

## RESEARCH ARTICLE

# Annual Financial Impact of Thyroidectomies for Nodular Thyroid Disease in China

Xiao-Yun Liu<sup>1&</sup>, Li-Jun Zhu<sup>2&</sup>, Dai Cui<sup>1</sup>, Zhi-Xiao Wang<sup>1</sup>, Huan-Huan Chen<sup>1</sup>, Yu Duan<sup>1</sup>, Mei-Ping Shen<sup>3</sup>, Zhi-Hong Zhang<sup>4</sup>, Xiao-Dong Wang<sup>1</sup>, Jia-Wei Chen<sup>1</sup>, Erik Karl Alexander<sup>5</sup>, Tao Yang<sup>1\*</sup>

### Abstract

A large proportion of patients with thyroid nodules in China undergo thyroidectomy in order to get confirmatory histology diagnosis. The financial impact of this modality remains to be investigated. To evaluate rationality of performing thyroidectomy without a routine FNA preoperatively from the economic perspective, we conducted a retrospective, observational study of all archival thyroidectomies with records of cost per stay (CPS), cost per day (CPD) and length of stay (LOS) from 2008 to 2013 in the First Affiliated Hospital of Nanjing Medical University. We compared all the parameters between cancer and non-cancer thyroidectomies. We recruited 6, 140 thyroidectomies with valid records of CPS, CPD and LOS in this period. The CPS of cancer thyroidectomy was significantly higher than non-cancer thyroidectomy. The percentage of cancer thyroidectomy increased from 26.5% to 41.6%. The percentage of annual cost of cancer thyroidectomies rose from 30.2% to 45.2%. The LOS for cancer and non-cancer thyroidectomy decreased while the CPD increased in the past six years. The estimated national cost in 2012 for all thyroidectomies would be USD 1.86 billion with USD 1.09 billion for non-cancer thyroidectomies. We have witnessed great improvement in the healthcare for patients with thyroid nodules in China. However, given limited healthcare resources, currently thyroid FNA for more precise preoperative diagnosis may help to curb the rapidly increasing demand in healthcare costs in the future for nodular thyroid disease in China.

**Keywords:** Thyroid nodule - thyroidectomy - thyroid cancer - cost - papillary thyroid carcinoma

*Asian Pac J Cancer Prev*, 15 (14), 5921-5926

### Introduction

Thyroid nodule is very common worldwide (Han et al., 2011; Jameson, 2012). The prevalence of thyroid nodule is about 18-40% in adult Chinese (Chen et al., 2013; Guo et al., 2013; Liu et al., 2013). However, only 5-10 percent of all thyroid nodules are malignant. Familial history of thyroid cancer, a low dietary iodine intake, younger age, higher thyrotropin levels, and micro-calcifications within the nodules are considered to be the predictors of malignancy (Othman et al., 2009; Yang et al., 2011; Xhaard et al., 2014). With the improvement in ultrasound (Phuttharak et al., 2009; Cheng et al., 2013; Wu et al., 2013), thyroid FNA (Cibas et al., 2008) and cytopathology reporting system update (Cibas and Ali, 2009), many patients do not need to undergo thyroidectomy to obtain confirmatory diagnosis of thyroid nodules. According to the recent guideline from American Thyroid Association (ATA) (American Thyroid Association Guidelines Taskforce on Thyroid et al., 2009), thyroid FNA under the

guidance of ultrasound is the essential mainstay step when making the diagnosis of thyroid nodules (Frates et al., 2006; Yassa et al., 2007; Cheng et al., 2013; Gupta et al., 2013). However, variation exists from country to country, even different regions within one country (Haymart et al., 2013; Van den Bruel et al., 2013). In China, a large proportion of patients still undergo thyroidectomy for diagnostic purpose. In the belief of surgeons, general practitioners and even endocrinologists, histological diagnosis would be the final judgment for thyroid nodules. You never know it is benign or malignant until you take it out. This is true especially when thyroid FNA results turn out to be indeterminate. When a nodule is indeterminate by FNA, the optimal way is to repeat FNA or undergo molecular tests (Alexander, 2008; Nikiforov et al., 2009; Nikiforov et al., 2011; Alexander et al., 2012; Kim and Alexander, 2012; Zhou et al., 2012; Nikiforov et al., 2013; Ranjbari et al., 2013; Alexander et al., 2014). Surgery, however, should be regarded as the last resort if all the other options still fail to produce satisfactory results.

