ORIGINAL ARTICLE

Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only

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December 8, 2022

BACKGROUND Screening for prostate cancer is burdened by a high rate of overdiagnosis. The most appropriate algorithm for population-based screening is unknown.

METHODS We invited 37,887 men who were 50 to 60 years of age to undergo regular prostate-specific antigen (PSA) screening. Participants with a PSA level of 3 ng per milliliter or higher underwent 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.

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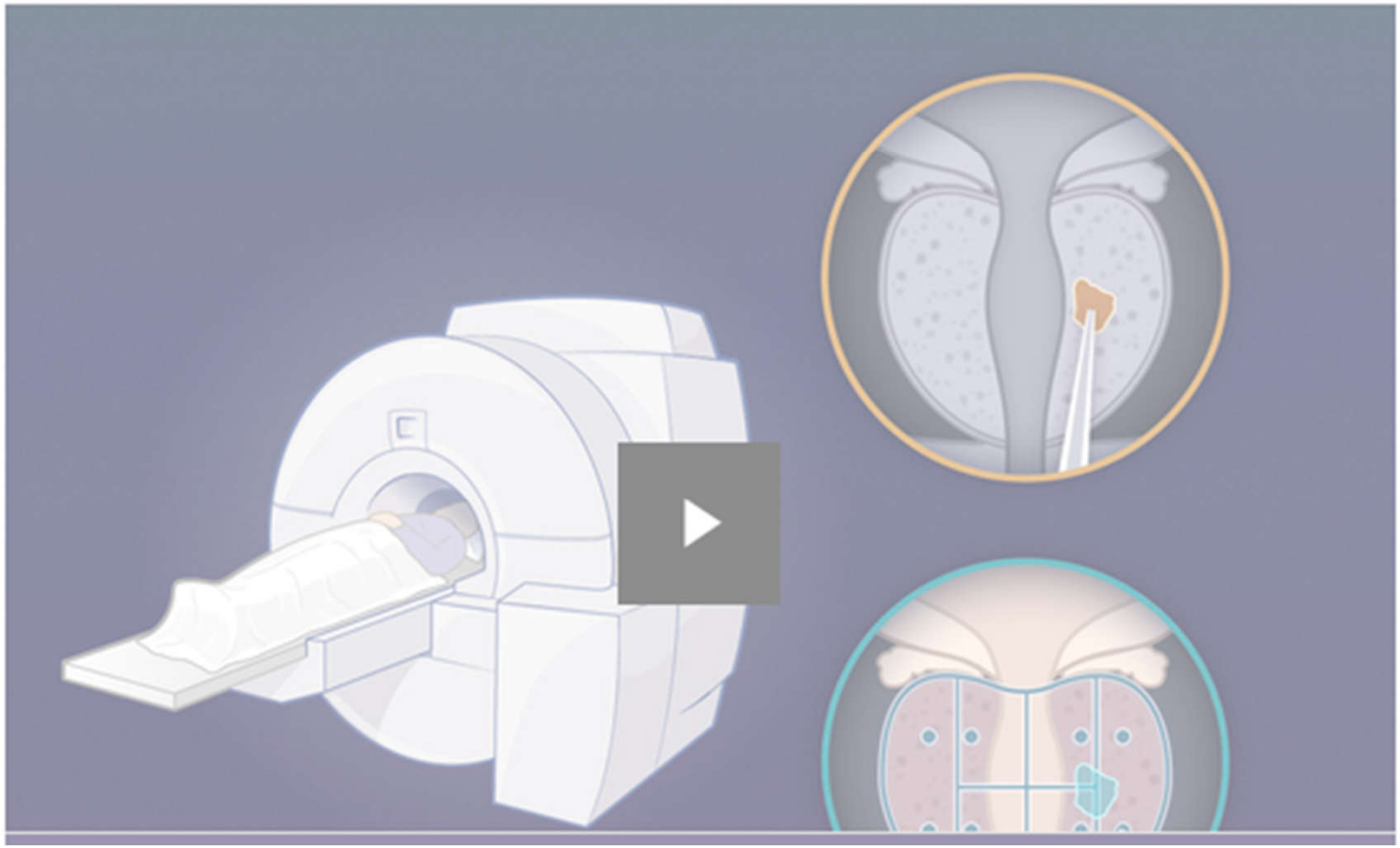
Omitting Systematic Biopsy in Prostate Cancer Screening



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Figures/Media

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.)

