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After PSA screening, MRI-targeted vs. systematic biopsy detected fewer clinically insignificant prostate cancers

magnetic resonance imaging (MRI) of the prostate, one third of the participants were randomly assigned to a reference group that underwent systematic biopsy as well as targeted biopsy of suspicious lesions shown on MRI. The remaining participants were assigned to the experimental group and underwent MRI-targeted biopsy only. The primary outcome was clinically insignificant prostate cancer, defined as a Gleason score of 3+3. The secondary outcome was clinically significant prostate cancer, defined as a Gleason score of at least 3+4. Safety was also assessed.

Results: Of the men who were invited to undergo screening, 17,980 (47%) participated in the trial. A total of 66 of the 11,986 participants in the experimental group (0.6%) received a diagnosis of clinically insignificant prostate cancer, as compared with 72 of 5994 participants (1.2%) in the reference group, a difference of -0.7 percentage points (95% confidence interval [CI], -1.0 to -0.4; relative risk, 0.46; 95% CI, 0.33 to 0.64; P<0.001). The relative risk of clinically significant prostate cancer in the experimental group as compared with the reference group was 0.81 (95% CI, 0.60 to 1.1). Clinically significant cancer that was detected only by systematic biopsy was diagnosed in 10 participants in the reference group; all cases were of intermediate risk and involved mainly low-volume disease that was managed with active surveillance. Serious adverse events were rare (<0.1%) in the two groups.

Conclusions: The avoidance of systematic biopsy in favor of MRI-directed targeted biopsy for screening and early detection in persons with elevated PSA levels reduced the risk of overdiagnosis by half at the cost of delaying detection of intermediate-risk tumors in a small proportion of patients. (Funded by Karin and Christer Johansson's Foundation and others; GÖTEBORG-2 ISRCTN Registry number, ISRCTN94604465.).

Dietary sugar consumption and health: umbrella review

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ABSTRACT

OBJECTIVE

To evaluate the quality of evidence, potential biases, and validity of all available studies on dietary sugar consumption and health outcomes.

DESIGN

Umbrella review of existing meta-analyses.

DATA SOURCES

PubMed, Embase, Web of Science, Cochrane Database of Systematic Reviews, and hand searching of reference lists.

INCLUSION CRITERIA

Systematic reviews and meta-analyses of randomised controlled trials, cohort studies, case-control studies, or cross sectional studies that evaluated the effect of dietary sugar consumption on any health outcomes in humans free from acute or chronic diseases.

RESULTS

The search identified 73 meta-analyses and 83 health outcomes from 8601 unique articles, including 74 unique outcomes in meta-analyses of observational

of sugar sweetened beverage consumption was associated with a 4% higher risk of gout (class III evidence) and each 250 mL/day increment of sugar sweetened beverage consumption was associated with a 17% and 4% higher risk of coronary heart disease (class II evidence) and all cause mortality (class III evidence), respectively. In addition, low quality evidence suggested that every 25 g/day increment of fructose consumption was associated with a 22% higher risk of pancreatic cancer (class III evidence).

CONCLUSIONS

High dietary sugar consumption is generally more harmful than beneficial for health, especially in cardiometabolic disease. Reducing the consumption of free sugars or added sugars to below 25 g/day (approximately 6 teaspoons/day) and limiting the consumption of sugar sweetened beverages to less than one serving/week (approximately 200-355 mL/week) are recommended to reduce the adverse effect of sugars on health.

SYSTEMATIC REVIEW REGISTRATION

WHAT IS ALREADY KNOWN ON THIS TOPIC

Sugar consumption could have negative effects on health, especially obesity, diabetes, cardiovascular disease, hyperuricaemia, gout, ectopic fatty accumulation, dental caries, and some cancers

Deficiencies in study design, varying measurements, inconsistent findings, and different definitions of exposure make drawing final conclusions on associations difficult

Comprehensive evaluation of the quality of existing evidence on the associations of sugar consumption with all health outcomes is needed

WHAT THIS STUDY ADDS

High dietary sugar consumption is generally more harmful than beneficial for health, especially in cardiometabolic disease

Evidence of the association between dietary sugar consumption and cancer remains limited but warrants further research

Existing evidence is mostly observational and of low quality, and further randomised controlled trials are needed

of type 2 diabetes mellitus.

