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Thyroid Nodules: Reducing Overdiagnosis and Investigations

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Introduction

Thyroid nodules (TN) are incredibly common, with approximately 5% of the population presenting with palpable TN.[1] However, the widespread utilization of sensitive imaging techniques over the past few decades has led to a rapid increase in their prevalence.[2] Notwithstanding the clinically palpable TN, the rate of incidental nodules picked up on imaging studies varies remarkably with the underlying imaging modality. For instance, the prevalence of TNs on computed tomography (CT) scans of the neck is reported to be 16.5%,[3] FDG-PET to be 2%[1] and on neck ultrasounds (US) well over 50%.[3] The prevalence of TN is higher in females and increases with age, and while there has been little change in the overall reported incidence of palpable TNs, the rising prevalence can be almost exclusively attributed to the expanded use of imaging, particularly the widespread availability of sensitive US. It is estimated that over 60% of the population may have at least one TN.[1]

The Dark Side of Enhanced Diagnosis

Despite the overall low risk of malignancy in most TN thyroid nodules (~5%),[4] it is the exclusion of cancer that remains the over-riding concern for both patients and care providers. This strategy has led to the inevitable cascade of further investigations and the resulting enhanced case finding of subclinical thyroid malignancies.

Such an approach can have a lasting negative impact on patients as they undergo workup. In a study of 2,834 patients undergoing thyroid US, those diagnosed with TN experienced psychological distress and sleep disturbances compared with those without nodules.[5] Their distress and sleep quality further worsened after undergoing fine needle aspirate biopsy. In a qualitative study interviewing patients undergoing surgery for either confirmed thyroid cancer or indeterminate results, both groups expressed similar anxiety and a sense of urgency to have surgery to "get it out".[6] Even with indeterminate results, patients experience fear, worry, and a sense of major disruption to their lives. Regardless of whether the final pathology is malignant or benign, patients undergoing total thyroidectomy develop worsening fatigue post-operatively, with an odds ratio of 10.4 for developing asthenia (chronic fatigue syndrome) compared with those who undergo thyroid lobectomy.[7] These findings underscore the importance of careful consideration and patient-centred discussions when deciding on treatment for TN.

Thyroid Cancer in Thyroid Nodules – Putting Things in Perspective

The incidence of thyroid cancer has mirrored the rising incidence of TNs in developed countries. A Canadian study[8] reported a 5-to 6-fold increase in thyroid cancer diagnoses over the past four decades despite no change in the overall mortality. A recent study from Korea also showed a 15-fold increase in detection of thyroid cancer in the population from 1993 to 2011, which was directly attributable to increased use of screening US in asymptomatic patients,[9] while mortality rates remained stable. Another nationwide Korean study[10] attributed over 97% of the increase in incidence of thyroid cancer cases from 1999 to 2008 to the increased detection of small thyroid cancers with a 100% 5-year survival rate. Thyroid cancers detected through over diagnosis are estimated to account for 70–80% of cases in women and 45% of cases in men in many developed countries.[9] Furthermore, subclinical thyroid cancer is found in 6–35% of autopsies, with a stable prevalence across the age groups, further highlighting that not all thyroid cancers that are treated impact morbidity or mortality.[11] In fact, recent Canadian guidelines provide a robust framework for otherwise low recurrence risk thyroid cancer, indicating that certain patients, may only need active surveillance as the risk of

mortality and recurrence is very low.[12] Overall, the available evidence supports the need for de-emphasizing aggressive management of these small incidental cancers. Future studies should explore strategies to mitigate the fear of underdiagnosis among both patients and clinicians.

Tackling Inappropriate Thyroid Imaging

As discussed in the previous section, it is evident that the imaging studies such as sensitive US, account for the rising incidence of benign and malignant TNs. When adequately used, thyroid US is an excellent imaging modality to assess the anatomy of the thyroid gland; however there is consistent evidence from the literature that up to one-third of these scans do not have a sound basis for the request and include vague indications such as choking sensation or swallowing difficulties.[13] Indeed, a previous study conducted at our own centre reported that approximately 19% of scans were performed with no clear indication.[14] Furthermore, rates of US requests have continued to increase annually by as much as 20% with no clear strategy to minimize inappropriate thyroid US requests.[13]