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RESEARCH Open Access

Comprehensive analysis of the differences between left- and right-side colorectal cancer and respective prognostic prediction

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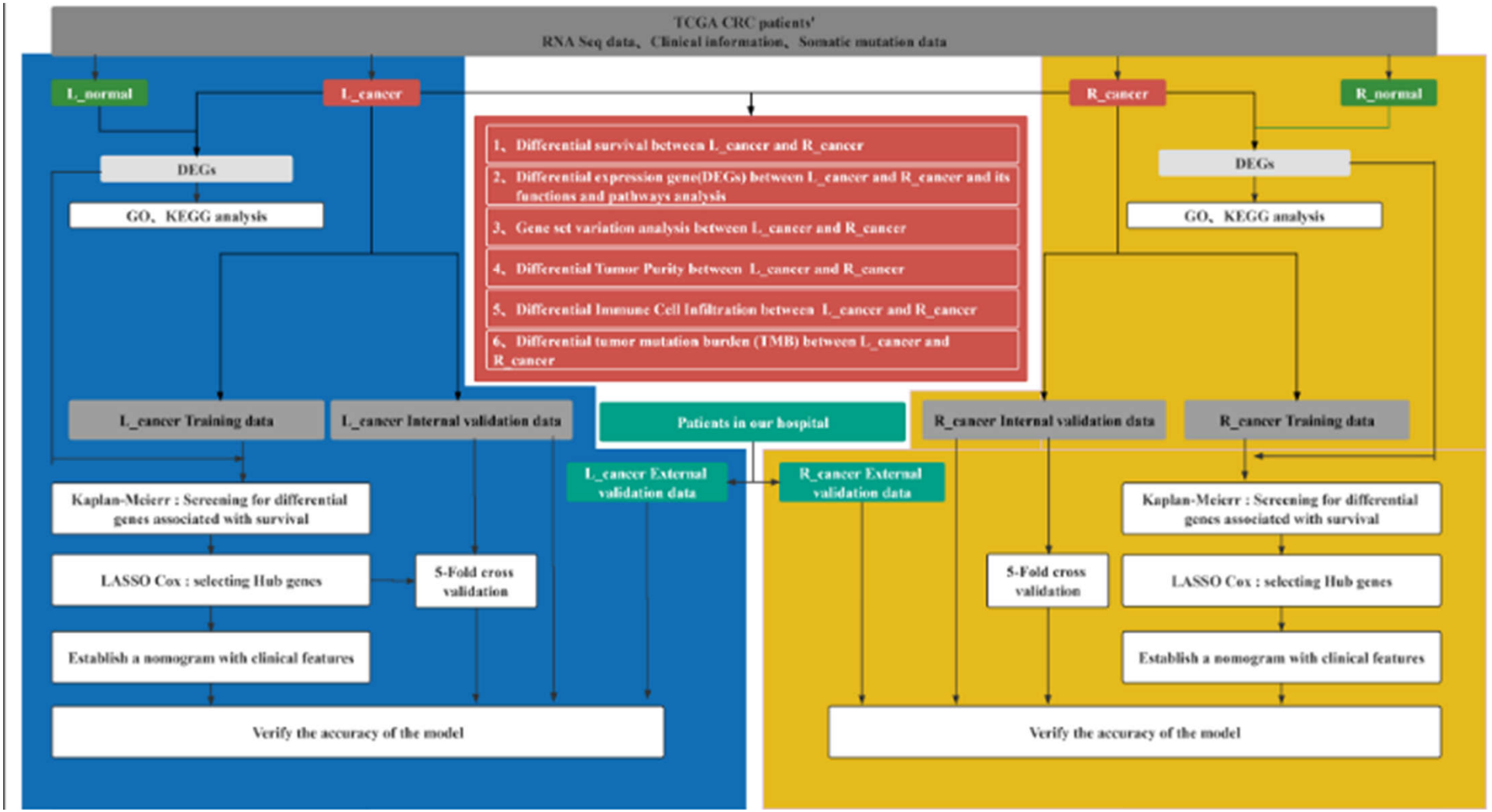
Abstract

Background: Previous studies have reported that the tumor heterogeneity and complex oncogenic mechanisms of proximal and distal colon cancer (CRC) are divergent. Therefore, we aim to analyze the differences between left-sided CRC (L_cancer) and right-sided CRC (R_cancer), as well as constructing respective nomograms.

