Which risk stratification system is best for thyroid nodules?

By Amerigo Allegretto, AuntMinnie.com staff writer

February 9, 2023 -- The American College of Radiology (ACR) TI-RADS system is best for risk stratification of thyroid nodules found on ultrasound, according to a Korean study published February 8 in the *American Journal of Roentgenology*.

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Diagnostic Performance of Six Ultrasound Risk Stratification Systems for Thyroid Nodules: A Systematic Review and Network Meta-Analysis

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ABSTRACT :

Please see the **Editorial Comment** by Luyao Shen discussing this article.

Background: Risk stratification systems for evaluating thyroid nodules on ultrasound use varying approaches to classify levels of suspicion for malignancy, leading to variable performance.

Objective: To perform a network meta-analysis comparing the diagnostic performance for detection of thyroid cancer of six risk stratification systems used to evaluate thyroid nodules on ultrasound.

Evidence Acquisition: Five bibliometric databases were searched for studies published through August 31, 2022 that compared at least two of six ultrasound risk stratification systems [American Association of Clinical Endocrinologists/American College of Endocrinology/Associazione Medici Endocrinologi (AACE/ACE/AME); American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS); American Thyroid Association (ATA); European Thyroid Association Thyroid Imaging Reporting and Data System (EU-TIRADS); Korean Thyroid Association/Korean Society of Thyroid Radiology Thyroid Imaging Reporting and Data System (K-TIRADS); Thyroid Imaging Reporting and Data System developed by Kwak et al. (Kwak TIRADS)], in terms of diagnostic performance for detection of thyroid cancer using a cytologic or histologic reference standard. Studies' risk of bias was evaluated using the Newcastle-Ottawa Scale. Meta-analysis was performed of each system to identify the risk category threshold having the highest accuracy as well as the sensitivity and specificity at this threshold. Network meta-analyses was used to perform hierarchical ranking and identify the systems having highest sensitivities and specificities at each system's most accurate threshold.

Evidence Synthesis: The analysis included 39 studies with 49,661 patients. All studies were of fair (n=17) or good (n=22) image quality. The most accurate risk category thresholds were class 3 (high risk) for AACE/ACE/AME, TR5 (highly suspicious) for ACR TI-RADS, EU-TIRADS 5 (high risk) for EU-TIRADS, 4c (moderate concern but not classic for malignancy) for Kwak TIRADS, K-TIRADS 5 (high suspicion) for K-TIRADS, and high suspicion for ATA. At these thresholds, the systems had sensitivity of 65–77% and specificity of 82–90%. Network meta-analysis identified highest sensitivity and highest specificity for ACR TI-RADS, followed by K-TIRADS.

Conclusion: ACR TI-RADS had the highest diagnostic performance among six risk stratification systems for thyroid nodules on ultrasound.

Clinical Impact: This network meta-analysis can inform decisions regarding implementation of the risk stratification systems and aid future system updates.

	EU-TIRADS	AACE/ACE/AME	ATA	Kwak TI-RADS	K-TI
Sensitivity	5%	20%	39%	67%	8
Specificity	8%	27%	33%	62%	7
Accuracy	14%	66%	30%	50%	6

Review Access to health care CPD

Pharmacologic prevention of migraine

Velina Tzankova MD, Werner J. Becker MD, Tommy L.H. Chan MBBS

■ Cite as: *CMAJ* 2023 February 6;195:E187-92. doi: 10.1503/cmaj.221607

See a related review article at www.cmaj.ca/lookup/doi/10.1503/cmaj.211969 and a first-person account of trying to access migraine treatment at www.cmaj.ca/lookup/doi/10.1503/cmaj.221783

Key points

- Oral medications traditionally used for the prevention of migraine and known to be effective include anti-epileptic, β-blocker, antihypertensive and antidepressant drugs.
- OnabotulinumtoxinA (Botox) injection is indicated for prevention in patients with chronic migraine, as it has very few drug interactions or systemic or long-term adverse effects; however, it must be administered by a trained provider.
- The newer calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs) specifically target migraine pathophysiology and are effective and safe treatment options particularly for patients who have contraindications to or have previously not responded to other therapies.
- Lifestyle changes, behavioural therapies and certain supplements can augment migraine prevention.

