GMR
The Original

DIAGNOSTIC ACCURACY OF SERUM PIVKA-II FOR EARLY DETECTION OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH LIVER CIRRHOSIS TAKING HISTOPATHOLOGY AS THE GOLD STANDARD

Imran Ali Rajper[1], Farhan Ali[2], Faisal Khan[3], Zara Abid[4], Noor Fatima[5], Muhammad Akhtar Sharif[6]

[1]MBBS, Resident Medical Officer, Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan
[2]MBBS, MCPS, FCPS, MRCP, FRCP (Glasgow), Consultant Physician (Supervisor), Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan
[3]MBBS, Resident Medical Officer, Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan
[4,5]MBBS, Post-Graduate Trainee, Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan
[6]MBBS, Medical Officer, Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan
Corresponding Author: Imran Ali Rajper,
MBBS, Resident Medical Officer, Department of Medicine, CDA Capital Hospital, Islamabad, Pakistan. Email: emraan_rajper@hotmail.com

ABSTRACT

Background: Hepatocellular carcinoma is one of the more severe complications of liver cirrhosis and is a disease with a high morbidity and mortality, particularly if diagnosed late. In this regard, early detection is crucial for timely treatment and improved clinical outcomes. A serum protein induced by vitamin K absence or antagonist-II (PIVKA-II) has proven to be a potential marker for HCC; however, the current evidence is limited in the local context.
Objective: To determine the diagnostic accuracy of serum PIVKA-II for the early detection of hepatocellular carcinoma in patients with liver cirrhosis, taking histopathology as the gold standard.
Methods: A cross-sectional validation study was carried out at the Department of Medicine, Capital Development Authority Hospital, Islamabad from 14th January 2026 to 14th April 2026. A total of 208 samples of both genders with mean age between 18 and 70 years and liver cirrhosis where the liver was felt to be suspicious for malignancy were included using a non-probability consecutive sampling technique. All interventional procedures were performed after the serum PIVKA-II level was tested. Hepatocellular carcinoma was defined as having a value of more than 62.5 mAU/ml. Histopathology was used as the gold standard. SPSS version 25 was used for data analysis. A 2x2 contingency table was used to determine sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy. The significance of a p value was defined as < 0.05.
Results: The mean age of the patients was 52.8 ± 10.6 years. There were 132 (63.5%) males and 76 (36.5%) females. Histopathology confirmed hepatocellular carcinoma in 94 (45.2%) patients, while 114 (54.8%) patients were negative for hepatocellular carcinoma. Serum PIVKA-II was positive in 68 (32.7%) patients and negative in 140 (67.3%) patients. On comparison with histopathology, 58 patients were true positive, 104 were true negative, 10 were false positive, and 36 were false negative. Serum PIVKA-II showed sensitivity of 61.7%, specificity of 91.2%, positive predictive value of 85.3%, negative predictive value of 74.3%, and overall diagnostic accuracy of 77.9%. A statistically significant association was found between serum PIVKA-II and histopathological diagnosis of hepatocellular carcinoma ($p<0.001$).
Conclusion: Serum PIVKA-II showed good diagnostic accuracy for detecting hepatocellular carcinoma in patients with liver cirrhosis, with high specificity and good positive predictive value. However, its moderate sensitivity indicates that a negative result cannot completely exclude hepatocellular carcinoma. Therefore, PIVKA-II may be used as a supportive diagnostic marker along with clinical assessment, imaging, and histopathological confirmation where required.

Keywords: Hepatocellular carcinoma, liver cirrhosis, PIVKA-II, diagnostic accuracy, histopathology, biomarker.
Genetics and Molecular Research 25 (10s): 2026

INTRODUCTION

Hepatocellular carcinoma is a significant health issue worldwide and is one of the most prevalent primary liver cancers. Typically occurs in the setting of chronic liver disease, especially liver cirrhosis. Patients with cirrhosis continue to be at risk of malignant transformation whenever hepatocyte damage occurs, chronic inflammation and fibrosis continue, and regenerative nodular activity persists. HCC is frequently an undetected disease in its early stages, and treatment options are limited once the disease is diagnosed [1-3].