Methods: We enrolled 335 colon cancer patients (146 L_cancer patients and 189 R_cancer patients) from The Cancer Genome Atlas (TCGA) data sets, and 102 pairs of color cancer tissue and adjacent normal tissue (51 L_cancer patients and 51 R_cancer patients) from our hospital. Firstly, we analyzed the differences between the L_cancer patients and R_cancer patients, and then established the L_cancer and R_cancer prognostic models using LASSO Cox.

Results: R_cancer patients had lower survival than L_cancer patients. R_cancer patients had higher ESTIMATE and immune scores and lower tumor purity. These patterns of expression of immune checkpoint-related genes and TMB level were higher in R_cancer than in L_cancer patients. Finally, we using Lasso Cox regression analyses established a prognostic model for L_cancer patients and a prognostic model for R_cancer patients. The AUC values of the risk score for OS in L_cancer were 0.862 in the training set and 0.914 in the testing set, while those in R_cancer were 0.835 in the training set and 0.857 in the testing set. The AUC values in fivefold cross-validation were between 0.727 and 0.978, proving that the two prognostic models have great stability. The nomogram of L_cancer included prognostic genes, age, pathological M, pathological stage, and gender, the AUC values of which were 0.800 in the training set and 0.905 in the testing set. Meanwhile, the nomogram of R_cancer comprised prognostic genes, pathological N, pathological T, and age, the AUC values of which were 0.836 in the training set and 0.850 in the testing set. In the R_cancer patients, high-risk patients had a lower proportion of 'B cells memory', 'Dendritic cells resting', immune score, ESTIMATE score, immune checkpoint-related genes, and HLA-family genes, and a higher proportion of 'T cells follicular helper', 'Dendritic cells activated', and 'Mast cells activated'.


TCGA CRC patients'
RNA Seq data、Clinical information、Somatic mutation data
L_normal
L_cancer
R_cancer
R_normal
1、Differential survival between L_cancer and R_cancer
2、Differential expression gene(DEGs) between L_cancer and R_cancer and its functions and pathways analysis
3、Gene set variation analysis between L_cancer and R_cancer
4、Differential Tumor Purity between L_cancer and R_cancer
5、Differential Immune Cell Infiltration between L_cancer and R_cancer
6、Differential tumor mutation burden (TMB) between L_cancer and R_cancer
DEGs
GO、KEGG analysis
DEGs
GO、KEGG analysis
L_cancer Training data
L_cancer Internal validation data
Patients in our hospital
R_cancer Internal validation data
R_cancer Training data
L_cancer External validation data
R_cancer External validation data
Kaplan-Meierr : Screening for differential genes associated with survival
LASSO Cox : selecting Hub genes
5-Fold cross validation
Establish a nomogram with clinical features
Verify the accuracy of the model
Kaplan-Meierr : Screening for differential genes associated with survival
5-Fold cross validation
LASSO Cox : selecting Hub genes
Establish a nomogram with clinical features
Verify the accuracy of the model

Conclusions

We found significant differences between L_cancer and R_cancer patients, including clinical features, transcriptome, TMB, immune microenvironment landscape, suggesting that colon cancer can be classified and analyzed into different clinical types with respect to their differences in anatomical location and gene expression, thus aiding in the early diagnosis and prognosis of colon cancer. We established two clinical predictive nomograms in combination with clinical features to provide a basis for the personalized and precise treatment of L_cancer and R_cancer. These hub genes may become promising biomarkers for the diagnosis, treatment, and prognosis of colon cancer. Moreover, The findings support previous studies suggesting that proximal and distal CRC can be classified differently in terms of epidemiology, pathology, and genetics.

Review

JOURNAL
OF HEPATOLOGY

Blood-based biomarkers for hepatocellular carcinoma screening: Approaching the end of the ultrasound era?