Conclusions and recommendations

This umbrella review shows that high dietary sugar consumption, especially intake of sugars that contain fructose, is harmfully associated with large numbers of health outcomes. Evidence for the harmful associations between dietary sugar consumption and changes in body weight (sugar sweetened beverages), ectopic fat accumulation (added sugars), obesity in children (sugar sweetened beverages), coronary heart disease (sugar sweetened beverages), and depression (sugar sweetened beverages) seems to be more reliable than that for other outcomes. Evidence of the association between dietary sugar consumption and cancer remains limited but warrants further research. In combination with the WHO and WCRF/AICR recommendations and our findings, we recommend reducing the consumption of free sugars or added sugars to below 25 g/day (approximately six teaspoons a day) and limiting the consumption of sugar sweetened beverages to less than one serving a week (approximately 200-355 mL/week).[38 119] To change sugar consumption patterns, especially for children and adolescents, a combination of widespread public health education and policies worldwide is urgently needed.

CLINICAL IMAGING

BREAST IMAGING | ARTICLES IN PRESS

To scan or not to scan: effect of scanning the axilla of all patients undergoing diagnostic breast ultrasound

Iris Chen • Aleksandar Kitich • Melissa Joines • ... Jane Dascalos • Anne Hoyt • Hannah

Show all authors

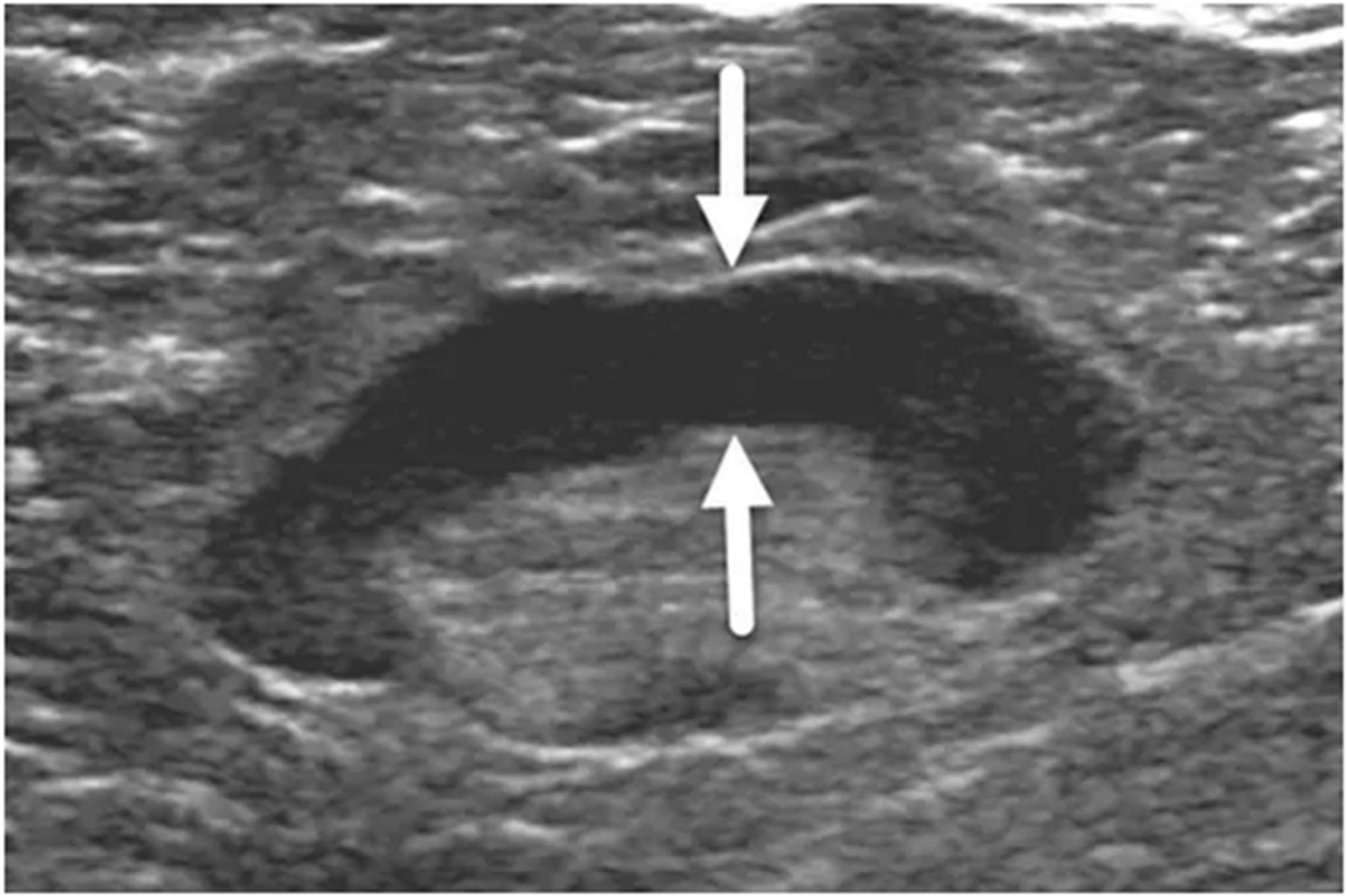
the axilla. Descriptive statistics were performed with a 5% level of significance.