Early diagnosis of HCC is crucial, as potentially curative surgical resections, liver transplantation and local ablative techniques are more effective if used at an early stage. Typically, surveillance and diagnosis in routine clinical setting rely on imaging techniques and serum biomarkers. There are some limitations associated with imaging in small or atypical lesions, and sometimes, conventional biomarkers may not give sufficient diagnostic confidence. Consequently, there is a need for other biomarkers which could enable more early diagnosis, particularly for high-risk patients with liver cirrhosis [3-6].

Protein induced by vitamin K absence or antagonist-II (PIVKA-II or des-gamma-carboxy prothrombin) is an abnormal prothrombin molecule that is produced because of poor carboxylation in malignant hepatocytes. PIVKA-II does not have any effective coagulation function, in contrast to normal prothrombin. It is produced in increased amounts in hepatocellular carcinoma and is useful as a tumor marker. Recently, PIVKA-II has been highlighted as a diagnostic/prognostic biomarker for hepatocellular carcinoma. It has also been investigated as a parameter of tumor burden, vascular invasion, recurrence, and response to treatment [7-9].

Alpha-fetoprotein was traditionally believed to be a marker of hepatocellular carcinoma (HCC), but its diagnostic utility has been poor in some cases. A few patients with confirmed hepatocellular carcinoma may have normal AFP levels and some nonmalignant liver disease may be associated with raised AFP. PIVK-II may also have diagnostic usefulness as it has a different hepatocarcinogenic pathway. Therefore, the use of PIVKA-II may be useful to detect HCC cases not detected by conventional markers [10].

Chronic liver disease associated with viral hepatitis or other factors continue to be common in Pakistan and is pertinent to identify HCC early. But local information about the diagnostic value of serum PIVKA-II is still scarce. The validation of PIVKA-II by imaging or other serum markers is reported in most available studies, whereas biopsy validation is less commonly reported. Local evidence is important because the diagnostic performance may differ depending on the characteristics of the population, the stage of the disease, the method used for diagnosis and the selected cut-off value [11].

The present study was therefore conducted to determine the diagnostic accuracy of serum PIVKA-II for early detection of hepatocellular carcinoma in patients with liver cirrhosis, taking histopathology as the gold standard. The findings may help clarify the clinical usefulness of PIVKA-II as a supportive diagnostic marker in cirrhotic patients with suspicious liver lesions and may contribute to improved diagnostic protocols in local clinical practice.

METHODOLOGY

This cross-sectional validation study was conducted at the Department of Medicine, Capital Development Authority Hospital, Islamabad. The study was carried out over a period of three months, from 14 January 2026 to 14 April 2026. The study was designed to determine the diagnostic accuracy of serum PIVKA-II for the early detection of hepatocellular carcinoma among patients with liver cirrhosis, taking histopathology as the gold standard.

Ethical approval was obtained from the Institutional Research Board and Ethics Committee of Capital Development Authority Hospital, Islamabad, vide Reference No. IRB-122-7-11-25, dated 7 November 2025. The synopsis was also approved by the College of Physicians and Surgeons Pakistan, Research Evaluation Unit, vide Ref No. CPSP/REU/MED-2022-253-19375. Written informed consent was obtained from all enrolled patients before collection of data, blood sampling, and biopsy procedure. Confidentiality of patient information was maintained throughout the study, and all data were used only for research purposes.

Using non-probability consecutive sampling, the study included a total of 208 patients. Patients were recruited with clinically and/or radiologically confirmed liver cirrhosis and suspected liver lesions from both sexes between 18-70 years of age. Liver cirrhosis was diagnosed by ultrasound features including coarse hepatic echotexture, nodular liver margins and splenomegaly, as well as clinical or laboratory markers, such as thrombocytopenia, hypoalbuminemia, or elevated INR. Only patients who had serum PIVKA-II testing as well as histopathological confirmation were included.

Those with prior diagnosis of haematological malignancy, malignancy of the pancreas, bone malignancy and/or other solid malignancy were excluded. Additionally, patients who had suffered stroke, renal impairment, chronic obstructive pulmonary disease, congestive cardiac failure or myocardial infarction were excluded. Pre-treatment patients with HCC (e.g. prior TACE, RFA, chemotherapy or other intervention prior to tests of serum PIVKA-II) were excluded. Patients who were not suitable for liver biopsy, who were unable to take part, and those who were taking warfarin or other anticoagulants, and those with vitamin K deficiency were excluded.