<sup>1</sup>Department of Endocrinology, <sup>2</sup>Department of Surgery, <sup>4</sup>Department of Pathology, The First Affiliated Hospital of Nanjing Medical University, <sup>3</sup>Department of Children's Health Care, Nanjing Maternity and Child Health Care Hospital Affiliated to Nanjing Medical University, Nanjing, China, <sup>5</sup>Thyroid Unit, Division of Endocrinology, Metabolism and Diabetes, Department of Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, USA <sup>&</sup>Equal contributors \*For correspondence: yangt@njmu.edu.cn

On the contrary, the percentage of patients receiving thyroid FNA is below 15% in many surgery departments specialized for thyroid nodules in China. Many surgeons still mainly rely on frozen section to guide further surgery range. This belief leads to a large proportion of thyroidectomies with final benign histology. However, considering the highly limited healthcare resources in China, the financial impact of this modality remains to be investigated. The aim of current study was to evaluate rationality of performing thyroidectomy without a routine FNA preoperatively from economic perspective in a large tertiary hospital of eastern China.

## Materials and Methods

We collected data from the Record Room and Register and Reporting system in the First Affiliated Hospital of Nanjing Medical University, one of the largest hospitals of eastern China. We coined the two data resources by the same admission number. Specifically, we reviewed all thyroid histopathological reports and valid records of cost per stay (CPS), length of stay (LOS) and cost per day (CPD) of each case in Record Room from January 2008 to December 2013. We only recruited cases with thyroidectomy as the only purpose of the admission for nodular thyroid disease. We divided histopathology results into two main categories: cancer and non-cancer groups. All pathological findings were confirmed by experienced endocrine pathologist (Z.Z.). Cases combined with other clinically irrelevant comorbidities were excluded in our final analysis. CPS, LOS and CPD were obtained by chart review at a Record Room by D.C., Z.W., H.C. and Y.D. We obtained valid data for CPS, LOS and CPD in 6,140 thyroidectomies in the six-year period. All the cost was converted to USD according to the yearly average exchange rate between RMB and USD.

Quantitative data were shown as mean±SD, whereas numbers and percentage were provided for qualitative data. Quantitative data were compared using independent samples T-test. Percentages were compared using the  $\chi^2$  test. All tests were 2-sided and a  $p < 0.05$  was considered statistically significant. Statistical analyses were performed with SPSS software, version 13.0 for Windows (SPSS Inc, Chicago, IL, USA).

This study was reviewed and deemed exempt from written informed consent by the Institutional Review Board (IRB) of the First Affiliated Hospital of Nanjing Medical University. It was approved by the IRB for analysis.

## Results

### Baseline characteristics of non-cancer and cancer thyroidectomies

We recruited 6,140 cases altogether with the mean age at 48.09±13.75 years old 78.7% being female. The cancer group was significantly younger than non-cancer group (Table 1. 44.52±14.05 years vs. 49.71±13.30 years,  $p < 0.01$ ). However, no gender difference was found between the two groups. There was more bilateral thyroidectomies in cancer group than in the non-cancer

group (48.4% vs. 27.2%,  $p < 0.01$ ). In cancer group, majority of the cases were papillary thyroid carcinoma (PTC), followed by other types (Table 2).

### Mean CPS for non-cancer and cancer thyroidectomies from 2008 to 2013

The mean CPS for cancer thyroidectomies was all higher than CPS for non-cancer thyroidectomies with statistical significance ( $p < 0.01$ , Table 3) over the six-year period. The mean CPS for cancer and non-cancer thyroidectomies both increased in this period. For non-cancer thyroidectomies, the mean CPS increased from USD 1,093±281 in 2008 to USD 2,055±576 in 2013 with increment of 88% ( $p < 0.01$ , compared with 2008), while for cancer thyroidectomies the mean CPS increased from USD 1,306±366 to USD 2,381±714 with augmentation of 82% ( $p < 0.01$ , compared with 2008).

### Numbers of patients receiving non-cancer and cancer thyroidectomies from 2008 to 2013

There was a leap for the number of benign thyroidectomies from 573 in 2008 to 716 in 2009, however the number remained steadily in the following years from 729 in 2010 to 772 in 2013, on the contrary the number of cancer patients increased year by year, especially with a leap from 390 in 2012 to 549 in 2013 (Table 3). The total number of patients receiving all kinds of thyroidectomies grew from 780 to 1,321 with increment of 69.36%. As expected, the percentage of cancer patients among all patients receiving thyroidectomies increased from 26.54% in 2008 to 41.56% in 2013 (Table 3,  $p < 0.01$ , compared with 2008) in the past six years.