Results

Of the 19,695 diagnostic ultrasounds performed during this timeframe, there were 91 (0.5%) incidental axillary findings given a BIRADS category 3 or 4, and none of these findings resulted in the diagnosis of an occult breast cancer. One biopsy-proven SLL/CLL lymphoma was diagnosed that was otherwise clinically occult.

Conclusion

Routine axillary scanning in all patients undergoing a diagnostic breast ultrasound at a large multi-site institution yields a low rate of incidental findings and has minimal impact on detection of cancer.



Experts recently questioned the necessity of scanning the axilla region during diagnostic breast ultrasound, as new data indicate that it is minimally beneficial for cancer detection.

World Journal of Hepatology

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ORIGINAL ARTICLE

Retrospective Cohort Study

Adherence to guideline-directed hepatocellular carcinoma screening: A single-center US experience

William W King, Raymond Richhart, Tyler Culpepper, Maneola Mota, Debdeep Banerjee, Media Ismael, Joydeep Chakraborty, Michael Ladna, Walid Khan, Nicole Ruiz, Jake Wilson, Ellery Altshuler, Virginia Clark, Roniel Cabrera

uary 21, 2023
February 21, 2023
e: March 27, 2023

METHODS

The authors identified patients with cirrhosis seen in a subspecialty hepatology clinic and determined whether they underwent appropriate screening, defined as two cross-sectional images between five and seven months apart. The authors characterized the primary driver of screening failure. Finally, other hepatologists were surveyed to determine provider perceptions of screening failure causes.

RESULTS

1034 patients were identified with an average age of 61 years and a mean MELD of 8.1 ± 3.8. Hepatitis C virus was the most common cirrhosis etiology. 489 (47%) underwent appropriate screening. No demographic or clinical differences were detected between those who underwent appropriate screening and those who did

not. The most common etiologies of screening failure, in descending order, were: radiology unable to schedule timely imaging, provider did not order imaging, patient canceled follow up appointment, appointments scheduled too far apart, lost to follow up, no-show to radiology appointment, and provider canceled appointment. Hepatologists surveyed believed the most common cause of screening failure was no-show to radiology.

CONCLUSION

Rates of screening were poor even in a subspecialty hepatology clinic. Screening failure was mostly due to systemic factors such as radiology availability and time between hepatology appointments rather than individual error.

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CLINICAL and MOLECULAR HEPATOLOGY

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Review

Neuropilins as potential biomarkers in hepatocellular carcinoma: a systematic review of basic and clinical implications