Neehar D. Parikh[1,2,*], Nabihah Tayob[3], Amit G. Singal[4]

Summary

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related death worldwide, in part because of inadequate early detection strategies. Current recommendations for screening consist of semi-annual abdominal ultrasound with or without serum alpha-fetoprotein in patients with cirrhosis and in demographic subgroups with chronic hepatitis B infection. However, this screening strategy has several deficiencies, including suboptimal early-stage sensitivity, false positives with subsequent harms, inter-operator variability in ultrasound performance, and poor adherence. A blood-based biomarker with sufficient performance characteristics for early-stage disease could overcome several of these barriers to improving early-stage detection. However, prior to use of a biomarker for screening in clinical practice, a multistep validation is required in order to understand test performance characteristics. These steps include case-control validation, followed by validation in prospective cohorts of at-risk patients. Until recently, we lacked adequate longitudinal validation cohorts for early HCC detection; however, several validation cohorts are maturing, including the Hepatocellular Carcinoma Early Detection Study and the Texas Hepatocellular Carcinoma Consortium, which will allow for rigorous validation of candidate biomarkers. While there are several promising biomarkers awaiting validation, in order to supplant abdominal ultrasound, a candidate biomarker must show adequate test performance and overcome practical hurdles to ensure adoption in clinical practice. The promise of blood-based biomarkers is significant, especially given the limitations of ultrasound-based screening; however, they require adequate validation and several logistical obstacles must be overcome prior to clinical implementation.

Keypoints

- HCC is a leading cause of cancer-related mortality and early detection has been associated with improved survival.
- Semi-annual ultrasound-based screening has several limitations which limits its effectiveness as an early detection strategy.
- Prior to clinical utilisation, biomarkers require rigorous evaluation to determine performance parameters *vs.* a comparable gold standard.
- Several existing biomarkers have undergone early-stage validation, with limited data in small phase III cohorts. Further reporting of phase III results in larger cohorts will enable selection of candidate biomarkers for further testing.
- Maturing well-powered phase III cohorts will facilitate validation of candidate biomarkers. Promising biomarkers can go on to larger phase IV/V validation studies for clinical implementation.

Table 1. Select phase II biomarkers for early-stage hepatocellular carcinoma detection.

Biomarker	Early detection performance
Osteopontin[82–84]	Sensitivity: 49% Specificity: 72%
Midikine[85]	Sensitivity: 87% Specificity: 90%
Dikkopf-1[86,87]	Sensitivity: 41%–74% Specificity: 87%
Glypican-3[88–90]	Sensitivity: 55% Specificity: >95%
Alpha-1 fucosidase[91]	Sensitivity: 56% Specificity: 69%
Golgi Protein-73[92,93]	Sensitivity: 62%–79% Specificity: 62%–88%
Squamous cell carcinoma antigen[94–97]	Data for early-stage HCC not available