Table 1: Medications traditionally used for migraine prevention[6]

Drug	Drug class	Target daily dose	Canadian Headache Society	
			Levels of evidence*	Strength of recommendation†
Topiramate	Anti-epileptic	100 mg	High	Strong
Propranolol	β-blocker	80–160 mg	High	Strong
Metoprolol	β-blocker	100–200 mg	High	Strong
Amitriptyline	Antidepressant	10–100 mg	High	Strong
Nadolol	β-blocker	80–160 mg	Moderate	Strong
Candesartan	Angiotensin receptor blocker	16 mg	Moderate	Strong
Gabapentin‡	Antidepressant	1200–3600 mg	Moderate	Strong
Divalproex sodium	Anti-epileptic	500–1500 mg	High	Weak
Flunarizine	Calcium channel blocker	10 mg	High	Weak
Pizotifen	Serotonin antagonist	1.5–4.0 mg	High	Weak
Venlafaxine	Antidepressant	150 mg	Low	Weak
Lisinopril	Angiotensin-converting enzyme inhibitor	20 mg	Low	Weak
Verapamil	Calcium channel blocker	120–480 mg	Low	Weak
OnabotulinumtoxinA (chronic migraine only)	Neurotoxin	155–195 units	Not applicable	Not applicable

Box 1: Evidence used in this review

We conducted a targeted search of Google Scholar and PubMed to identify original research, review articles and clinical practice guidelines published through November of 2021, using search terms that included, but were not limited to, "migraine acute treatment," "migraine preventive treatment," "migraine CGRP monoclonal antibodies," "migraine 5-HT1F," "migraine behavioural treatments," and "migraine neuromodulation." We also consulted the most recent guidelines from the Canadian Headache Society and the American Headache Society, and the *International Classification of Headache Disorders, 3rd edition*.

Box 2: Unanswered questions

- How does the efficacy and safety of onabotulinumtoxinA compare with calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs)?
- What is the efficacy and safety of the concurrent use of gepants and CGRP mAbs with other drugs (e.g., CGRP mAbs and onabotulinumtoxin A; CGRP mAbs and gepants; triptans and gepants)?
- How safe are gepants and CGRP mAbs in specific populations such as older adults, patients with autoimmune diseases and those with moderate-to-high cardiovascular risk factors?
- What is the safety of CGRP mAbs when used for longer than 5 years?

ment choice is influenced by patient comorbidities, individual preferences, medication adverse effects and drug coverage. Medications should be started at a low dose and titrated slowly until the minimum effective or maximum tolerated dose is reached. An 8- to 12-week trial at a therapeutic dose is reasonable to determine efficacy. If a medication is ineffective, clinicians should consider a medication from a different drug class. Tapering the dose, and possibly stopping the medication, can be considered after an adequate treatment response has been maintained for 6–12 months.[3]

Patient involvement is crucial to a successful preventive treatment plan, which requires long-term commitment and careful adherence to treatment, as well as communication with their

ANNALS OF SURGERY

ORIGINAL ARTICLES

Low Preoperative Serum Creatinine is Common and Associated With Poor Outcomes After Nonemergent Inpatient Surgery

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Annals of Surgery 277(2):p 246-251, February 2023. | **DOI:** 10.1097/SLA.0000000000005760

Background:

The association between low creatinine and poor surgical outcomes is not well understood.

Methods:

We identified patients with creatinine in the 7 days preceding nonemergent inpatient surgery in the American College of Surgeons National Surgical Quality Improvement Program database from 2005 to 2020. Multivariable logistic regression was used to examine the association between creatinine and 30-day mortality and major complications.

Results:

Of 1,809,576 patients, 27.8% of males and 23.5% of females had low preoperative serum creatinine, 14.6% experienced complications, and 1.2% died. For males, compared with the reference creatinine of 0.85 to 1.04, those with serum creatinine ≤0.44 had 55% increased odds of mortality [adjusted odds ratio (aOR), 1.55; 95% CI, 1.29-1.86] and 82% increased odds of major complications (aOR, 1.82; 95% CI, 1.69-1.97). Similarly, for females, compared with the reference range of 0.65 to 0.84, those with serum creatinine ≤0.44 had 49% increased odds of mortality (aOR, 1.49; 95% CI, 1.32-1.67) and 76% increased odds of major complications (aOR, 1.76; 95% CI, 1.70-1.83). These associations persisted for the total cohort, among those with mildly low albumin, and for those with creatinine values measured 8 to 30 days preoperatively.

Conclusions:

A low preoperative creatinine is common and associated with poor outcomes after nonemergent inpatient surgery. A low creatinine may help identify high-risk patients who may benefit from further evaluation and optimization.

Original Article

Hepatology

Statin Use and Reduced Hepatocellular Carcinoma Risk in Patients With Nonalcoholic Fatty Liver Disease

Biyao Zou [*] [‡], Michelle C. Odden [‡], Mindie H. Nguyen [*] [‡]

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chemoprevention and treatment. Nonalcoholic fatty liver disease (NAFLD) is expected to become the leading cause of hepatocellular carcinoma (HCC). We aimed to investigate the association between statin initiation and the risk of HCC among patients with NAFLD.

Methods

In this study using the Optum de-identified Clinformatics database, Cox proportional hazards regression model was performed to determine the risk of HCC in statin initiators versus nonusers. We incorporated inverse probability of treatment weighting (IPTW) to minimize potential confounding.