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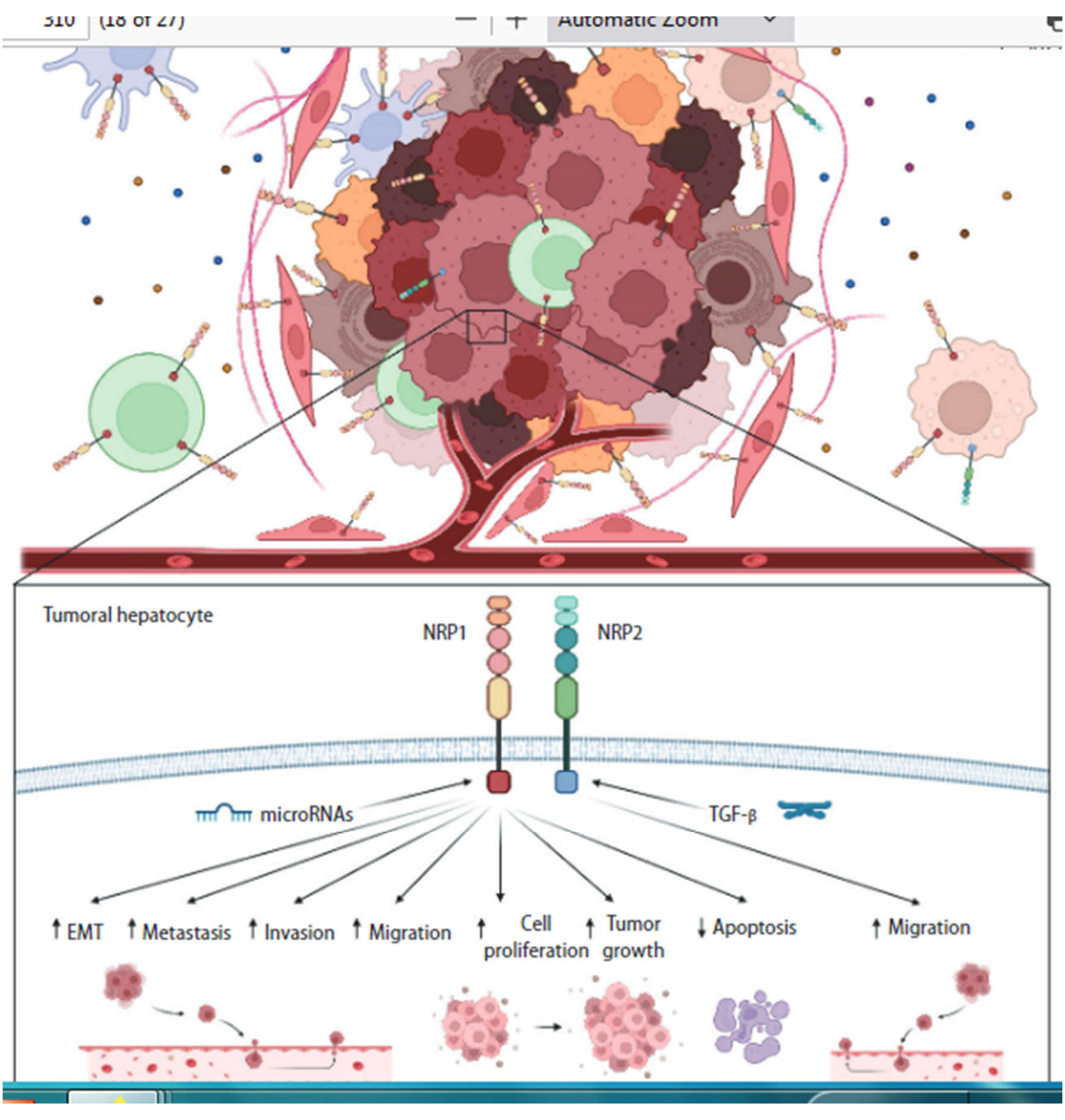
Hepatocellular carcinoma (HCC) is one of the most common and deadly cancers worldwide and is characterized by complex molecular carcinogenesis. Neuropilins (NRPs) NRP1 and NRP2 are the receptors of multiple proteins involved in key signaling pathways associated with tumor progression. We aimed to systematically review all the available findings on their role in HCC. We searched the Scopus, Web of Science (WOS), PubMed, Cochrane and Embase databases for articles evaluating NRPs in preclinical or clinical HCC models. This study was registered in PROSPERO (CRD42022349774) and include 49 studies. Multiple cellular and molecular processes have been associated with one or both NRPs, indicating that they are potential diagnostic and prognostic biomarkers in HCC patients. Mainly NRP1 has been shown to promote tumor cell survival and progression by modulating several signaling pathways. NRPs mainly regulate angiogenesis, invasion and migration and have shown to induce invasion and metastasis. They also regulate the immune response and tumor microenvironment, showing a crucial interplay with the hypoxia response and microRNAs in HCC. Altogether, NRP1 and NRP2 are potential biomarkers and therapeutic targets, providing novel insight into the clinical landscape of HCC patients. **(Clin Mol Hepatol 2023;29:293-319)**