For incidentally detected TN noted on CT or MRI, the American College of Radiology (ACR) recommends further clarification with thyroid US only for nodules that are >1.5 cm in size in patients >35 years and nodules that are >1 cm in those <35 years.[15] The risk of malignancy in nodules smaller than 1 cm identified on CT scans is very low, estimated at 0.1% (confidence interval [CI] 0–0.8) compared to 11.7% (CI 3.9–19.4) for nodules over 1 cm, and 24.9% (CI 0–52.7) for those exceeding 1.5 cm.[3] Despite this, guidelines[16,17] suggest performing US to further characterize any nodule detected on other imaging, regardless of size. Given that over 30% of thyroid US are requested following incidental findings on other imaging studies,[18] having clearer guidance and unified cutoffs for these thyroid incidentalomas may assist in decreasing over-investigation of TN.

While strategies to curb unnecessary thyroid US may vary by region, a tantalizing option is to enhance the integration of artificial intelligence (AI) in vetting US requests. A recent study reported that an AI based algorithm could evaluate the appropriateness for thyroid US referrals with a high level of accuracy.[19] To date, no published studies have evaluated effective interventions to address this important issue. Though restricting access to neck US is neither feasible nor advisable, regional audits on the inappropriate US requests could help identify problem areas and support developing tailored strategies to be put in place.

Reducing Thyroid Nodule Related Investigations

Once a functioning nodule has been excluded, further TN investigations are guided by sonographic features. The introduction of risk scores, such as the ACR Thyroid Imaging Reporting and Data System (TIRADS) system,[20] has improved standardization of nodule management. However, a Canadian retrospective review conducted before the implementation of ACR TIRADS revealed that 71% of US reports did not include the dominant nodule's three-dimensional size, 68% omitted echogenicity, and 46% did not provide an estimate for the risk of malignancy/recommendation for biopsy.[21] While multiple risk stratification systems exist, including the American Thyroid Association (ATA) guidelines, European Thyroid Imaging and Reporting Data System (EU-TIRADS), and the Korean Thyroid Association/Korean Society of Thyroid Radiology Guidelines (K-TIRADS), the ACR TIRADS has the highest size thresholds for biopsy resulting in 19.9–46.5% reduction in unnecessary fine needle aspirate biopsies (FNAB) compared to other scoring systems.[22] Regardless of the risk scoring system chosen, standardized implementation has been shown to significantly improve the quality of US reports and the classification reporting rates compared with radiology groups that do not adopt a systematic approach.[23] Developing standardized reporting forms through local consensus and education, providing reminders at the point of care, and conducting audits with feedback are viable strategies to improve the adoption of risk scoring systems. These efforts could help decrease the number of thyroid biopsies performed while increasing the rates of malignancy or intermediate cytology findings.[24]

Though FNABs are useful and accurate when benign or malignant results are reported, with false negative or positive rates <3%, at least 20% of FNABs result in indeterminate results. These indeterminate nodules have varying risk of malignancy that can be institution dependent but are most often benign and there is no consensus on management. A recent meta-analysis surmised that repeating FNAB can yield a more definitive

result in up to two-thirds of patients (50% benign, 15% malignant)[25]. Multiple thyroid nodule guidelines also recommend considering molecular testing[16,17] for indeterminate TNs. Molecular testing is used much more widely in the United States and is becoming available in Canada. There are several commercially available molecular tests which examine a variety of somatic mutations, gene expression profiles, and microRNA-based classifiers, each offering different positive and negative predictive values.[16] Publicly funded molecular testing has been implemented in both Alberta and Quebec. In Quebec, recent academic centres using Thyroseq v3 have demonstrated a benign call rate of 72.6% and found the test to be cost effective.[26] However, their analysis included non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in the "malignant" category and assumed that most Bethesda III and IV nodules measuring 1-4 cm would undergo diagnostic lobectomy, an approach that may not reflect standard practice in other centres. Unfortunately, it is still unclear whether molecular testing impacts rates of thyroid surgery. A recent large database analysis of patients in the United States who had undergone thyroid FNAB showed a steady trend of decreases in thyroidectomy surgeries after the release of the 2015 ATA guidelines. Notably, this decline was not impacted by molecular testing.[27] Regions with low adoption of molecular testing showed no differences in thyroidectomy rates compared with high testing adoption areas. In fact, low-adoption states appeared to have greater decline in thyroidectomy rates, likely reflecting the overall trend of more conservative management of low-risk thyroid cancers. Perhaps developing more nuanced decision-making nomograms that incorporate results from both molecular testing and clinical variables may enhance the accuracy of selecting surgical candidates.[28]

Conclusion

Overdiagnosis of TN is a growing worldwide concern, posing potential harm to both the healthcare system and patients. To address this, multi-targeted strategies need to be adopted, which should include reducing inappropriate US requests and minimizing subsequent investigations. Above all, engaging patients in a clear discussion in advance about the pros and cons of imaging including the possibility of incidental findings, will help them in making informed decisions.

