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Original Article

Surveillance Imaging and GAAD/GALAD Scores for Detection of Hepatocellular Carcinoma in Patients with Chronic Hepatitis

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Abstract

Background and Aims: Early detection of hepatocellular carcinoma (HCC) is crucial for improving survival in patients with chronic hepatitis. The GALAD algorithm combines gender (biological sex), age, α-fetoprotein (AFP), *Lens culinaris* agglutinin-reactive fraction of AFP (AFP-L3), and protein induced by vitamin K absence or antagonist-II (PIVKA-II) for HCC detection. Similarly, the GAAD algorithm incorporates gender (biological sex), age, AFP, and PIVKA-II. This study aimed to assess the clinical utility of AFP-L3 in the GALAD algorithm and its potential synergies with ultrasound. We compared the clinical performance of GALAD with GAAD; AFP; AFP-L3; and PIVKA-II, with or without ultrasound, in Taiwanese adults. ***Methods:*** A total of 439 serum samples were analyzed using a Cobas® e 601 analyzer (healthy controls, n = 200; chronic liver disease controls, n = 177; HCC cases, n = 62). Performance was assessed through receiver operating characteristic curve analyses to calculate the area under the curve. ***Results:*** The area under the curve for differentiating early-stage HCC from patients with chronic liver disease was optimal for PIVKA-II (84.9%), GAAD (79.8%), and GALAD (79.4%), with slightly improved performance for detecting all-stage HCC. Clinical performance was unaffected by disease stage or etiology. Sensitivity for early-stage HCC was highest for GAAD (57.6%) and GALAD (57.6%). Sensitivity for each strategy was further enhanced when combined with ultrasound, regardless of disease stage or etiology ($P < 0.01$). ***Conclusions:*** These findings indicate that the role of AFP-L3 in the GALAD algorithm is minimal, supporting the use of GAAD for HCC detection. A combination of GAAD, GALAD, or PIVKA-II with ultrasound may improve diagnostic efficiency compared with recommended strategies.

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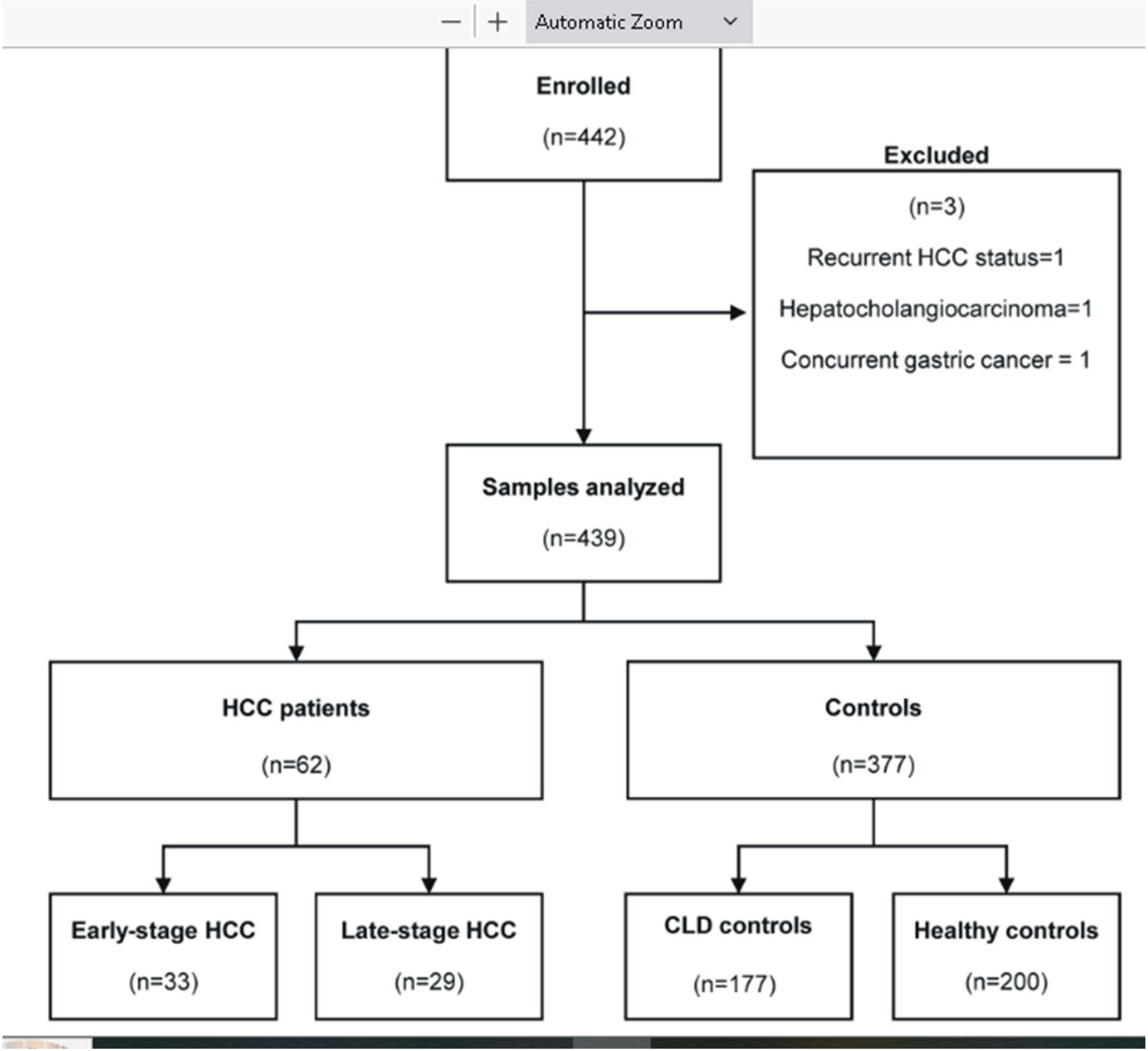
Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer and the second most common cause of cancer-related death in Asia.[1] In 2020, there were approximately 609,596 new cases of liver cancer in Asia, with an age-standardized rate of 11.6 per 100,000 persons.[1] Taiwan alone reported 10,988 new cases in 2020,[2] equating to nearly 30 people receiving a diagnosis of liver cancer daily.[2] HCC is often associated with cirrhosis caused by hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, particularly in Asia.[3,4] For example, in Taiwan, between 2011 and 2019, viral hepatitis-induced HCC accounted for 78.7% of all HCC cases in males and 70.5% in females.[5]