### Total annual cost for thyroidectomies of non-cancer and cancer patients from 2008 to 2013

We next determined the annual total cost of non-cancer and cancer thyroidectomies in the period. It was shown that the total annual cost for non-cancer thyroidectomies increased from USD 0.626 million in 2008 to USD 1.586

**Table 1. Baseline Characteristics of Non-cancer and Cancer Thyroidectomies**

	non-Cancer	Cancer	Total	P
Number	4,229	1,911	6,140	
Mean Age (y)	49.71±13.30	44.52±14.05	48.09±13.75	<0.01
Gender				
Male	890 (21.0%)	418 (21.9%)	1,308 (21.3%)	0.463
Female	3,339 (79.0%)	1,493 (78.1%)	4,832 (78.7%)	
Surgical approach				
Unilateral	3,071 (72.6%)	983 (51.4%)	4,054 (66.0%)	<0.01
Bilateral	1,151 (27.2%)	925 (48.4%)	2,076 (33.8%)	<0.01
Other	7 (0.2%)	3 (0.2%)	10 (0.2%)	1

Other: substernal thyroidectomy

**Table 2. Cancer Type Distribution in the Cohort**

Cancer types	Number	Percent
PTC	1,675	87.65%
FTC	111	5.81%
MTC	33	1.73%
ATC	4	0.21%
Other cancer types	88	4.60%
Total	1,911	100.00%

\*Abbreviations: PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; MTC, medullary thyroid carcinoma; ATC, anaplastic thyroid carcinoma

**Table 3. Cost per Stay (CPS), Length of Stay (LOS) and Cost per Day (CPD) for Non-Cancer and Cancer Thyroidectomies from 2008 to 2013**

	2008	2009	2010	2011	2012	2013
Number of Patients						
Non-cancer	573	716	729	738	701	772
Cancer	207	194	267	304	390	549
Total	780	910	996	1,042	1,091	1,321
Cancer Patients Ratio	26.54%	21.32%	26.81%	29.17%	35.75%	41.56% <sup>b</sup>
Cost Per Stay (CPS)						
Non-cancer (in USD)	1,093±281	1,206±308	1,323±347	1,359±314	1,729±430	2,055±576 <sup>b</sup>
Cancer (in USD)	1,306±366 <sup>a</sup>	1,524±552 <sup>a</sup>	1,611±539 <sup>a</sup>	1,677±627 <sup>a</sup>	2,169±713 <sup>a</sup>	2,381±714 <sup>a, b</sup>
p value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Annual Total Cost						
Non-cancer (in thousand USD)	626	864	965	1,003	1,212	1,586
Cancer (in thousand USD)	270	296	430	510	846	1,307
Total (in thousand USD)	897	1,159	1,395	1,513	2,058	2,893
Annual cancer thyroidectomies cost percentage	30.15%	25.50%	30.83%	33.69%	41.11%	45.17%
Length Of Stay (LOS)						
Non-Cancer	9.36±3.50	8.73±3.32	8.3±3.32	7.31±2.51	7.00±2.08	6.67±2.45 <sup>b</sup>
Cancer	10.68±3.85 <sup>a</sup>	10.02±4.37 <sup>a</sup>	9.98±4.12 <sup>a</sup>	8.56±3.12 <sup>a</sup>	8.41±3.12 <sup>a</sup>	7.47±2.88 <sup>a, b</sup>
p value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Cost Per Day (CPD)						
Non-Cancer (in USD)	125±35	148±41	171±51	199±60	263±87	333±114 <sup>b</sup>
Cancer (in USD)	130±35 <sup>a</sup>	160±43 <sup>a</sup>	173±52 <sup>a</sup>	204±58 <sup>a</sup>	276±98 <sup>a</sup>	345±118 <sup>a, b</sup>
p value	0.121	<0.01	0.677	0.204	0.032	0.072
Yearly average exchange rate (1RMB to USD in each year)	0.14415	0.14661	0.14794	0.15496	0.15865	0.16155