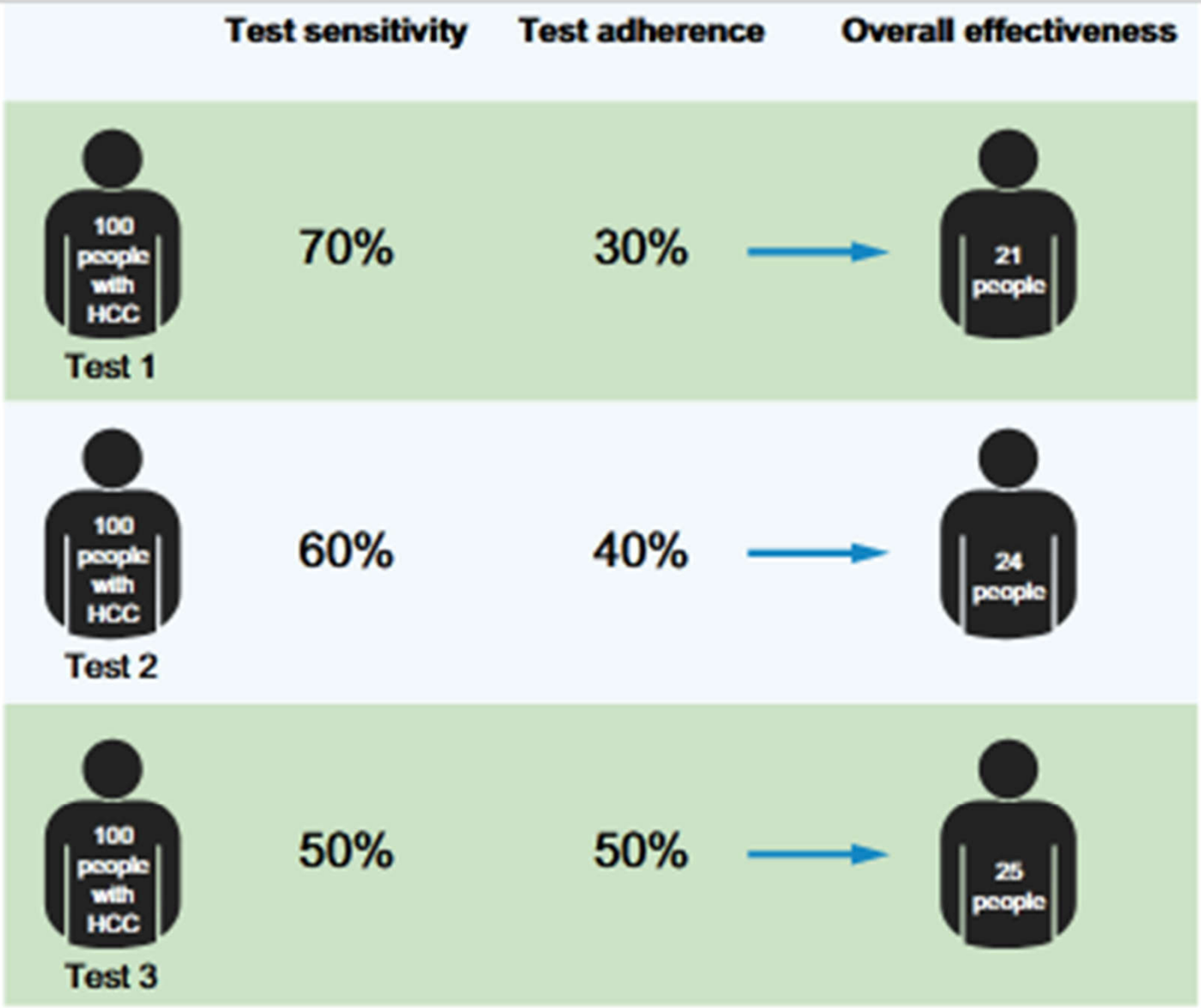


Fig. 2. Schematic of the interplay between test sensitivity and adherence that determines overall effectiveness. HCC, hepatocellular carcinoma.