Keywords: Biomarker; Hepatocellular carcinoma; Neuropilins; Systematic review


Tumoral hepatocyte
NRP1
NRP2
microRNAs
TGF-β
↑ EMT
↑ Metastasis
↑ Invasion
↑ Migration
↑ Cell proliferation
↑ Tumor growth
↓ Apoptosis
↑ Migration

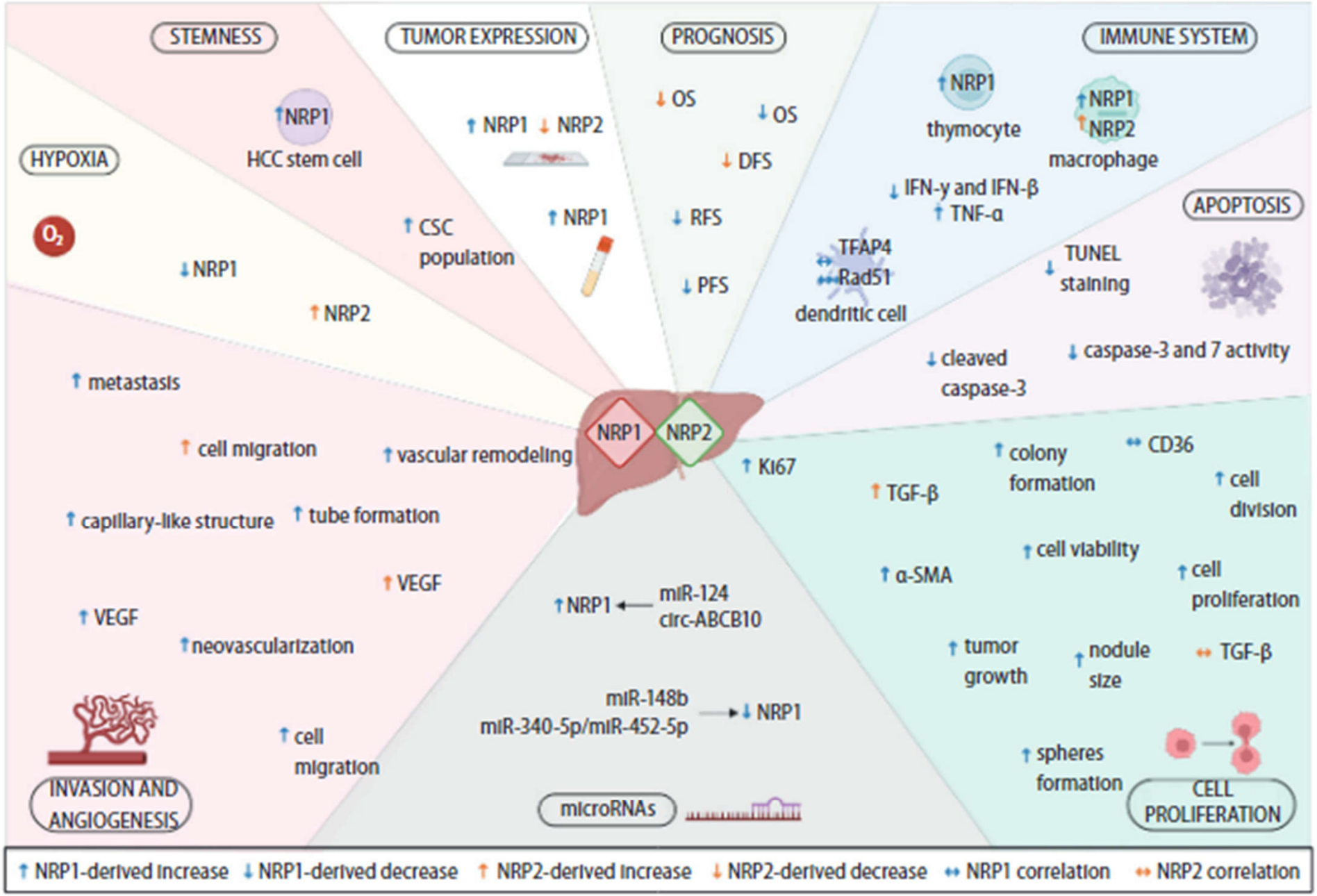


Figure 3. Main findings from the studies included in this systematic review describing modulatory effects associated to NRP1 and NRP2 in HCC. Specific modulatory effects exerted by both NRPs are graphically shown, together with correlations observed in different cellular processes and molecular mechanisms. α-SMA, α smooth muscle actin; CSC, cancer stem cell; DFS, disease-free survival; IFN-β, interferon beta; IFN-γ, interferon gamma; OS, overall survival; PFS, progression-free survival; RFS, recurrence-free survival; TFAP4, transcription factor activating enhancer binding protein 4; TGF-β, transforming growth factor beta; TNF-α, tumoral necrosis factor-α; VEGF, vascular endothelial growth factor.