<sup>a</sup>compared between non-cancer and cancer group; <sup>b</sup>compared between 2013 and 2008

**Table 4. Estimated National-wide Cost for Thyroidectomies in 2012**

	The First Affiliated Hospital of Nanjing Medical University	National Estimation
Number of all surgeries	40,851	36,902,500
Number of thyroidectomies	1,091	985,548
Cost for thyroidectomy (USD, Million)	2.06	1,858.80
Non-cancer thyroidectomy (USD, Million)	1.21	1,094.93
Cancer thyroidectomy (USD, Million)	0.85	763.87

million in 2013 with the increment of 153%, while the total cost for cancer thyroidectomies rose from USD 0.270 million to USD 1.307 million in 2013 more than 4.5 times in 2008. The total cost of all thyroidectomies was raised from USD 0.897 million to USD 2.893 million in the same period more than tripled in 2008 (Table 3). In the meantime the percentage of the cost of annual cancer thyroidectomies in all thyroidectomies grew from 30.15% to 45.17%, almost reaching half of all the costs.

#### Average length of stay (LOS) of non-cancer and cancer thyroidectomies from 2008 to 2013

With more patients receiving thyroidectomies, the average length of stay (LOS) shrank both in non-cancer thyroidectomies and in cancer thyroidectomies. For non-cancer thyroidectomy cohort, the average LOS decreased from 9.36±3.50 days in 2008 to 6.67±2.45 days in 2013 with significance (Table 3,  $p<0.01$ , compared with 2008). While the average LOS for cancer thyroidectomies

decreased from 10.68±3.85 in 2008 to 7.47±2.88 days in 2013 (Table 3,  $p<0.01$  compared with 2008). The LOS for non-cancer thyroidectomy was all shorter than cancer thyroidectomy in each year significantly (Table 3,  $p<0.01$ ).

#### Mean cost per day (CPD) of non-cancer and cancer thyroidectomies from 2008 to 2013

Due to increased total cost of both kinds of thyroidectomies with decreased LOS in each group, CPD of each group was expected to grow in the six years. As we can draw from Table 3 that, the mean CPD for non-cancer thyroidectomies grew from USD 125±35 in 2008 to USD 333±114 in 2013 more than 2.5 times of 2008 (Table 3,  $p<0.01$ , compared with 2008). In the meantime the CPD for cancer rose from USD 130±35 to USD 345±118 in 2013 similarly (Table 3,  $p<0.01$ , compared with 2008). The mean CPD for cancer thyroidectomies was significantly higher than that of non-cancer thyroidectomies in the year 2009 and 2012 ( $p<0.01$  in 2009 and  $p=0.032$  in 2012), however only similar trend was shown in 2008, 2010, 2011 and 2013 without statistical significance.

#### Estimated national-wide cost for thyroidectomies

According the data from National Bureau of Statistics of the People's Republic of China, in 2012 there were 36.9025 million surgeries of all kinds national wide (<http://data.stats.gov.cn/workspace/index?m=hgnd>). In the meantime, the number of all surgeries in the First Affiliated Hospital of Nanjing Medical University was 40,851. According to the ratio, we estimated the national cost of thyroidectomies in 2012 (Table 4). The estimated national cost in 2012 for all thyroidectomies would be USD 1.86 billion with USD 1.09 billion for non-cancer thyroidectomies.

## Discussion

Our study evaluated the healthcare situation of thyroid nodules in China from a novel and unique perspective. The total annual cost for all thyroidectomies has more than tripled in recent six years reaching USD 2.893 million from one single comprehensive tertiary teaching hospital. Part of this was due to increased amount of thyroidectomies and notably the increased percentage of cancer patients which might be caused by the increased incidence in thyroid cancer itself (Haymart et al., 2013) and improved general healthcare standards. As expected, the CPS of cancer thyroidectomies was generally higher than that of non-cancer patients. The other part was due to the increased CPS for all kinds of thyroidectomies with more advanced technology applied during thyroidectomy and increased cost of general health care resources and inflation to some degree. The increasing cost seemed to be synchronous with the steady rising of the national annual income per capita. The annual average growth of CPS for non-cancer and cancer thyroidectomy was around 17.6% and 16.4% doubled the CPS for other admission with annual increment around 8% as reported by Zhao (Zhao et al., 2013) or 7% by Zhou (Zhou et al., 2011). However the increment was exaggerated due to increased yearly average exchange rate between RMB and USD (Table 3). If costs were designated in RMB the annual increment would be 13.4% for non-cancer thyroidectomy and 12.6% for cancer thyroidectomy. We have achieved decreased LOS in the past six years for both kinds of thyroidectomy similar to the findings by Zhao (Zhao et al., 2013) meaning more cost-efficient way has been applied for patients receiving thyroidectomy.

