Pediatric Thyroid Nodule Score (PTNS): Derivation and Validation of a Predictive Score for Thyroid Nodule Assessment in Children

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Conclusions

- Bivariate analysis demonstrates multiple parameters that distinguish thyroid cancer from benign disease.
- Logistic regression models identified palpable lymph nodes on physical exam, preoperative TSH level and multiple ultrasound features as risk factors for thyroid cancer with an > 80% chance of accurate differentiation between thyroid cancer and benign disease.

Background

- Although differentiated thyroid carcinoma in children is rare, the incidence is increasing.
- 25-30% of thyroid nodules in children and adolescents are malignant.
- The clinical challenge is to identify nodules requiring further intervention.
- Clinical assessment includes history, physical examination, biochemical evaluation, ultrasound (US) and ultrasound guided fine-needle aspiration (FNA).
- Current modalities, in isolation, have poor ability to reliably differentiate benign from malignant nodules.

Objective

To derive a predictive score that integrates clinical, biochemical, radiological and cytopathological parameters to define malignancy risk of a pediatric thyroid nodule.

Patients and Methods

- Inclusion criteria:
  - Patients < 18 years assessed for thyroid nodules between 1992-2015 at Sick Kids.
  - Histopathologically confirmed papillary or follicular thyroid carcinoma, or benign thyroid nodular disease.
  - Non-operative patients with FNA and > 2 year ultrasound follow-up without radiological change.
- Exclusion criteria:
  - Patients with medullary thyroid carcinoma.
- Methodology: review of patient charts including clinical data, radiology and pathology reports.
- Statistical analysis:
  - Multiple imputation analysis to account for missing values.
  - Bivariate analyses using Student's T-test, Chi-square or Fisher's Exact Test.
  - Variables with P-value < 0.2 were included in backward elimination logistic regression analysis.
  - Variables with P-value < 0.3 were retained in the logistic regression models.
  - Model estimate of > 0.8 is considered as strong.

Results

Table 1: Baseline clinical characteristics.

	Thyroid cancer (N=84)	Benign disease (N=94)
Gender (no. of females:males)	64:20	66:28
Mean ± SDS age (years)	12.9 ± 2.7	12.4 ± 3.3
Ionizing radiation exposure (no.)	3	4
Childhood cancer survivor (no.)	4	4
Acquired thyroid disease* (no.)	17	15
Family history thyroid ca (no.)	9	8

* euthyroidism with positive antibodies, Hashimoto, Graves' disease

Table 2: Identified parameters using bivariate analyses.

	Thyroid cancer (N=84)	Benign disease (N=94)	P-value
Demographics			
Mode of discovery: - Incidental finding on imaging - Patient/caregiver - Physician	 12% 46% 42%	 18% 52% 30%	0.18
Physical examination			
Palpable lymph nodes	27%	4%	<0.001
Biochemical evaluation			
Mean ± SDS TSH level (mIU/l)	2.14 ± 1.8	1.28 ± 1.1	0.07
Ultrasound features			
Calcifications	75%	36%	<0.001
Hypoechogenicity	41%	18%	0.003
Heterogeneity	92%	71%	0.003
Irregular margins	60%	37%	0.01
>50% cystic	3%	33%	<0.001
Suspicious lymphadenopathy	36%	5%	<0.001
Incomplete halo	48%	31%	0.17
Cytopathological features			
Benign Suspicious + malignant Indeterminate	9% 74% 15%	62% 0% 6%	<0.001

Table 3: Logistic regression analysis.

	Odds ratio	Lower and upper control limit
Calcifications on US	3.02	1.26-7.23
Heterogeneity on US	2.60	0.91-7.45
Palpable lymph nodes	2.42	0.36-16.4
Suspicious lymphadenopathy on US	2.21	0.43-11.4
Hypoechogenicity on US	1.75	0.70-4.36
Mode of discovery	1.74	1.00-3.03
TSH level	1.14	0.87-1.50
>50% cystic on US	0.12	0.03-0.46

Model estimate: 0.82 (0.78-0.85)

Future directions

- We will continue to refine the statistical model and explore other mathematical models to develop a predictive score for clinical use.
- External validation using an independent cohort from Montreal Children's Hospital is pending.

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Thyroid

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