Canadian Association of Radiologists Journal 68 (2017) 425–430

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Ultrasonography / Échographie

Risk Stratification in Multinodular Goiter: A Retrospective Review of Sonographic Features, Histopathological Results, and Cancer Risk

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Abstract

Purpose: In the management of thyroid nodules, although the potential for malignancy exists, there is also the potential for overtreatment of subclinical disease. Although the TI-RADS (Thyroid Imaging-Reporting and Data System) system outlines a risk stratification score based on suspicious ultrasound findings, it has not been universally accepted. Many TI-RADS 2 or 3 patients proceed to fine needle aspiration biopsy (FNAB), potentially unnecessarily. The aim of the study was to identify whether lesions within a multinodular goiter (MNG) without suspicious features can be followed with ultrasound rather than biopsied as is recommended for single nodules.
Methods: Pathology records were retrospectively analysed for proven MNGs over a 5-year period. A total of 293 cases were identified. FNAB, prebiopsy ultrasound images, and reports were identified for each case. Images were reviewed and assessed for sonographically suspicious criteria guided by TI-RADS. Logistic regression was applied to determine if any sonographic features were associated with neoplasia. Odds ratios with 95% confidence intervals were calculated.
Results: Of 293 samples, 14 (4.7%) were neoplastic. Having no suspicious features conferred an average risk of 0.0339 (95% confidence interval: 0.02831-0.04087) of neoplasia. Risk of neoplasm significantly increased by having 1 and >1 suspicious feature ($P < .001$). Regarding cytological results, of 237 patients with Thy-2 cytology, 159 were followed up and 8 had a neoplasm.
Conclusion: Ultrasound can be used to estimate risk of neoplasia in MNG. In the absence of suspicious radiological findings, follow-up with ultrasound rather than FNAB may be appropriate in patients who have a low clinical suspicion for neoplasia.

Résumé

Objectif : Dans un contexte de prise en charge des nodules thyroïdiens, il peut y avoir malignité, mais également surtraitement d'une affection subclinique. Le système TI-RADS (Thyroid Imaging-Reporting and Data System) calcule un score de stratification du risque fondé sur l'observation de caractéristiques suspectes par échographie. Toutefois, il n'est pas universellement reconnu. Dans bien des cas, les patients qui obtiennent le score 2 ou 3 selon le système TI-RADS subissent ensuite une cytoponction, potentiellement inutile. La présente étude avait pour objectif de déterminer si les lésions d'un goitre multinodulaire ne présentant pas de caractéristiques suspectes peuvent faire l'objet d'un suivi par échographie, plutôt que d'une biopsie, comme il est recommandé de le faire pour un nodule unique.
Méthodes : Une analyse rétrospective sur une période de cinq ans a été réalisée afin de relever les cas avérés de goitre multinodulaire dans les dossiers de pathologie. Au total, 293 cas englobant une cytoponction, des images échographiques avant la biopsie et des rapports ont été isolés. Les images ont été examinées et évaluées en fonction des aspects échographiques suspects définis par le système TI-RADS. Une régression logistique a été réalisée afin de déterminer si les caractéristiques échographiques observées étaient associées à une néoplasie. Les rapports des cotes avec intervalles de confiance de 95 % ont été calculés.
Résultats : Quatorze (4,7 %) des 293 échantillons étaient néoplasiques. L'absence de caractéristiques suspectes était associée à un risque moyen de 0,0339 (intervalle de confiance de 95 %: de 0,02831 à 0,04087) de néoplasie. Le risque de néoplasie augmentait notablement en présence d'une ou de plusieurs caractéristiques suspectes ($P < 0{,}001$). En ce qui concerne les résultats cytologiques, 159 des 237 patients affichant le score TI-RADS 2 ont fait l'objet d'un suivi et 8 ont présenté une néoplasie.

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0846-5371/$ - see front matter
http://dx.doi.org/10.1016/j.carj.2017.03.002

Conclusion : L'échographie peut servir à estimer le risque de néoplasie en présence d'un goitre multinodulaire. En l'absence d'aspects radiologiques suspects, il peut être approprié d'effectuer un suivi par échographie au lieu d'une cytoponction chez les patients pour lesquels le niveau de suspicion clinique est faible.