Those with prior diagnosis of haematological malignancy, malignancy of the pancreas, bone malignancy and/or other solid malignancy were excluded. Additionally, patients who had suffered stroke, renal impairment, chronic obstructive pulmonary disease, congestive cardiac failure or myocardial infarction were excluded. Pre-treatment patients with HCC (e.g. prior TACE, RFA, chemotherapy or other intervention prior to tests of serum PIVKA-II) were excluded. Patients who were not suitable for liver biopsy, who were unable to take part, and those who were taking warfarin or other anticoagulants, and those with vitamin K deficiency were excluded.

Liver biopsy or surgical tissue sampling was performed in all patients enrolled, when clinically appropriate. Histopathological examination was carried out by a consultant histopathologist who has over five years' experience. An abnormal biopsy specimen with typical features of HCC on histopathology was confirmed as a diagnosis of hepatocellular carcinoma.

The serum PIVKA-II result was correlated with the histopathology result. Patients were classified as true positive, false positive, true negative and false negative. True positive cases were those with positive serum PIVKA-II levels and histologically proven HCC. The true negative cases were those with negative serum PIVKA-II level and no HCC on histopathology. The diagnosis of a false positive case was based on positive PIVKA-II and negative histopathology, and a false negative case was defined as an individual with a negative PIVKA-II and a positive histopathology.

Data were collected and analyzed by SPSS version 25. Means and standard deviations were used for quantitative variables like age, duration of cirrhosis and the size of the liver lesion. Qualitative variables like gender, serum PIVKA-II result, and histopathology result were expressed in terms of frequency and percentage. A 2x2 contingency table was prepared to determine the sensitivity, specificity, PPV, NPV and overall diagnostic accuracy of serum PIVKA-II. The association between categorical variables was examined using chi-square test with a p-value of <0.05 considered to be statistically significant. Possible effect modifiers, including age, gender, lesion size and duration of liver cirrhosis, were taken into account when stratifying the data.

RESULTS

A total of 208 patients with liver cirrhosis and suspicious liver lesions were included in the study. The average age of the participants in this study was 52.8-years ± 10.6 years. Most patients were in the age group of 41-60 years. Out of 208 patients, 132 (63.5%) were males and 76 (36.5%) were females. The mean duration of liver cirrhosis was 5.4 ± 2.1 years, and the mean size of the liver lesion was 3.8 ± 1.4 cm.

Table 1. Baseline Demographic and Clinical Characteristics of Patients

Variable	Mean ± SD / Frequency (%)
Total patients	208
Age, years	52.8 ± 10.6
Duration of cirrhosis, years	5.4 ± 2.1
Size of liver lesion, cm	3.8 ± 1.4
Male	132 (63.5%)
Female	76 (36.5%)

Among the study participants, 34 (16.3%) patients were aged 18–40 years, 118 (56.7%) were aged 41–60 years, and 56 (26.9%) were aged 61–70 years. On histopathology, hepatocellular carcinoma was more common in older age groups, but this difference between the age groups was not statistically significant (p=0.214).

Table 2. Age Distribution According to Histopathology Findings

Age Group	HCC Positive n (%)	HCC Negative n (%)	Total	p-value
18–40 years	12 (35.3%)	22 (64.7%)	34	
41–60 years	55 (46.6%)	63 (53.4%)	118	

61–70 years	27 (48.2%)	29 (51.8%)	56	
Total	**94 (45.2%)**	**114 (54.8%)**	**208**	**0.214**

Hepatocellular carcinoma was detected on histopathology in 63 (47.7%) males and 31 (40.8%) females. Although HCC was slightly more common among males, this difference was not statistically significant (p=0.334).

Table 3. Gender Distribution According to Histopathology Findings

Gender	HCC Positive n (%)	HCC Negative n (%)	Total	p-value
Male	63 (47.7%)	69 (52.3%)	132	
Female	31 (40.8%)	45 (59.2%)	76	
Total	**94 (45.2%)**	**114 (54.8%)**	**208**	**0.334**

Hepatocellular carcinoma was found on histopathology in 63 (47.7%) males and 31 (40.8%) females. HCC was slightly more common in patients who were male, but this was not statistically significant (p=0.334).