Automatic Zoom
Enrolled
(n=442)
Excluded
(n=3)
Recurrent HCC status=1
Hepatocholangiocarcinoma=1
Concurrent gastric cancer = 1
Samples analyzed
(n=439)
HCC patients
(n=62)
Controls
(n=377)
Early-stage HCC
(n=33)
Late-stage HCC
(n=29)
CLD controls
(n=177)
Healthy controls
(n=200)

AFP for HCC screening in cohorts from the UK, Switzerland, and China.[32–34]

A limitation of our study is that the enrolled patients were not matched for age or gender, resulting in an older, predominantly male cohort. However, this population was intended for HCC surveillance, and our study aimed to reflect the real-world population that would undergo HCC surveillance in Taiwan. The issue of age and gender bias in the GAAD algorithm has been investigated previously.[21] After performing several simulations to address this bias between HCC cases and CLD controls for the GAAD score, the study found that results remained stable when cases were matched across all investigated sample sizes. Further validation through larger phase 3/4 case-matched studies is required to assess the benefit-

Research Letter

September 19, 2024

Transperineal vs Transrectal Prostate Biopsy—The PREVENT Randomized Clinical Trial

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(Prostate Imaging Reporting and Data System [PI-RADS] score ≥3 or ≥4) for biopsy indication.

Results Data were synthesized from 80 114 men from 12 studies. Compared with standard PSA-based screening, the MRI pathway (sequential screening, PI-RADS score ≥3 cutoff for biopsy) was associated with higher odds of csPCa when tests results were positive (OR, 4.15; 95% CI, 2.93-5.88; $P \leq .001$), decreased odds of biopsies (OR, 0.28; 95% CI, 0.22-0.36; $P \leq .001$), and insignificant cancers detected (OR, 0.34; 95% CI, 0.23-0.49; $P = .002$) without significant differences in the detection of csPCa (OR, 1.02; 95% CI, 0.75-1.37; $P = .86$). Implementing a PI-RADS score of 4 or greater threshold for biopsy selection was associated with a further reduction in the odds of detecting insignificant PCa (OR, 0.23; 95% CI, 0.05-0.97; $P = .048$) and biopsies performed (OR, 0.19; 95% CI, 0.09-0.38; $P = .01$) without differences in csPCa detection (OR, 0.85; 95% CI, 0.49-1.45; $P = .22$).

Conclusion and relevance The results of this systematic review and meta-analysis suggest that integrating MRI in PCa screening pathways is associated with a reduced number of unnecessary biopsies and overdiagnosis of insignificant PCa while maintaining csPCa detection as compared with PSA-only screening.

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JGHF Journal of Gastroenterology and Hepatology Foundation

Original Article - Hepatology (Clinical)

Cirrhosis in primary practice: many patients remain potentially undiagnosed and are not receiving liver cancer surveillance

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were reviewed to identify outcomes of interest.

Results

One hundred seventy-one patients with confirmed cirrhosis across nine general practices were identified (74% male, mean age: 61.2 years). There was significant variation in the rate of cirrhosis diagnosis between practices (range 31.7–637.9 per 100 000 patients, $P < 0.0001$). Patients with cirrhosis had predominately compensated disease (75% Child–Pugh A) and common etiologies of cirrhosis were alcohol (49%), hepatitis C (47%), and metabolic dysfunction-associated steatotic liver disease (29%). Forty-two patients (25%) had received appropriate HCC surveillance. Predictors of inadequate HCC surveillance were time from last specialist correspondence (odds ratio [OR] = 1.06 per month increase, 95% confidence interval [CI]: 1.02–1.10, $P = 0.002$) and hepatitis B (OR = 0.24, 95% CI: 0.06–0.98, $P = 0.047$). Specialist correspondence with primary care was older than 2 years or absent in 37% of cases.