Key Words: Thyroid; Ultrasound; Fine needle aspiration and biopsy; Nodules

There is a high prevalence of thyroid nodules in the population, with estimates up to 67% [1]. Although the vast majority is asymptomatic, they are being diagnosed with greater frequency due to improved access to cross-sectional imaging and ultrasound as well as advances in ultrasound technology. These allow for detection of small subcentimetre nodules. As a result, there are more people being diagnosed with multinodular goiter (MNG), posing a challenge to clinicians.

Similarly, the incidence of thyroid cancer has been rising [2] and indeed doubled in Florida over the course of 10 years [3]. A landmark study in *JAMA* [4] that has been supported in other studies [5] concluded that the increased incidence represented "detection of subclinical disease" rather than an increase "in the true occurrence of thyroid cancer." Fortunately, majority of neoplastic thyroid disease is treatable with excellent 5-, 10-, and even 20-year survival rates [1,6]. Therefore, the challenge is diagnosing early clinically significant thyroid disease and avoiding potential risk of overtreatment.

The guidelines are clear for the management of solitary solid thyroid nodule >10 mm found on ultrasound [7]; however, there is less clear guidance in MNGs. Several attempts have been made to predict cancer risk based on ultrasound findings including the TI-RADS (Thyroid Imaging-Reporting and Data System) system [8]. However, no one system of reporting has been widely adopted nor stratification of risk widely accepted. Consequently, approaches to the management of thyroid nodules in MNGs vary. Most approaches, however, including at our institution and as described in the literature [9], tend to biopsy the largest lesion as well as any lesion with suspicious features (hypoechoic, irregular margin, microcalcification) or guided by the British Thyroid Association's U score [10]. This may lead to some patients having unnecessary fine needle aspiration biopsy (FNAB).

The aim of our study was to retrospectively examine if the principals of TI-RADS for single thyroid nodules could be applied to MNG as well as investigate whether the cytological results added to risk stratification of malignancy beyond the ultrasound findings alone. Our hypothesis was that patients whose ultrasound showed no suspicious features (guided by the Horvath et al TI-RADS) [8] were as likely to have a thyroid neoplasm as those patients with Thy-2 cytology. This could mean that a cohort of patients with MNG need not proceed to FNAB as it did not further stratify their risk.

Methods

Study Population

The institutional review board approved this study. Histopathological records from 2008-2012 for thyroid FNAB were collected from a tertiary referral centre and cross-referenced with a radiology Radiological Information System/Picture Archive and Communication System (RIS/PACS) system. Over this 5-year period, histopathological records showed 576 patients underwent thyroid nodule FNAB, of which 397 had prebiopsy ultrasound and ultrasound-guided FNAB according to the RIS/PACS system. A total of 179 biopsies were done without ultrasound guidance (this practice is no longer carried out at our institution) and as such were excluded. Following review of these ultrasound scans and reports, 293 of these 397 patients were multinodular (as opposed to single nodules) and were included for analysis. All patients with at least 3 nodules >5 mm were included in the study (although there were no samples with exactly 2 nodules). Lesions smaller than 5 mm tend to have low diagnostic yield when biopsied and may be of lesser clinical significance [11]. Histopathological records obtained for these 293 thyroid FNAB were reported according the Thy1-5 classification system as recommended by the Royal College of Pathologists: Thy1 (n = 25), Thy2 (n = 237), Thy3 (n = 25), Thy4 (n = 1), and Thy5 (n = 5). This scoring system is closely analogous but not identical to the Bethesda system employed in most North American institutions. Details of the study population are described in Figure 1. The average age was 53.72 (range 19-91) years and there were 49 men and 240 women. All those who returned Thy1 cytology were repeated and if this repeat was carried out within the time frame of this study they were included for analysis.

Imaging and Image Analysis

All thyroid ultrasounds and biopsies were carried out and reported on by 5 consultant radiologists who used real-time ultrasound to locate the nodules. The target lesion was biopsied using sterile technique and at least 2 samples were taken. A Consultant Pathologist specializing in head and neck pathology checked samples for adequacy at the time of biopsy.

TI-RADS outlines solid components on marked hypoechoic nodules, microlobulations or irregular margins, and microcalcifications as sonographic features suspicious for malignancy. In this study we retrospectively applied this classification to static ultrasound thyroid images and