CONCLUSIONS AND FUTURE PERSPECTIVES

To the best of our knowledge, this article is the first systematic review focusing on the role of NRPs in HCC, summarizing all the results obtained from preclinical and clinical studies (Fig. 3). Increasing evidence suggests vital roles for these receptors (NRP1 and NRP2) in tumor-associated processes. The results summarized here suggest that NRP1 could act as a potential diagnostic biomarker and, with NRP2, an interesting prognostic biomarker in HCC patients. The NRPs have modulatory effects on different signaling pathways that promote tumor progression and are crucial mediators of the HCC cell invasion and migration abilities. The tumor-associated immune response is also strongly associated with NRPs, mainly NRP1, and the tumor microenvironment, in which different tumor cell populations have higher NRP1 levels. The interplay between miRNAs and NRPs has gained interest since several miRNAs directly modulate NPR1, restraining tumor cell proliferation. In summary, NRPs appear to have critical roles in various processes involved in tumor development and progression, suggesting the potential of both, but mainly NRP1, as tumor biomarkers and potential targets for improving the HCC patient outcomes.

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Review

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Clinical and Molecular Hepatology 2023;29:263-276

The role of different viral biomarkers on the management of chronic hepatitis B

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Chronic hepatitis B infection is a major public health challenge. With the advancement in technology, various components of the viral cycle can now be measured in the blood to assess viral activity. In this review article, we summarize the relevant data of how antiviral therapies impact viral biomarkers, and discuss their potential implications. Viral nucleic acids including hepatitis B virus (HBV) double-stranded deoxy-ribonucleic acid (DNA) and to a lesser extent, pre-genomic RNA, are readily suppressed by nucleos(t)ide analogues (NUCs). The primary role of these markers include risk prediction for hepatocellular carcinoma (HCC) and risk stratification for partial cure, defined as off-therapy virological control, or functional cure, defined as hepatitis B surface antigen (HBsAg) seroclearance plus undetectable serum HBV DNA for ≥6 months. Viral translational products including hepatitis e antigen, quantitative HBsAg and hepatitis B core-related antigen can be reduced by NUCs and pegylated interferon a. They are important in defining disease phase, delineating treatment endpoints, and predicting clinical outcomes including HCC risk and partial/ functional cure. As the primary outcome of phase III trials in chronic hepatitis B is set as HBsAg seroclearance, appropriate viral biomarkers can potentially inform the efficacy of novel compounds. Early viral biomarker response can help with prioritization of subjects into clinical trials. However, standardization and validation studies would be crucial before viral biomarkers can be broadly implemented in clinical use. **(Clin Mol Hepatol 2023;29:263-276)**

Keywords: Chronic hepatitis B; Hepatitis B core antigen; Viremia; Treatment outcome

