATERIALS AND METHODS

We did a retrospective analysis of all patients with adrenal lesions and paragangliomas admitted in Endocrine Surgery ward, King George's Medical University between June 1, 2016 and October 30, 2017. We had total of 34 patients with adrenal lesions/paragangliomas under evaluation.

RESULTS

Mean age was 35 years (2–62 years), F:M ratio—20:14, side—right:left: bilateral—26:6:2, functional tumors in 80% of patients, surgeries done—57% laparoscopic and 43% open transperitoneal, histologies-pheochromocytoma (n = 11), myelolipoma (n = 11), adrenocortical carcinoma (ACC, n = 5), teratoma (n = 1), neuroblastoma (n = 1), cortical adenoma (n = 3), metastasis (n = 1), and paraganglioma (n = 1). Mean tumor size 12.5 cm (5.2–28 cm). Difficulties we faced in diagnosis include a patient with large 18 × 16 cm right adrenal mass nonfunctional, heterogeneous mass with calcifications. We found difficulties in resection over the subhepatic area and areas where the tumor was going retrocaval. We did open transperitoneal right adrenalectomy. Histopathology was adrenal teratoma. Other patient with 25 × 22 cm large right adrenal myelolipoma with hemorrhage confined to retroperitoneum had open trans-peritoneal right adrenalectomy. We found difficulties in dissecting the planes, which were disrupted by contained hematoma. Another patient a 13 years aged boy with large 25 × 22 × 20 cm right adrenal mass abutting liver, IVC, kidney with few areas with loss of fat planes. Biochemical workup showed high 24 hours urinary normetanephrines. He was given alpha-blockers and then had incisional biopsy reported as neuroblastoma. Metaiodobenzylguanidine scan was positive. In view of the pathology and large mass with resectability, we planned him for chemotherapy to downstage the disease and help in resection. He got cisplatin, etoposide, doxorubicin, and cyclophosphamide regimen and became symptomatically better with tumor reduced to 10 cm size and underwent successful surgery. We had a difficult time of decision making to operate or downstage by systemic therapy. Then two patients with adrenocortical carcinoma (ACC) infiltrating adjacent structures had difficult intraoperative resections and one child 2 years age with ACC with aorta being encased by large 25 × 20 cm left adrenal mass was planned for neoadjuvant chemotherapy (etoposide, doxorubicin, and cisplatin).

CONCLUSION

Giant adrenal tumors pose challenge in surgical planning, approach, and resection, and need careful planning and multidisciplinary team approach to have best outcomes.

Spontaneous Adrenal Hemorrhage—A Mixed Bag: 18 Cases from a Single Institution

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INTRODUCTION

Spontaneous adrenal hemorrhage is a rare clinical entity, which can lead to adrenal crisis, shock, and death. We conducted this study to analyze the etiopathogenesis, clinical presentation, imaging, and treatment of patients with spontaneous adrenal hemorrhage.

MATERIALS AND METHODS

Retrospective study of 18 patients with spontaneous adrenal hemorrhage managed between 2005 and 2017 at a single institution.

RESULTS

Mean age was 39 years (27–59 years) with eight males (44%) and ten females (56%). Most common presenting symptom was abdominal pain 10/18 (55.6%). Pheochromocytoma-like spells were present in 4/18 (22.2%). Contrast-enhanced computed tomography (CECT) was the most common imaging modality used 16/18 (88%). Imaging revealed bilateral adrenal hemorrhage in 6/18 (33%). Adrenal insufficiency was detected in 7/18 (38.9%) and these patients received steroid cover. Etiology included idiopathic 6 (33.3%), antiphospholipid antibody syndrome 5 (27.8%), pheochromocytoma 4 (22.2%), associated with pregnancy, trauma, and myelolipoma in 1 (11.1%) each respectively. Nine (50%) patients could be managed conservatively, while eight (44.4%) required adrenalectomy. There were no mortalities.

CONCLUSION

A high index of clinical suspicion should be raised in patients presenting with abdominal pain and pheochromocytoma-like spells. The detection of an unexplained adrenal hemorrhage should prompt one to look for predisposing conditions like antiphospholipid antibody. Patients with adrenal hemorrhage should be evaluated for adrenal insufficiency and if present supplementary therapy needs to be initiated. Abdominal CECT is a good imaging modality for this condition. As seen in our case series not all patients with adrenal hemorrhage require an adrenalectomy.

