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Novel Biomarkers in Hepatocellular Carcinoma from Embryo-genic Antigens to cfDNA

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 February 2025 and was last updated on 7 February 2025.

INTRODUCTION

Review question / Objective In patients with hepatocellular carcinoma, how do novel biomarkers compare to traditional biomarkers in terms of diagnostic accuracy, prognostic value and clinical utility.

Rationale Hepatocellular carcinoma, being a leading cause of cancer-related mortality relies mainly on the biomarker alpha-fetoprotein, which has suboptimal sensitivity and specificty. The rationale of our review is identifying novel biomarkers that could aid us in early detection and deciding on better treatment options for patients with HCC.

Condition being studied Hepatocellular carcinoma, most common primary liver cancer and a leading cause of cancer-related mortality.

METHODS

Search strategy Systematically searching medical databases for studies related to novel biomarkers in hepatocellular carcinoma (HCC) using specific keywords and inclusion criteria to select relevent studies.

Participant or population Patients diagnosed with hepatocellular carcinoma.

Intervention The review evaluates biomarkers for HCC, including circulating cell-free DNA (cfDNA), circulating tumor cells (CTCs), microRNAs (miRNAs), inflammatory-based markers, and other novel molecular markers. and checking the potential use of these biomarkers to improve diagnostic accuracy.

Comparator The conventional biomarkers, particullary alpha-fetoprotein.

Study designs to be included Original artices, clinical trials and experimental studies.

Eligibility criteria Articles on hepatocellular carcinoma diagnosis, prediction and prognosis progress were included;
Specific studies on liver transplantation, drug-related studies, or other types of cancer were excluded.

Information sources Electronic databases (PubMed, Scopus and Clarivate Web of Science.)

Main outcome(s) The main outcome of this review is evaluating the diagnostic accuracy of novel biomarkers for hepatocellular carcinoma, particularly in early detection and staging, and to compare their performance to the current gold standard, alpha-fetoprotein (AFP) and ultrasound (US). The review focuses on metrics such as sensitivity, specificity, positive and negative predictive value, diagnostic accuracy, and diagnostic odds ratio (DOR). Data from studies published between 2015 and 2024 were synthesized to assess these biomarkers' effectiveness, with the aim of providing a comprehensive understanding of their potential clinical application in HCC diagnosis.

Quality assessment / Risk of bias analysis The quality of the listed studies was evaluated using appropriate risk of bias instruments.

Strategy of data synthesis The data was summarized and analyzed in a narrative format, with tables and figures included when necessary. Results were shown as percentages with 95% confidence intervals. For non-normally distributed data, sample sizes were presented as the median and interquartile range. Microsoft Excel (Version 2402) was used for the analysis.

Subgroup analysis Subgroups include patients who were positive for different novel biomarkers, the analysis was performed in comparision with the traditional biomarker, alpha-fetoprotein or in comparision with other biomarkers. results were mainly shown as percentages with 95% confidence intervals.

Sensitivity analysis No formal sensitivity analysis was conducted in this review.

Country(ies) involved Romania, Israel.

Keywords “HCC”, “hepatocellular carcinoma", “biomarkers”, “GPC3”, “AFP”, “cfDNA”; Mesh “Carcinoma, Hepatocellular/Diagnosis”.

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