Results

Among 272,431 adults with NAFLD diagnosis, IPTW model shows that statin initiators had 53% less risk of developing HCC compared with nonusers (hazard ratio [HR], 0.47; 95% confidence interval, 0.36–0.60). In the subcohort with fibrosis-4 index data available, statin initiation was associated with 56% hazard reduction of developing HCC in NAFLD after adjusting for fibrosis-4 index score (HR, 0.44; 0.30–0.65). The association between statin initiation and lower risk of HCC development was observed for both lipophilic statin (HR, 0.49; 0.37–0.65) and hydrophilic statin (HR, 0.40; 0.21–0.76). Moreover, we observed greater hazards reduction as the dose and duration of statin use increased. NAFLD patients with more than 600 cumulative defined daily doses of statin had 70% reduction in hazards of developing HCC (HR, 0.30; 0.20–0.43).

Conclusions

Our study provides strong evidence for the association between statin initiation and reduced risk of HCC development in NAFLD patients. These findings imply that statin can be used as a protective medication for NAFLD patients to reduce the risk of HCC.

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Gastroenterology

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Low Hepatitis B Core–Related Antigen Levels Correlate Higher Spontaneous Seroclearance of Hepatitis B Surface Antigen in Chronic Hepatitis B Patients With High Hepatitis B Surface Antigen Levels

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baseline were associated with an increased likelihood of HBsAg seroclearance (log rank $P < .001$). When restricting the study population to 1539 patients with HBsAg levels >1000 IU/mL, only HBcrAg <10,000 U/mL (vs ≥100,000 U/mL) served as an independent viral predictor for HBsAg seroclearance, with adjusted hazard ratio of 1.95 (95% CI, 1.16–3.27). In contrast to the late decline of HBsAg levels (5–9 years before HBsAg seroclearance), HBcrAg levels became undetectable 10–14 years before HBsAg seroclearance. This finding was confirmed by the different annual HBsAg seroclearance rates in the first and second decades of follow-up (0.97% vs 3.75%; $P < .001$) in patients achieving undetectable HBcrAg levels.

Conclusions

Lower serum HBcrAg levels were associated with increased probability of HBsAg seroclearance over time. In patients with HBsAg levels >1000 IU/mL, clearing HBcrAg may serve as an early biomarker for HBsAg seroclearance.

Stroke indicator found on MRI could help with treatment strategies

By Amerigo Allegretto, AuntMinnie.com staff writer

February 15, 2023 -- Percent insular ribbon infarction (PIRI) on MRI helps classify patients with slowly progressive stroke who could benefit from late-window endovascular thrombectomy (EVT), a study published February 15 in the *American Journal of Roentgenology* has found.

AJR American Journal of Roentgenology

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Percent Insular Ribbon Infarction for Predicting Infarct Growth Rate and 90-Day Outcomes in Large-Vessel Occlusive Stroke: Secondary Analysis of Prospective Clinical Trial Data

Robert W. Regenhardt, MD, PhD[a,b], Aneesh B. Singhal, MD[a], Julian He, MD[c], R. Gilberto Gonzalez, MD, PhD[c,d,e] ... Show all

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Background: Insight into the natural history of infarct growth could help identify patients with slowly progressing stroke who may benefit from delayed endovascular thrombectomy (EVT).