Conclusions

There was a 20-fold difference in the rate of cirrhosis diagnosis between general practices within Sydney, suggesting a large proportion of patients remain undiagnosed. Three quarters of patients with diagnosed cirrhosis are not receiving appropriate HCC surveillance.

Commentary

Time to step into better heart failure therapy

Jonathan Howlett MD

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See related research at www.cmaj.ca/lookup/doi/10.1503/cmaj.240116.

In this issue of *CMAJ*, Van and colleagues present a cost–utility analysis of several different strategies for introduction of guideline-directed medical therapy (GDMT) to patients with heart failure.[1] This well-executed study shows the potential of simultaneous initiation of 3–4 drugs used to treat heart failure to improve outcomes at an attractive cost. I discuss why these findings are important and next steps for evidence generation and health-system readiness.

Heart failure is an increasingly common and fatal disease and causes a heavy patient, health care–system, and cost burden.[2] Approximately half of all heart failure is due to poor left ventricular systolic function (heart failure with reduced ejection fraction [HFrEF]), which in past years carried a median survival less than 5 years after diagnosis. Fortunately, management of this condition has undergone a revolution. Currently, optimal therapy includes 4 classes of disease-modifying drugs (β adrenergic receptor blockers, angiotensin receptor–neprilysin inhibitors, mineralocorticoid receptor antagonists, and sodium–glucose cotransporter-2 inhibitors [SGLT2Is]), which have dramatically improved prognosis.[3] Recently, an analysis of several landmark randomized controlled trials (RCTs) confirmed that initial inclusion of all 4 drug classes, now termed GDMT, reduces 2-year mortality in patients with HFrEF from 35% to 10%, a 73% risk reduction[4] compared with a diuretic alone. However, little guidance for clinicians (apart from expert opinion) exists as to the best manner to achieve GDMT.[5,6]

As a result, clinical practice has mirrored the approach taken in clinical trials — adding medications to background therapy 1 at a time, titrating to target or tolerated doses before repeating the process with the next medication. Data from registries of

Key points

- Heart failure is an increasingly common and fatal disease and causes a heavy patient, health care–system, and cost burden.
- A cost-effectiveness study looking at different scenarios of achieving optimal treatment for patients with heart failure — that is, 4 classes of disease-modifying drugs — found that more aggressive drug-titration strategies offered the largest gains in quality-adjusted life years.
- Further work is to identify patient profiles that require tailored approaches to titration.
- Implementation of simultaneous initiation of heart failure therapy should include use of titration aids and expanded practice models, and they should focus on safety, tolerability, and efficiency.

ively deliver optimal GDMT to patients with HFrEF.

Owing to the large number of patients with heart failure, widespread implementation of rapid sequence therapy would require changes in health care delivery. Randomized controlled trials should now focus on addressing the manner in which to initiate GDMT and the implementation of successful strategies. Factors to consider include simultaneous drug administration, titration aids and technology, and identification of patients who are not suitable for aggressive strategies.[12] Valuable human resources such as nurses and pharmacists remain underused and should be included in this research. In today's reality of limited health care resources, evaluation of the relative cost benefits of newly developed treatment strategies will help shape future practice, leading to better care for patients with heart failure.

Original Research | Breast Imaging | October 23, 2024

Automated Breast Ultrasound With Remote Reading for Primary Breast Cancer Screening: A Prospective Study Involving 46 Community Health Centers in China

Authors: Xiaozhi Dang, M.B., Yi Gao, Ph.D., Yan Ju, M.S., Xiaojie Yuan, Ph.D., Huan Lin, M.D., Yi Ren, M.D., Yao Xiao, M.B., Rui Shu, M.M., Xiang Gu, M.B., Wo
Kyung Moon, M.D., Ph.D., and Hongping Song, M.D., Ph.D. | AUTHOR INFO & AFFILIATIONS

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Results: The final analysis included 5978 enrolled participants (median age, 46 years [IQR 40-52 years]) who underwent screening ABUS at the community health centers with subsequent remote reading. A total of 24 ABUS-detected cancers and two interval cancers were diagnosed. The cancer detection rate was 4.0 per 1000 women (95% CI: 2.7–5.9), and the AIR was 11.9% (95% CI: 11.1–12.7). A total of 95.8% (23/24) of ABUS-detected cancers were invasive. The 23 invasive cancers had a median diameter of 10.0 mm; 73.9% (17/23) were node-negative. Sensitivity was 92.3% (95% CI: 75.9–97.9), and specificity was 88.4% (95% CI: 87.6–89.2). The biopsy rate was 1.7% (95% CI: 1.4–2.0), and the PPV of biopsy was 24.0% (95% CI: 16.7–33.2).

Conclusion: ABUS screening with remote reading met benchmark performance for cancer detection in comparison to mammography, with infrequent interval cancers.

Clinical Impact: ABUS with remote reading holds promise in enhancing access to breast cancer screening and early detection in low-resource settings or underserved regions where mammographic screening is not established.

THE END