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Research Article

Role of Contrast-Enhanced CT and Serum Alpha-Fetoprotein in Early Detection of Hepatocellular Carcinoma

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Abstract:

Early detection of hepatocellular carcinoma (HCC) remains a global challenge due to its asymptomatic course and high mortality. Serum alpha-fetoprotein (AFP) is widely used in surveillance but suffers from limited sensitivity and specificity, especially for small lesions. Contrast-enhanced computed tomography (CECT) provides dynamic imaging characteristics of hepatic nodules but is not always conclusive in differentiating benign from malignant lesions. This prospective study evaluated the diagnostic performance of serum AFP, CECT, and their combination in detecting early-stage HCC among high-risk patients with chronic liver disease. A total of 210 patients undergoing HCC surveillance were enrolled. Serum AFP levels were quantified, and all participants underwent multiphasic CECT. Histopathology or 12-month imaging follow-up served as reference standard. AFP alone demonstrated moderate sensitivity (68%) but low specificity (62%), while CECT showed higher sensitivity (82%) and specificity (79%). The combined approach significantly improved diagnostic accuracy (sensitivity 90%, specificity 83%, AUC 0.91). These findings underscore that integration of AFP and CECT enhances early detection of HCC compared to either modality alone, supporting their complementary role in surveillance protocols for at-risk populations.

Keywords: Hepatocellular carcinoma, contrast-enhanced CT, alpha-fetoprotein, early detection, diagnostic accuracy

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and a leading cause of cancer-related deaths worldwide. Despite therapeutic advances, prognosis remains poor due to late presentation and limited curative options at advanced stages. Early detection is critical, as patients diagnosed at early stages may benefit from potentially curative therapies including surgical resection, liver transplantation, or local ablative procedures.1-3

Surveillance of at-risk populations—particularly those with cirrhosis or chronic hepatitis B/C infection—is the cornerstone of early detection. Ultrasound and serum alpha-fetoprotein (AFP) remain the most widely used tools in surveillance programs. However, both methods have significant limitations. Ultrasound is highly operator dependent and may miss small or subdiaphragmatic lesions. AFP, while inexpensive and widely available, lacks sufficient accuracy for standalone use. Elevated AFP levels can occur in benign hepatic conditions such as hepatitis or cirrhosis, and nearly one-third of early-stage HCC cases may present with normal AFP.4-7

In recent years, imaging modalities have played a vital role in HCC detection. Contrast-enhanced CT (CECT) and MRI provide dynamic characterization of hepatic lesions based on vascularity. Typical imaging hallmarks of HCC include arterial phase hyperenhancement followed by washout in the portal venous or delayed phase. CECT is particularly valuable due to its accessibility, rapid acquisition, and ability to detect extrahepatic spread. However, it may be limited by radiation exposure and contrast-related risks, and some early or atypical HCC lesions may not display classical features.8-10

An integrated approach combining serum biomarkers with imaging has been proposed to optimize surveillance accuracy. AFP offers a biological dimension reflecting tumor biology, while CECT provides structural and vascular characterization. By leveraging their complementary strengths, clinicians may improve diagnostic yield and reduce false positives or negatives.

This study aimed to evaluate the individual and combined diagnostic performance of AFP and CECT in early HCC detection among high-risk patients. The hypothesis was that a combined strategy would outperform either modality alone in terms of sensitivity, specificity, and overall accuracy.

Methodology

Study design & setting: Prospective diagnostic accuracy study conducted in Services Institute of Medical Sciences / Services Hospital, Lahore a tertiary care hospital. Ethical approval obtained.

Sample size calculation: Using Epi Info v7.2, assuming expected sensitivity of 85% for combined AFP+CECT, with 95% confidence and 80% power, a minimum of 190 participants was required. To account for attrition, 210 patients were recruited.

Inclusion criteria:

- Adults ≥18 years with chronic liver disease (cirrhosis, chronic hepatitis B or C).
- Undergoing routine surveillance for HCC.

Exclusion criteria:

- Prior history of HCC.
- Contraindication to iodinated contrast (renal dysfunction, allergy).
- Pregnancy.

Procedures:

- Serum AFP measured using chemiluminescent immunoassay. Cut-off >20 ng/mL considered positive.
- Multiphasic CECT (arterial, portal venous, delayed phases) performed on all participants. Lesions demonstrating arterial enhancement with venous/delayed washout considered radiologically positive for HCC.
- Reference standard: histopathology for resected/biopsied lesions or ≥12 months of follow-up imaging confirming stability/ progression.

Statistical analysis: Diagnostic accuracy metrics (sensitivity, specificity, PPV, NPV, ROC curves) calculated for AFP, CECT, and combined approach. Chi-square test used for comparisons. Significance set at $p < 0.05$.

Results

Table 1: Baseline Demographics

Variable	Total (n=210)
Age (years, mean ± SD)	58.6 ± 10.7
Male sex, n (%)	144 (68.6%)
Cirrhosis etiology – HBV/HCV/Alcohol/Other	76/62/42/30
Child-Pugh A/B/C (%)	61/29/10
HCC confirmed cases (%)	94 (44.8%)

Interpretation: Majority of participants were middle-aged males with cirrhosis; nearly 45% had confirmed HCC.

Table 2: Diagnostic Accuracy of AFP vs CECT

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
AFP (>20 ng/mL)	68	62	59	70	0.67
CECT	82	79	77	84	0.83

Interpretation: CECT outperformed AFP in both sensitivity and specificity.

Table 3: Combined AFP + CECT Approach

Approach	Sensitivity (%)	Specificity (%)	AUC	p-value vs CECT
AFP+CECT (parallel testing)	90	83	0.91	0.02

Interpretation: Combined testing significantly improved diagnostic accuracy compared to CECT alone.

Discussion

This study confirms that serum AFP alone has limited utility in detecting early HCC, consistent with global surveillance challenges. Its sensitivity of 68% and specificity of 62% underscore that

a substantial proportion of patients may be misclassified if AFP is used in isolation. 11-13 CECT demonstrated higher diagnostic accuracy, identifying typical enhancement patterns in early lesions. Its sensitivity of 82% and specificity of 79% are comparable with recent literature, affirming its central role in HCC detection.14-15 Importantly, the combined AFP+CECT approach yielded the highest accuracy, with sensitivity reaching 90% and specificity 83%. This reinforces the complementary nature of biochemical and imaging modalities. The improved performance likely arises from AFP capturing biologically active tumors not yet radiologically typical, while CECT detects structural lesions that may be AFP-negative.16-18 Clinically, this integrated approach supports current guidelines advocating multimodal surveillance in high-risk patients, particularly those with cirrhosis. Early detection allows curative options such as resection or transplantation, significantly improving survival.19-20 The study's strengths include prospective design, standardized imaging protocol, and histopathological confirmation where feasible. However, limitations include single-center scope, lack of MRI comparison, and potential selection bias from tertiary care setting. Future research should validate these findings in multicenter cohorts, incorporate novel biomarkers (e.g., AFP-L3, des-γ-carboxy prothrombin), and evaluate cost-effectiveness of combined strategies.

Conclusion

CECT provides superior diagnostic accuracy to AFP alone in early HCC detection, but their combination significantly enhances sensitivity and specificity. Integrating serum biomarkers with imaging should be the preferred surveillance strategy for high-risk populations.

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