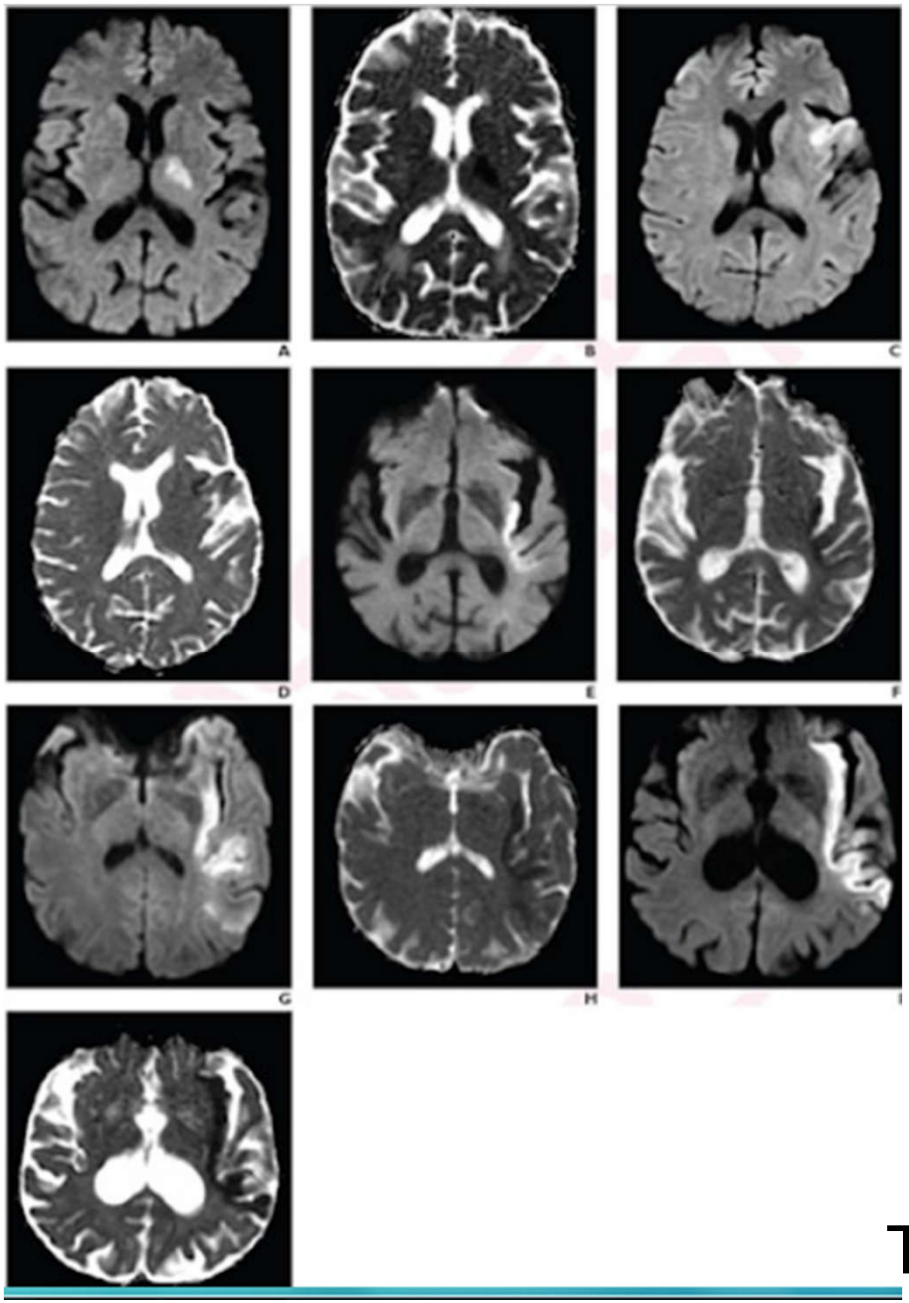
Objective: To evaluate associations of percent insular ribbon infarction (PIRI) with infarct growth rate (IGR) and 90-day outcomes in patients with large-vessel occlusion (LVO) stroke.

Methods: This retrospective study was a secondary analysis of a prior clinical trial that enrolled patients with acute stroke not treated with reperfusion therapies from January 2007 to June 2009. The present analysis evaluated 31 trial patients (median age, 71 years; 12 female, 19 male) with anterior-circulation LVO who underwent serial MRI examinations. Two neuroradiologists independently scored PIRI on presentation MRI examinations based on the ratio of the length of the portion of the insula showing restricted diffusion to the insula's total length using a previously described 0-4 scale; scores were categorized [mild (0-1), moderate (2), or severe (3-4)], and discrepancies were resolved by consensus. Ninety-day modified Rankin Scale (mRS) was obtained. As part of earlier clinical trial analysis, collateral pattern on CTA was classified (symmetric, malignant, other), and infarct volumes were measured on DWI during the initial 48 hours after presentation and on FLAIR at 90 days.

Results: Inter-rater agreement for PIRI category was strong (K=0.890). PIRI was mild in 10, moderate in 4, and severe in 17 patients. For mild, moderate, and severe PIRI, median onset-to-presentation IGR was 1.6, 8.5, and 17.5 cc/h ($p<.001$); median presentation-to-48-hour IGR was 0.3, 0.2, and 1.2 cc/h ($p=.005$); median 90-day infarct volume was 9.4, 39.8, and 108.6 cc ($p=0.01$); 90-day mRS ≤2 occurred in 78%, 67%, and 6% of patients ($p=.001$). In multivariable models controlling for age, ICA occlusion, and collateral pattern, PIRI category independently predicted onset-to-presentation IGR ($\beta=1.5$), presentation-to-48-hour IGR ($\beta=1.3$), and 90-day mRS ≤2 (OR=0.2). For predicting 90-day mRS ≤2, mild-to-moderate PIRI had sensitivity of 90.0% and specificity of 84.2%; symmetric collateral pattern had sensitivity of 70.0% and specificity of 73.7%.

Conclusion: PIRI was independently associated with IGR and 90-day outcome.

Clinical Impact: PIRI may help identify patients who could benefit from late-window EVT when requiring transfer to EVT-



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