However, there is still a great difference compared with the situation of thyroidectomies in developed countries, for example, the United States. In the US, the CPS of one thyroidectomy for malignancy including fees for surgeon, anaesthesia and hospitality would be USD 6,814.81 (Lubitz et al., 2014) or USD 5,447 to 6,587 as reported by Sosa (Sosa et al., 2007). In Singapore the mean cost of thyroidectomy was SGD 3,929 in 2001 (Ramanujam and Cheah, 2005). In our analysis, the average CPS of malignant thyroidectomy in 2013 was CNY 14,735.92 (USD 2,381 and SGD 3,135) which was much cheaper than in the US and still cheaper than in Singapore in the year of 2001. In the meantime the LOS in China was much longer than developed countries. In Singapore the LOS was 3.3 days in 2001 (Ramanujam and Cheah, 2005) while in US the average LOS for thyroidectomy was 1.75 to 2.46 days (Sosa et al., 2007). As for the annual cancer patients percentage, we are lagging behind as well. According to the report published by Dr Alexander's group in 2007 (Yassa et al., 2007), the malignant rate was 56% in Brigham and Women's Hospital at that time. In comparison, the malignant rate was 41.56% in 2013 in our analysis (Table 3), higher than the situation in Malaysia (28.1%) (Othman et al., 2009). All these data have shown that there is still a major gap between China and developed countries. We are performing thyroidectomies with longer LOS, less CPS, most importantly less cancer patients percentage. The reason for this disparity lies that

many health care professionals in China including thyroid surgeons and even endocrinologists think that only surgery can be the final judgment for thyroid nodules and cannot be replaced by other modalities including thyroid FNA. The surgeons still depend largely on the frozen section to guide the surgery range.

According to Lubitz (Lubitz et al., 2014), the cost for ultrasound guided thyroid FNA in the US was USD 465.56. While in our hospital the average cost of thyroid FNA was CNY 276 (USD 45) including the cost for cytopathology review. If we could save one patient from unnecessary thyroidectomy by doing a FNA we could save 6.67 days of admission and CNY 2,055 from our healthcare insurance. In replace, more chances will be given to patients who truly need thyroidectomy for higher risk of malignancy. Given the high prevalence of thyroid nodule in our community (Guo et al., 2013) and limited healthcare resources, it is worthwhile to reconsider the algorithm when referring a patient for thyroidectomy.

In order to increase hospital beds and resources availability, several means have been applied resulting in decreased total cost of admission and improved patient flow. In Singapore, sub-specialization and a clinical thyroidectomy pathway were implemented in 2001 to save CPS from SGD 3,929 to SGD 3,524 and LOS from 3.3 days to 1.9 days (Ramanujam and Cheah, 2005). Vrabec (Vrabec et al., 2013) showed a designated short-stay hospital unit was an effective model for improving the timeliness of discharge for thyroidectomy patients compared to those admitted to a general care surgical ward. The patients in the short-stay unit were discharged often within 24 hours. However, Lang did not recommend discharging patients with thyroidectomy within 24 hours due to possible risks of hematoma between 6 to 24h after surgery (Lang et al., 2012). However, in China, according to the findings of our study, the most urgent means would be to decrease the non-cancer patients percentage instead of shortening LOS. One less non-cancer patient means extra 6.67 days for patients with higher risk for malignancy. And this patient would be saved from unnecessary thyroidectomy by one or two thyroid FNAs with total cost no more than CNY 552 (USD 89). That would be more cost-efficient than simply shortening LOS for all thyroidectomies.