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References

1. Russ G, Leboulleux S, Leenhardt S, Hegedüs L. Thyroid incidentalomas: epidemiology, risk stratification with ultrasound and workup. Eur Thyroid J. 2014;3(3):154–163. doi:10.1159/000365289
2. Acar T, Ozbek SS, Acar S. Incidentally discovered thyroid nodules: frequency in an adult population during Doppler ultrasonographic evaluation of cervical vessels. Endocrine. 2014;45(1):73-78. doi:10.1007/s12020-013-9949-3
3. Song Z, Wu C, Kasmirski J, Gillis A, Fazendin J, Lindeman B, et al. Incidental thyroid nodules on computed tomography: a systematic review and meta-analysis examining prevalence, follow-up, and risk of malignancy. Thyroid. 2024;34(11):1389-1400. doi:10.1089/thy.2024.0313
4. Grani G, Sponziello M, Pecce V, Ramundo V, Durante C. Contemporary thyroid nodule evaluation and management. J Clin Endocrinol Metab. 2020;105(9):2869–2883. doi:10.1210/clinem/dgaa322
5. Li R, Li G, Wang Y, Bao T, Lei Y, Tian L, et al. Psychological distress and sleep disturbance throughout thyroid nodule screening, diagnosis, and treatment. J Clin Endocrinol Metab. 2021;106(10):e4221-e4230. doi:10.1210/clinem/dgab224
6. Pitt SC, Saucke MC, Wendt EM, Schneider DF, Orne J, Macdonald CL, et al. Patients' reaction to diagnosis with thyroid cancer or an indeterminate thyroid nodule. Thyroid. 2021;31(4):580-588. doi:10.1089/thy.2020.0233
7. Luddy MK, Vetter R, Shank J, Goldner W, Patel A, Kotwal A, et al. Patient reported outcome measures of health-related quality of life and asthenia after thyroidectomy. J Surg Res. 2021;264:394-401. doi:10.1016/j.jss.2021.02.039
8. Topstad D, Dickinson JA. Thyroid cancer incidence in Canada: a national cancer registry analysis. CMAJ Open. 2017;5(3):E612-E616. doi:10.9778/cmajo.20160162
9. Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L. Worldwide thyroid-cancer epidemic? The increasing impact of overdiagnosis. N Engl J Med. 2016;375(7):614-617. doi:10.1056/NEJMp1604412
10. Park S, Oh CM, Cho H, Lee JY, Jung KW, Jun JK, et al. Association between screening and the thyroid cancer "epidemic" in South Korea: evidence from a nationwide study. BMJ. 2016;355:i5745. Published