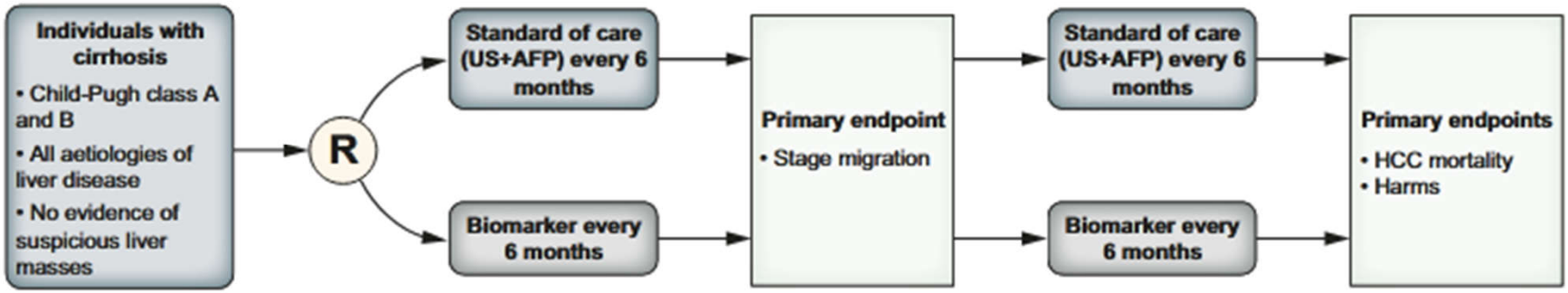
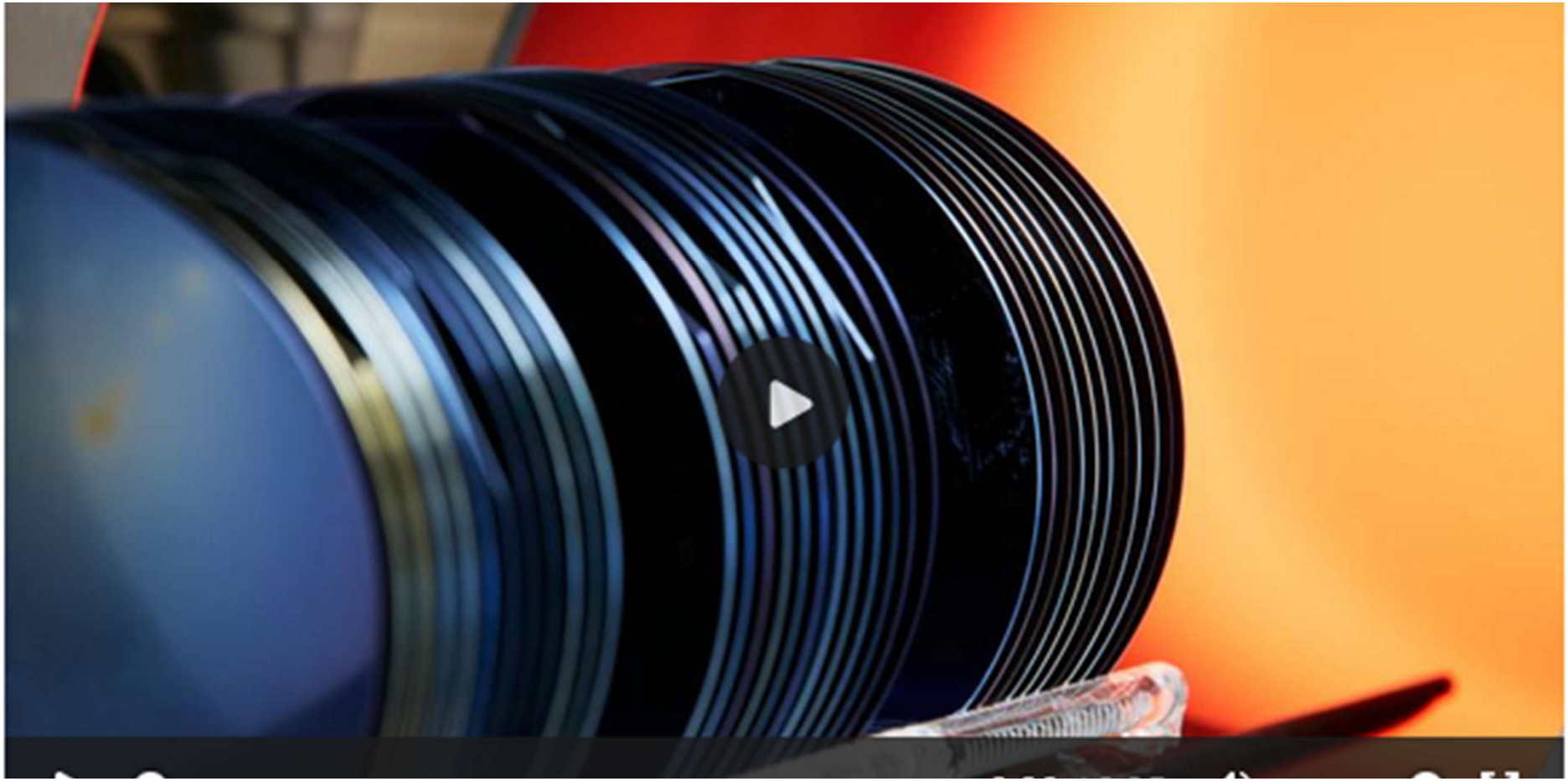


Fig. 3. Proposed schema for a phase IV clinical utility trial for HCC biomarker validation. AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma; US, ultrasound.

HCC,[75] the costs of any surveillance test will be an important to longitudinal cohorts, which can take years to mature. However,



PCCT reduces abdominal imaging radiation dose by almost 20%

By Kate Madden Yee, AuntMinnie.com staff writer

December 16, 2022 -- Photon-counting CT (PCCT) not only improves image quality for arterial phase abdominal scans compared to conventional CT, but it also reduces radiation dose by almost 20%, according to research presented at the 2022 RSNA meeting.

The findings are good news for oncology patients, wrote a team led by presenter Dr. Dirk Graafen, PhD, of Johannes Gutenberg-Universität Mainz in Germany.

"Image quality improvement of photon-counting detector CT for arterial-phase abdominal scans holds the potential to increase diagnostic certainty of oncologic imaging ... [and] further dose reduction might be achievable," the group explained.

Clinicians seek to reduce patient exposure to radiation, especially on CT imaging, which can impart high doses. Photon-counting CT shows promise for having considerable impact on abdominal oncologic imaging when it comes to reducing radiation dose, Graafen's team noted.