China expanded its population coverage by health insurance from around 29.7% in 2003 to over 90% at the end of 2010 (Tang et al., 2012). The rapidly increasing population coverage by government supported health insurance schemes has stimulated a demanding use of limited healthcare resources, and thus given rise to more challenges on cost control in China. We are facing unprecedented pressure to use limited healthcare resources as cost-efficient as possible. According to the estimation in our study, the estimated national cost in 2012 for non-cancer thyroidectomies would be USD 1.09 billion. That was 68% of the estimated overall societal cost of well differentiated thyroid cancer care in 2013 in the US which was USD 1.6 billion (Lubitz et al., 2014). Given the high prevalence of thyroid nodules in China and limited healthcare resources, cost-effective algorithm should be applied generally for all patients with thyroid nodule

as the first priority instead of shortening LOS. Surgery should no longer be considered as a diagnostic method anymore from the economic perspective with the data given by our study. Appropriate triage according to the recent American Thyroid Association (ATA) guideline (American Thyroid Association Guidelines Taskforce on Thyroid et al., 2009) should be suggested to raise the percentage of cancer patients and then to utilize healthcare resources more efficiently.

The main limitation of current study was that it was a single-centre study. The situation in the First Affiliated Hospital of Nanjing Medical University could only represent partial situation of the whole scenario. Variety in percentage of thyroidectomy in all surgeries is expected from region to region and from hospital to hospital. Multi-centre study is needed to further illustrate the issue.

To summarize, we have witnessed great improvement in the healthcare for patients with thyroid nodules in China with more percentage of patients getting thyroidectomies for malignant nodules and decreased annual cost percentage for benign nodules. However, great gap still exists between China and developed countries. Effective methods including thyroid FNA for more precise preoperative diagnosis should be utilized preoperatively in order to lower the non-cancer patient percentage which would be more cost-effective modality currently rather than shortening LOS.

## Acknowledgements

The study was supported by Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

## References

- Alexander EK (2008). Approach to the patient with a cytologically indeterminate thyroid nodule. *J Clin Endocrinol Metab*, **93**, 4175-82.
- Alexander EK, Kennedy GC, Baloch ZW, et al (2012). Preoperative diagnosis of benign thyroid nodules with indeterminate cytology. *N Engl J Med*, **367**, 705-15.
- Alexander EK, Schorr M, Klopper J, et al (2014). Multicenter clinical experience with the afirma gene expression classifier. *J Clin Endocrinol Metab*, **99**, 119-25.
- American Thyroid Association Guidelines Taskforce on Thyroid N, Differentiated Thyroid C, Cooper DS, et al (2009). Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*, **19**, 1167-214.
- Chen Z, Xu W, Huang Y, et al (2013). Associations of noniodized salt and thyroid nodule among the Chinese population: a large cross-sectional study. *Am J Clin Nutr*, **98**, 684-92.
- Cheng P, Chen ED, Zheng HM, et al (2013). Ultrasound score to select subcentimeter-sized thyroid nodules requiring ultrasound-guided fine needle aspiration biopsy in eastern China. *Asian Pac J Cancer Prev*, **14**, 4689-92.
- Cibas ES, Alexander EK, Benson CB, et al (2008). Indications for thyroid FNA and pre-FNA requirements: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. *Diagn Cytopathol*, **36**, 390-9.
- Cibas ES, Ali SZ (2009). The Bethesda System for Reporting Thyroid Cytopathology. *Thyroid*, **19**, 1159-65.
- Frates MC, Benson CB, Doubilet PM, et al (2006). Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. *J Clin Endocrinol Metab*, **91**, 3411-7.
- Guo H, Sun M, He W, et al (2013). The prevalence of thyroid nodules and its relationship with metabolic parameters in a Chinese community-based population aged over 40 years. *Endocrine*, **45**, 230-5.
- Gupta A, Ly S, Castroneves LA, et al (2013). A standardized assessment of thyroid nodules in children confirms higher cancer prevalence than in adults. *J Clin Endocrinol Metab*, **98**, 3238-45.
- Han MA, Choi KS, Lee HY, et al (2011). Current status of thyroid cancer screening in Korea: results from a nationwide interview survey. *Asian Pac J Cancer Prev*, **12**, 1657-63.
- Haymart MR, Banerjee M, Yang D, et al (2013). Variation in the management of thyroid cancer. *J Clin Endocrinol Metab*, **98**, 2001-8.
- Jameson JL (2012). Minimizing unnecessary surgery for thyroid nodules. *N Engl J Med*, **367**, 765-7.
- Kim MI, Alexander EK (2012). Diagnostic use of molecular markers in the evaluation of thyroid nodules. *Endocr Pract*, **18**, 796-802.
- Lang BH, Yih PC, Lo CY (2012). A review of risk factors and timing for postoperative hematoma after thyroidectomy: is outpatient thyroidectomy really safe? *World J Surg*, **36**, 2497-502.
- Liu Y, Huang H, Zeng J, et al (2013). Thyroid volume, goiter prevalence, and selenium levels in an iodine-sufficient area: a cross-sectional study. *BMC Public Health*, **13**, 1153.
- Lubitz CC, Kong CY, McMahon PM, et al (2014). Annual financial impact of well-differentiated thyroid cancer care in the United States. *Cancer*, **120**, 1345-52.
- Nikiforov YE, Ohori NP, Hodak SP, et al (2011). Impact of mutational testing on the diagnosis and management of patients with cytologically indeterminate thyroid nodules: a prospective analysis of 1056 FNA samples. *J Clin Endocrinol Metab*, **96**, 3390-7.
- Nikiforov YE, Steward DL, Robinson-Smith TM, et al (2009). Molecular testing for mutations in improving the fine-needle aspiration diagnosis of thyroid nodules. *J Clin Endocrinol Metab*, **94**, 2092-8.
- Nikiforov YE, Yip L, Nikiforova MN (2013). New strategies in diagnosing cancer in thyroid nodules: impact of molecular markers. *Clin Cancer Res*, **19**, 2283-8.
- Othman NH, Omar E, Naing NN (2009). Spectrum of thyroid lesions in hospital Universiti Sains Malaysia over 11 years and a review of thyroid cancers in Malaysia. *Asian Pac J Cancer Prev*, **10**, 87-90.
- Phuttharak W, Somboonporn C, Hongdomnern G (2009). Diagnostic performance of gray-scale versus combined gray-scale with colour doppler ultrasonography in the diagnosis of malignancy in thyroid nodules. *Asian Pac J Cancer Prev*, **10**, 759-64.
- Ramanujam LN, Cheah WK (2005). Improvements in health care for patients undergoing thyroidectomy. *Asian J Surg*, **28**, 266-70.
- Ranjbari N, Almasi S, Mohammadi-Asl J, et al (2013). BRAF mutations in Iranian patients with papillary thyroid carcinoma. *Asian Pac J Cancer Prev*, **14**, 2521-3.
- Sosa JA, Mehta PJ, Wang TS, et al (2007). Racial disparities in clinical and economic outcomes from thyroidectomy. *Ann Surg*, **246**, 1083-91.
- Tang S, Tao J, Bekedam H (2012). Controlling cost escalation of healthcare: making universal health coverage sustainable in China. *BMC Public Health*, **12**, S8.