Bilateral Malignant Struma Ovarii with Lung Metastasis: A Case Report from an Endocrine Surgery Center in East Coast Malaysia

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INTRODUCTION

Malignant struma ovarii (SO) is a rare tumor defined as a mature ovarian teratoma containing 50% or more thyroid tissue. It comprises 5% of all ovarian teratomas and mostly is benign and unilateral. Malignant transformation of SO occurs in less than 5% of all cases. It is even rare for bilateral and metastatic disease.

CASE REPORT

We present an interesting case of a 24-year-old, single, nulliparous lady who was asymptomatic. Incidentally during medical checkup noted to have bilateral ovarian mass. Computed tomography scan of abdomen, thorax, and pelvis performed prior to surgery revealed bilateral complex ovarian cystic lesions with multiple lung nodules (largest 0.9 cm) and presence of ascites. Tumor marker of CA-125 was 655. She was counseled for surgery and opted for exploratory laparotomy with right salpingo-oophorectomy and left cystectomy for fertility sparing. Intraoperative findings revealed bilateral ovarian tumor. Her right ovary measured 20 × 14 cm mass, multiloculated with solid area. Her left ovary had another mass measuring 6 × 8 cm mass, multiloculated with no solid area. Gross ascites noted. However, there was no peritoneal seeding. Histopathological examination revealed bilateral malignant papillary thyroid carcinoma with metastasis. Patient refused total thyroidectomy and subsequent radioactive iodine ablation therapy. She was started on low-dose thyroxine for thyroid suppression. It was amazing to see that the lung metastasis disappeared.

DISCUSSION

We will discuss about the management and prognosis of this rare disease.

Surgeon-performed Superficial Cervical Plexus Block for Thyroidectomy and Parathyroidectomy

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INTRODUCTION

Thyroidectomy has been performed conventionally under general anesthesia (GA) for decades and so has been neck exploration for parathyroidectomy. The need of GA makes these surgeries impossible in some patients with comorbidities and poor performance status. Focused parathyroidectomy is most commonly done with infiltration of local anesthetic. But this may sometimes be troublesome if the procedure gets prolonged or during deep dissection. Several studies have explored the effects of combining bilateral cervical plexus block with GA and have found this to be effective in controlling postoperative pain and nausea (Lin et al. *J Int Med Res* 2012;40:1390–1398). Combined superficial and deep cervical plexus block have been used as an anesthetic procedure in thyroidectomies but most commonly employed and studied for carotid endarterectomies (Kulkarni et al. *J Endocrinol Invest* 1996;19:714-718, Davies et al. *Reg Anesth* 1997;22:442-446, Pandit et al. *Anesth Analg* 2000;91:781-786, Stoneham et al. 1998;89:907-912, Howell. *Br J Anaesth* 2007;99:119-131, Lewis et al. *Lancet* 2008;372:2132-2142, McCleary et al. *Eur J Vasc Endovasc Surg* 2001;22:1-12). But deep cervical block needs ultrasonography (USG) guidance and expertise. It is also fraught with complications. Superficial cervical plexus, on the contrary, is easily learnt, administered, and is not associated with much complications (Aunac et al. *Anesth Analg* 2002;95:746-750, Lo Gerfo et al. *Thyroid* 1994;4:437-439, Kulkarni et al. *J Endocrinol Invest* 1996;19:714-718, Chauhan et al. *Reg Anesth* 1995;20:459, Pandit et al. *Br J Anaesth* 2007;99:159-169). In our observational study, we have evaluated superficial cervical block (unilateral or bilateral) performed by the surgeon himself as a safe and effective technique of anesthesia for thyroidectomy and parathyroidectomy.

AIMS AND OBJECTIVES

To study the safety and efficacy of surgeon performed superficial cervical block (unilateral/bilateral) for performing thyroidectomy and parathyroidectomy. Inclusion criteria: (1) All patients undergoing thyroidectomy or parathyroidectomy who could not be operated under GA due to comorbidities, poor performance status. (2) Patients operated on daycare basis due to dearth of GA slots/beds. Exclusion criteria: Patients with preoperative diagnosis of carcinoma. Study Population: Patients operated under Unit 1, Surgical Disciplines, All India Institute of Medical Sciences, New Delhi. Study Duration: May 2016 to November 2017. Sample Size: 120. Study Design: Institutional observational study.