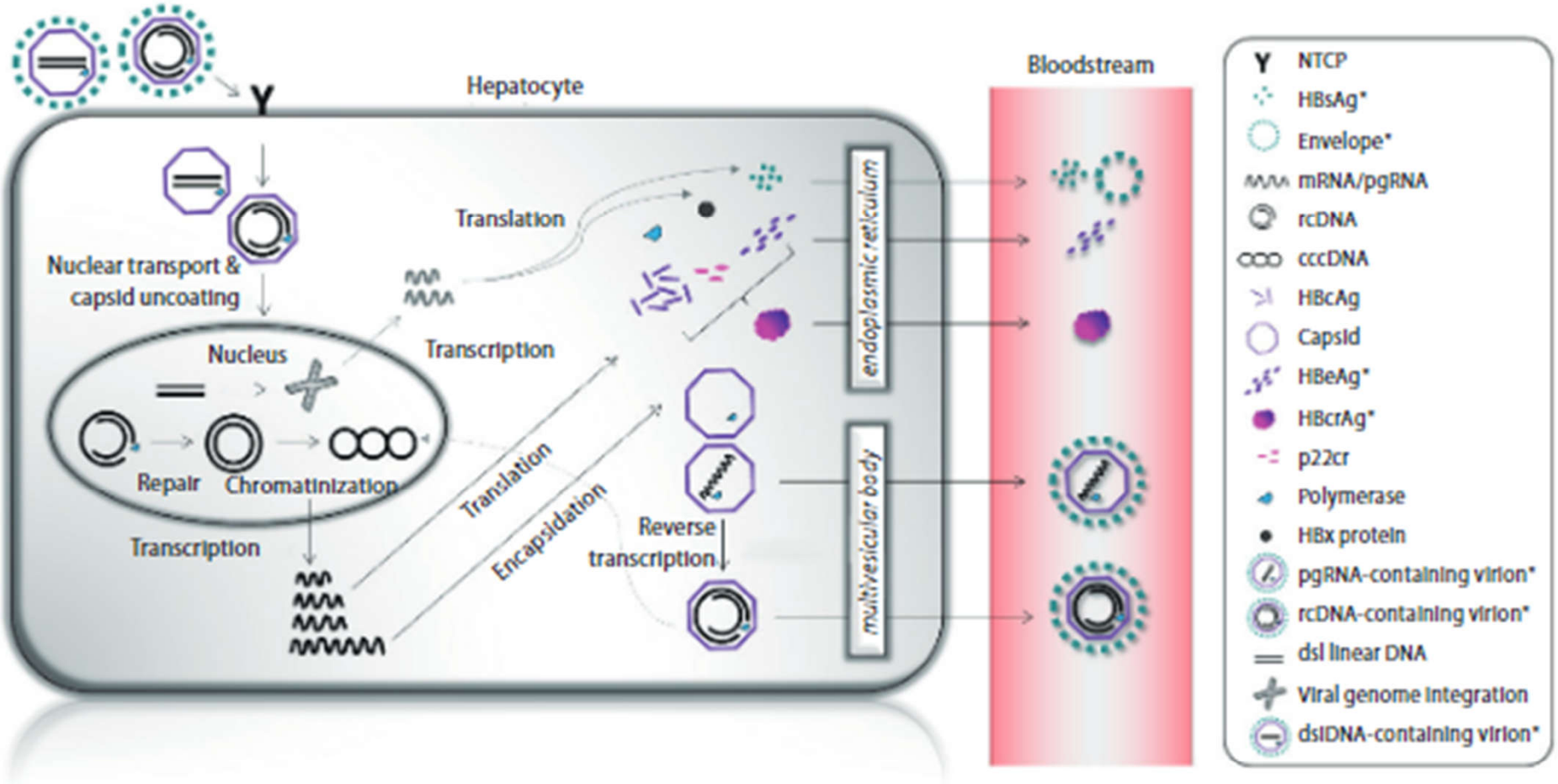

Figure 1. Viral cycle of hepatitis B virus. Those highlighted in asterisks are detectable in the bloodstream and can be used as viral biomarkers. These include HBsAg, HBeAg, HBcrAg, HBV DNA and pgRNA. cccDNA, covalently closed circular DNA; dslDNA, double-stranded linear DNA; HBV, hepatitis B virus; HBcAg, hepatitis core antigen; HBcrAg, hepatitis B core related antigen; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; mRNA, messenger RNA; NTCP, sodium taurocholate co-transporting polypeptide; pgRNA, pre-genomic RNA; rcDNA, relaxed circular DNA. *Detectable in the bloodstream.