- Van den Bruel A, Francart J, Dubois C, et al (2013). Regional variation in thyroid cancer incidence in Belgium is associated with variation in thyroid imaging and thyroid disease management. *J Clin Endocrinol Metab*, **98**, 4063-71.
- Vrabec S, Oltmann SC, Clark N, et al (2013). A short-stay unit for thyroidectomy patients increases discharge efficiency. *J Surg Res*, **184**, 204-8.
- Wu HX, Zhang BJ, Wang J, et al (2013). Conventional ultrasonography and real time ultrasound elastography in the differential diagnosis of degenerating cystic thyroid nodules mimicking malignancy and papillary thyroid carcinomas. *Asian Pac J Cancer Prev*, **14**, 935-40.
- Xhaard C, Ren Y, Clero E, et al (2014). Differentiated thyroid carcinoma risk factors in French Polynesia. *Asian Pac J Cancer Prev*, **15**, 2675-80.
- Yang Y, Li Q, Guo L, et al (2011). A retrospective analysis of thyroid cancer in China. *Asian Pac J Cancer Prev*, **12**, 2245-9.
- Yassa L, Cibas ES, Benson CB, et al (2007). Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. *Cancer*, **111**, 508-16.
- Zhao LP, Yu GP, Liu H, et al (2013). Control costs, enhance quality, and increase revenue in three top general public hospitals in Beijing, China. *PLoS One*, **8**, e72166.
- Zhou YL, Zhang W, Gao EL, et al (2012). Preoperative BRAF mutation is predictive of occult contralateral carcinoma in patients with unilateral papillary thyroid microcarcinoma. *Asian Pac J Cancer Prev*, **13**, 1267-72.
- Zhou Z, Gao J, Fox A, et al (2011). Measuring the equity of inpatient utilization in Chinese rural areas. *BMC Health Serv Res*, **11**, 201.