MATERIALS AND METHODS

Patients fulfilling the inclusion criteria were informed about the study. Those who gave consent were enrolled. Carcinoma was ruled out. Surgeon himself performed Superficial Cervical Plexus block without taking the aid of USG guidance with 0.5% Bupivacaine (@ maximum of 2 mg/kg). The operating time and incision length were noted. Patients were interviewed about the pain they experienced during and after the procedure. Other parameters like patient satisfaction due to absence of preoperative fasting, time of initiation of oral intake after surgery, duration of hospital stay, resumption of normal daily activities, and the need of analgesics were studied.

RESULTS

A total of 120 patients were operated, of whom 98 underwent thyroidectomies (hemi or total) and the rest underwent parathyroidectomies (focused or formal neck exploration). None of the patients had anesthetic agent or block associated complication. Some patients however complained of a tugging sensation, while dissecting over the trachea or at the tracheo-esophageal groove, which could be successfully tackled by local infiltration of anesthetic. One patient of thyroiditis with severe adhesions needed to be converted to general anesthesia as the bilateral block failed. Another patient posted for completion thyroidectomy felt extremely uncomfortable during dissection near the trachea and had to be administered GA. Patients could be discharged immediately after surgery and oral feeds were initiated as soon as the patient felt thirst or had a desire to eat. Most patients returned to work next day. The ones with poor performance status continued to be in their preoperative state as far as daily activities is concerned. Analgesics like oral nonsteroidal anti-inflammatory drugs and Paracetamol were sufficient and rarely required beyond 48 hours. For performing focused parathyroidectomy, which is otherwise done under local infiltration at incision site, there was an added advantage with this block with respect to intraoperative analgesia especially in cases where parathyroid identification got prolonged or deeper dissection became necessary.

CONCLUSION

Surgeon-performed superficial cervical block is a safe method of anesthesia for performing thyroidectomies and parathyroidectomies, obviating the need of general anesthesia and thereby leading to effective analgesia intraoperatively and postoperatively, early discharge, early initiation of feeds, and early resumption of normal daily activities. In case of focused parathyroidectomy, it is more effective than local infiltrative anesthesia given at site of incision especially in cases where parathyroid identification gets prolonged or deeper dissection is necessary.

A Comparative Study of Single-incision vs Robotic-assisted Laparoscopic Surgery for Adrenal Masses

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INTRODUCTION

Minimally invasive surgical procedures are gaining more attention over recent years in adrenal surgery. The aim of this study was to compare surgical outcomes of robotic multiport adrenalectomy (RMA) and single-incision laparoscopic adrenalectomy (SILA) procedures.

MATERIALS AND METHODS

Between May 2012 and June 2016, a total of 70 patients who underwent transabdominal RMA and SILA procedures, performed by two senior endocrine surgeons, were included in the study. Patients were divided into two study groups according to the surgical technique. Besides demographics, surgical outcomes including operative time, tumor size, estimated blood loss, conversion to open surgery, and length of hospital stay were compared.

RESULTS

There were 48 patients in the RMA group and 22 patients in the SILA group. Patient demographics including body mass index, gender, and age were similar between study groups. Tumor size was similar in both groups (4.3 ± 2.7 vs 3.2 ± 1.4 cm respectively, $p = 0.984$). Operative time was shorter for the RMA group (82.0 ± 35.4 vs 104.0 ± 38.3 minutes, $p = 0.022$), while the rate of conversion to open surgery was similar (6.2% for RMA vs 4.5% for SILA). Hospital stay was shorter for the robotic group (2.5 ± 0.8 vs 4.0 ± 2.9 days respectively, $p = 0.018$).

CONCLUSION

Several minimally invasive techniques and approaches have been successfully performed worldwide for the surgery of adrenal masses. Our study shows that the use of the robot decreases the operative time. However, on the contrary, SILA group had better cosmetic outcomes. Both minimal invasive techniques were feasible and safe in experienced hands.