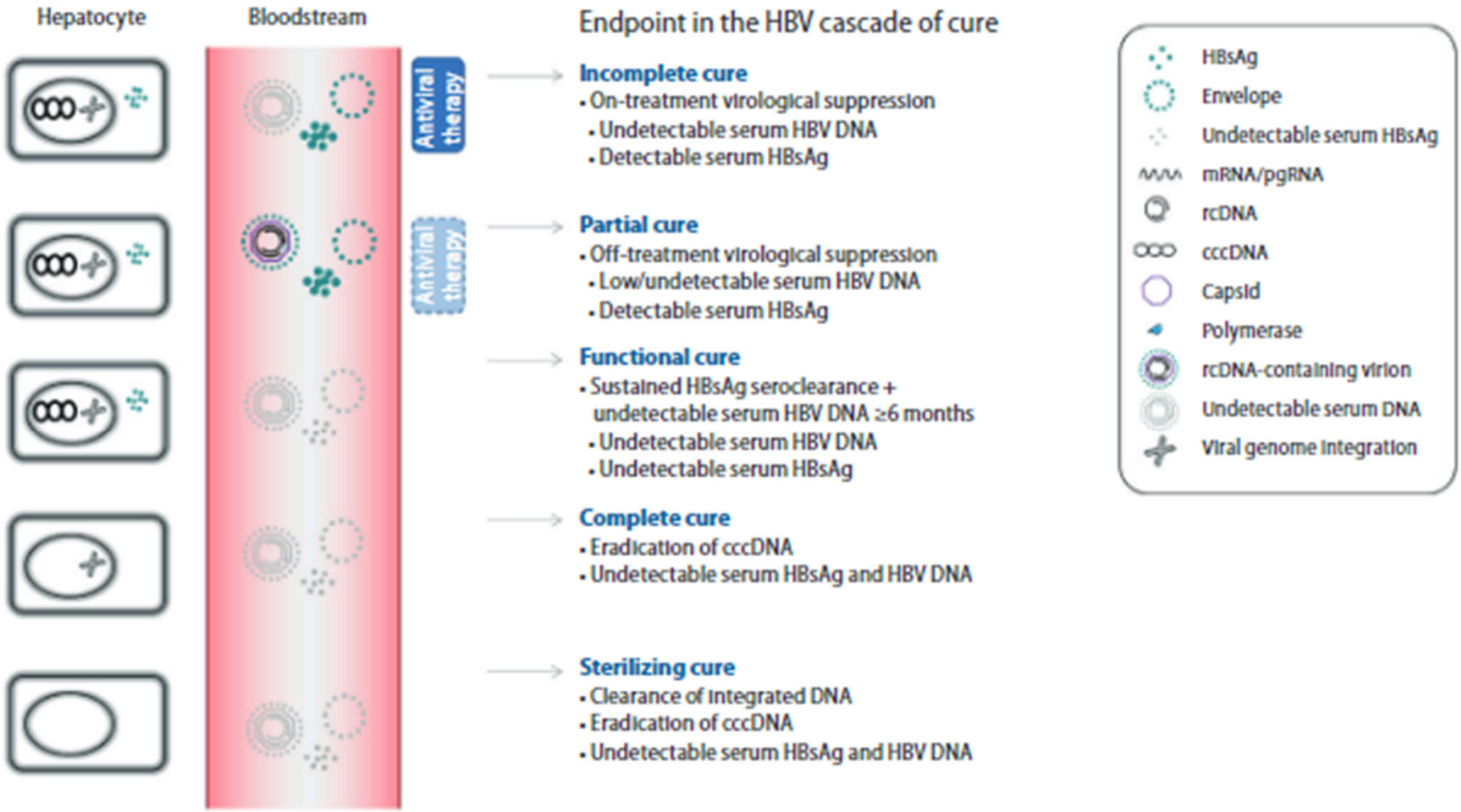

Figure 2. Treatment endpoints in the cascade of cure in chronic hepatitis B infection. cccDNA, covalently closed circular DNA; HBsAg, hepatitis B surface antigen; mRNA, messenger RNA; pgRNA, pre-genomic RNA; rcDNA, relaxed circular DNA; HBV, hepatitis B virus; DNA, double-stranded deoxy-ribonucleic acid.

CONCLUSION

Viral biomarker assessment is indispensable in clinical management and through the journey of novel drug discovery in the field of CHB. In the current era with highly effective NUC therapy as the mainstay of treatment, HBV DNA will be expectedly undetectable and novel transcriptional (HBV RNA) and translational markers (qHBsAg and HBcrAg) can provide further insights into treatment efficacy. Emerging data suggests these viral biomarkers can aid treatment decision, risk stratification for HCC and risk prediction for partial cure/functional cure. As the primary outcome of phase III trials is set on functional cure, viral biomarkers can potentially inform the efficacy of novel compounds or treatment approaches in the early course of treatment, and help with prioritization of subjects into clinical trials. Importantly, standardization and validation studies are necessary before viral biomarkers can be broadly implemented in clinical use. The role of viral biomarkers needs to be further explored to pave the way into elimination of viral hepatitis B.

THE END