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Recent progress in molecular mechanisms of postoperative recurrence and metastasis of hepatocellular carcinoma

Abstract

Hepatectomy is currently considered the most effective option for treating patients with early and intermediate hepatocellular carcinoma (HCC). Unfortunately, the postoperative prognosis of patients with HCC remains unsatisfactory, predominantly because of high postoperative metastasis and recurrence rates. Therefore, research on the molecular mechanisms of postoperative HCC metastasis and recurrence will help develop effective intervention measures to prevent or delay HCC metastasis and recurrence and to improve the long-term survival of HCC patients. Herein, we review the latest research progress on the molecular mechanisms underlying postoperative HCC metastasis and recurrence to lay a foundation for improving the understanding of HCC metastasis and recurrence and for developing more precise prevention and intervention strategies.

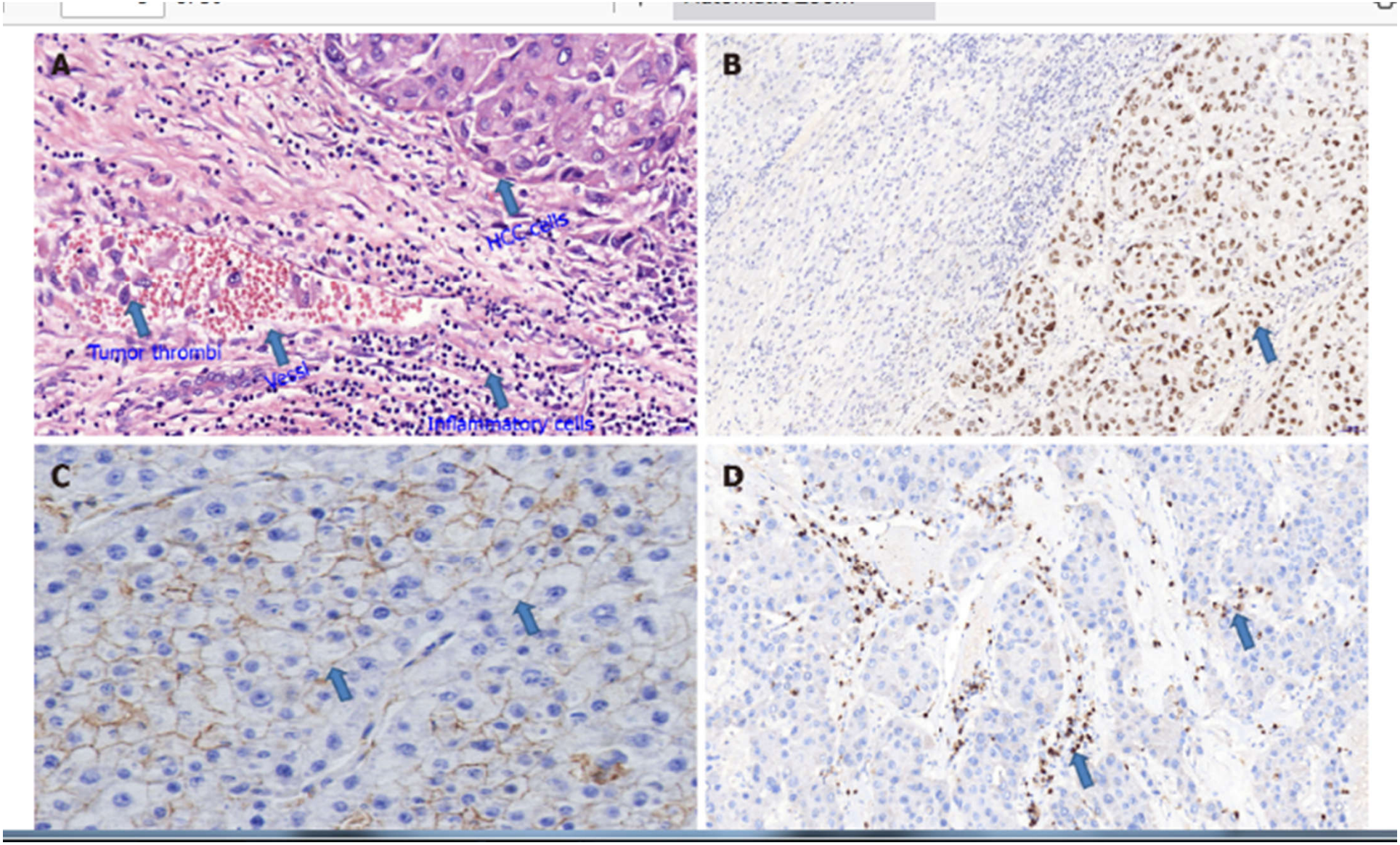
A
HCC cells
Tumor thrombi
Vessel
Inflammatory cells
B
C
D