2016 Nov 30. doi:10.1136/bmj.i5745
11. Arroyo N, Bell KJL, Hsiao V, Fernandes-Taylor S, Alagoz O, Zhang Y, et al. Prevalence of subclinical papillary thyroid cancer by age: meta-analysis of autopsy studies. J Clin Endocrinol Metab. 2022;107(10):2945-2952. doi:10.1210/clinem/dgac468
12. Paschke R, Ghaznavi S, Imran SA, Jacquier J, Lochnan H, Massicotte MH, et al. Follow-up and transition of care for low recurrence risk thyroid cancer patients in Canada. Eur Thyroid J. 2025;14(3):e250072. Published 2025 Jun 5. doi:10.1530/ETJ-25-0072
13. Edwards MK, Iñiguez-Ariza NM, Singh Ospina N, Lincango-Naranjo E, Maraka S, Brito JP. Inappropriate use of thyroid ultrasound: a systematic review and meta-analysis. Endocrine. 2021;74(2):263–269. doi:10.1007/s12020-021-02820-z
14. Landry BA, Barnes D, Keough V, Watson A, Rowe J, Mallory A, et al. Do family physicians request ultrasound scans appropriately? Can Fam Physician. 2011;57(8):e299-e304.
15. Hoang JK, Langer JE, Middleton WD, Wu CC, Hammers LW, Cronan JJ, et al. Managing incidental thyroid nodules detected on imaging: white paper of the ACR Incidental Thyroid Findings Committee. J Am Coll Radiol. 2015;12(2):143-150. doi:10.1016/j.jacr.2014.09.038
16. Durante C, Hegedüs L, Czarniecka A, Paschke R, Russ G, Schmitt F, et al. 2023 European Thyroid Association Clinical Practice Guidelines for thyroid nodule management. Eur Thyroid J. 2023;12(5):e230067. Published 2023 Aug 14. doi:10.1530/ETJ-23-0067
17. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26(1):1-133. doi:10.1089/thy.2015.0020
18. Soto Jacome C, Segura Torres D, Fan JW, Garcia-Bautista A, Golembiewski E, Duran M, et al. Drivers of thyroid ultrasound use: a retrospective observational study. Endocr Pract. 2023;29(12):948-954. doi:10.1016/j.eprac.2023.09.006
19. Jacome CS, Torres DS, Fan JW, Loor-Torres R, Duran M, Zahidy MA, et al. Thyroid ultrasound appropriateness identification through natural language processing of electronic health records. Mayo Clin Proc Digit Health. 2024;2(1):67-74. doi:10.1016/j.mcpdig.2024.01.001
20. Tessler FN, Middleton WD, Grant EG, Hoang JK, Berland LL, Teefey SA, et al. ACR thyroid imaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee. J Am Coll Radiol. 2017;14(5):587-595. doi:10.1016/j.jacr.2017.01.046
21. Karkada M, Costa AF, Imran SA, Hart RD, Bullock M, Ilie G, et al. Incomplete thyroid ultrasound reports for patients with thyroid nodules: implications regarding risk assessment and management. AJR Am J Roentgenol. 2018;211(6):1348-1353. doi:10.2214/AJR.18.20056
22. Hoang JK, Middleton WD, Tessler FN. Update on ACR TI-RADS: successes, challenges, and future directions, from the AJR special series on radiology reporting and data systems. AJR Am J Roentgenol. 2021;216(3):570-578. doi:10.2214/AJR.20.24608
23. Hu XY, Wu J, Seal P, Ghaznavi SA, Symonds C, Kinnear S, et al. Improvement in thyroid ultrasound report quality with radiologists' adherence to 2015 ATA or 2017 TIRADS: a population study. Eur Thyroid J. 2022;11(3):e220035. Published 2022 Jun 14. doi:10.1530/ETJ-22-0035
24. Edwards M, Brito JP, Salloum RG, Hoang J, Singh Ospina N. Implementation strategies to support ultrasound thyroid nodule risk stratification: a systematic review. Clin Endocrinol. 2023;99(4):417-427. doi:10.1111/cen.14942
25. Bayona A, Benavent P, Muriel A, Abuchaibe C, Sharpe SC, Tarasova V, et al. Outcomes of repeat fineneedle aspiration biopsy for AUS/FLUS thyroid nodules. Eur J Endocrinol. 2021;185(4):497-506. doi:10.1530/EJE-21-0330
26. Lévesque F, Payne RJ, Beaudoin D, Boucher A, Fortier PH, Massicotte MH, et al. Publicly funded molecular testing of indeterminate thyroid nodules: Canada's experience. J Clin Endocrinol Metab. 2025;110(4):e1031-e1037. doi:10.1210/clinem/dgae355
27. Huang Y, Chan SJ, Wright JD, Kuo JH, McManus CM, Lee JA, et al. Does the adoption of molecular testing cause decreased thyroidectomy rates in a national cohort? A quasiexperimental study of high- versus low-adoption states. Thyroid. 2024;34(3):388-398. doi:10.1089/thy.2023.0651
28. Wu J, Stewardson P, Eszlinger M, Khalil M, Ghaznavi S, Nohr E, et al. Development of a nomogram to integrate molecular testing and clinical variables to improve malignancy risk assessment among cytologically indeterminate thyroid nodules. Thyroid. 2025;35(5):508-515. doi:10.1089/thy.2024.0481