Table 1 Molecular mechanisms associated with postoperative hepatocellular carcinoma metastasis and recurrence in this review

Molecular marker	Association with HCC metastasis and recurrence	Ref.
Oncogenes and tumor suppressors		
Oncogens		
H-ras	Increased expression	Ma *et al*[9]
OPN	Increased expression	Yu *et al*[22]; Zhu *et al*[25]
S100A9	Increased expression	Chiou and Lee[29]; Liao *et al*[31]
Tumor suppressors		
Mutated p53	Increased expression	Nikolova *et al*[40]; Chaudhary *et al*[44]
Nm23	Decreased expression	Khera *et al*[50]
KAI1	Decreased or lost expression	Xu *et al*[55]
Tumor microenvironment		
Tumor stromal cells		
Immune cells		
T lymphocytes	Decreased expression	Cai *et al*[68]; Gabrielson *et al*[70]; Li *et al*[71]
NK cells	Decreased expression	Wu *et al*[85]; Lee *et al*[90]

Tumor microenvironment		
Tumor stromal cells		
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NK cells	Decreased expression	Wu *et al*[85]; Lee *et al*[90]
DCs	Decreased expression	Shi *et al*[108]
M2-TAMs	Increased expression	Yao *et al*[128]; Park *et al*[133]; Liao *et al*[134]
MDSCs	Increased expression	Kalathil and Thanavala[143]; Lu *et al*[147]
Tregs	Increased expression	Xiong *et al*[155]; Trehanpati and Vyas[159]
N2-TANs	Increased expression	Zhou *et al*[172]; Yang *et al*[175]
HSCs	Increased expression	Barry *et al*[198]; Cheng *et al*[200]
CAFs	Increased expression	Gao *et al*[217]; Zhang *et al*[220]
TECs	Increased expression	Tahmasebi *et al*[236]; Dong *et al*[239]
ECM		
Adhesion enhancement in tumor cell-ECM		
ICAM-1	Increased expression	Chen *et al*[255]
E-Cadherin	Decreased or lost expression	Ren *et al*[267]; He *et al*[269]

Onishi *et al. Cancer Drug Resist* 2020;3:385-400
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Cancer
Drug Resistance

Review

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MicroRNA and liver cancer

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Abstract

Hepatocellular carcinoma (HCC) is a major cause of cancer-related deaths worldwide. HCC is characterized by a poor prognosis and an ever increasing number of scientific studies aim to find new diagnostic, prognostic, and therapeutic targets. MicroRNAs (miRNAs), small non-coding RNAs that regulate the gene expression in many processes, have been shown to play a crucial role in regulating hepatocellular carcinoma. miRNAs may act as oncogenic miRNAs and tumor suppressor miRNAs and regulate cancer cell proliferation, invasion, and metastasis by being differently upregulated or downregulated and targeting the genes related with carcinogenesis. miRNAs secreted from cancer cells are found circulating in the blood, presenting an opportunity for their use as disease-related biomarkers. Moreover, extracellular vesicle-derived miRNAs are known to reflect the cell of origin and function and may provide effective biomarkers for predicting diagnosis and prognosis and new therapeutic target in HCC. In this article, we describe the most recent findings regarding the molecular mechanisms and gene regulation of microRNA in HCC, as well as their application in diagnosis/prognosis and treatment.

Core Tip: Surgical resection is currently a vital treatment option for patients with early and intermediate hepatocellular carcinoma (HCC). Unfortunately, the prognosis of HCC patients remains unsatisfactory due to high rates of postoperative metastasis and recurrence. Therefore, studies on the molecular mechanisms of postoperative HCC metastasis and recurrence will help develop effective intervention measures to prevent or delay HCC metastasis and recurrence and to improve the long-term survival of HCC patients. Herein, we review the latest research progress on the molecular mechanisms underlying postoperative HCC metastasis and recurrence to lay a foundation for improving the understanding of HCC metastasis and recurrence and for developing more precise prevention and intervention strategies.

THE END