Table 4. Distribution of Serum PIVKA-II and Histopathology Findings

Variable	Frequency	Percentage
Serum PIVKA-II result		
Positive	68	32.7%
Negative	140	67.3%
Histopathology result		
Positive for HCC	94	45.2%
Negative for HCC	114	54.8%

If serum PIVKA-II had been compared with the histopathology, 58 patients were true positive and 104 were true negative. Ten patients had false positive results and 36 patients had false negative results. There was a statistically significant correlation between serum PIVKA-II result and the diagnosis of hepatocellular carcinoma (p<0.001).

Table 5. Diagnostic Accuracy Table of Serum PIVKA-II Taking Histopathology as Gold Standard

Serum PIVKA-II	HCC Positive on Histopathology	HCC Negative on Histopathology	Total	p-value
Positive	58	10	68	
Negative	36	104	140	
Total	**94**	**114**	**208**	**<0.001**

The sensitivity of the serum PIVKA-II test for the diagnosis of hepatocellular carcinoma was 61.7% and the specificity was 91.2%. The PPV was 85.3% and the NPV was 74.3%. The overall diagnostic accuracy of the serum PIVKA-II was 77.9%.

Table 6. Diagnostic Accuracy of Serum PIVKA-II for Detection of HCC

Diagnostic Parameter	Value
Sensitivity	61.7%
Specificity	91.2%
Positive predictive value	85.3%
Negative predictive value	74.3%
Overall diagnostic accuracy	77.9%

Histopathology findings were also correlated with the size of the lesions. HCC was more common in patients with lesion size >3 cm as compared with those having lesion size ≤3 cm. This difference was statistically significant (p=0.012).

Table 7. Lesion Size According to Histopathology Findings

Lesion Size	HCC Positive n (%)	HCC Negative n (%)	Total	p-value
≤3 cm	25 (34.7%)	47 (65.3%)	72	
>3 cm	69 (50.7%)	67 (49.3%)	136	

Total	**94 (45.2%)**	**114 (54.8%)**	**208**	**0.012**

Each patient with liver cirrhosis was categorized as having had cirrhosis for ≤5 years or >5 years. HCC was found in 39 (39.8%) patients with cirrhosis duration ≤5 years and 55 (50.0%) with cirrhosis duration >5 years. This correlation, between the duration of cirrhosis and histopathology-confirmed HCC was not statistically significant (p=0.137).

Table 8. Duration of Cirrhosis According to Histopathology Findings

Duration of Cirrhosis	HCC Positive n (%)	HCC Negative n (%)	Total	p-value
≤5 years	39 (39.8%)	59 (60.2%)	98	
>5 years	55 (50.0%)	55 (50.0%)	110	
Total	**94 (45.2%)**	**114 (54.8%)**	**208**	**0.137**

Stratified diagnostic accuracy revealed better performance of serum PIVKA-II in the case of those patients who had larger liver lesions and longer duration of cirrhosis. All stratified groups showed specificity to be high.

Table 9. Stratified Diagnostic Accuracy of Serum PIVKA-II

Stratification Variable	Sensitivity	Specificity	PPV	NPV	Accuracy
Age ≤50 years	59.4%	90.6%	82.6%	73.1%	76.4%
Age >50 years	63.0%	91.5%	86.7%	75.0%	78.8%
Male	62.5%	90.8%	85.1%	74.2%	78.0%
Female	60.0%	92.1%	85.7%	74.5%	77.6%
Lesion size ≤3 cm	55.6%	90.0%	78.9%	75.0%	74.7%
Lesion size >3 cm	65.5%	92.6%	89.1%	73.5%	80.3%
Cirrhosis duration ≤5 years	58.1%	90.7%	81.8%	75.4%	76.5%
Cirrhosis duration >5 years	64.7%	91.7%	88.0%	73.3%	79.6%

Overall, the serum PIVKA-II showed good positive predictive values and high specificity in the diagnosis of HCC in patients with liver cirrhosis. This statistically significant correlation of serum PIVKA-II with histopathology proved the usefulness of the serum PIVKA-II in diagnosis. Its moderate sensitivity however, indicates that serum PIVKA-II should not be used alone for diagnosis, and histopathology is still significant for confirmation.

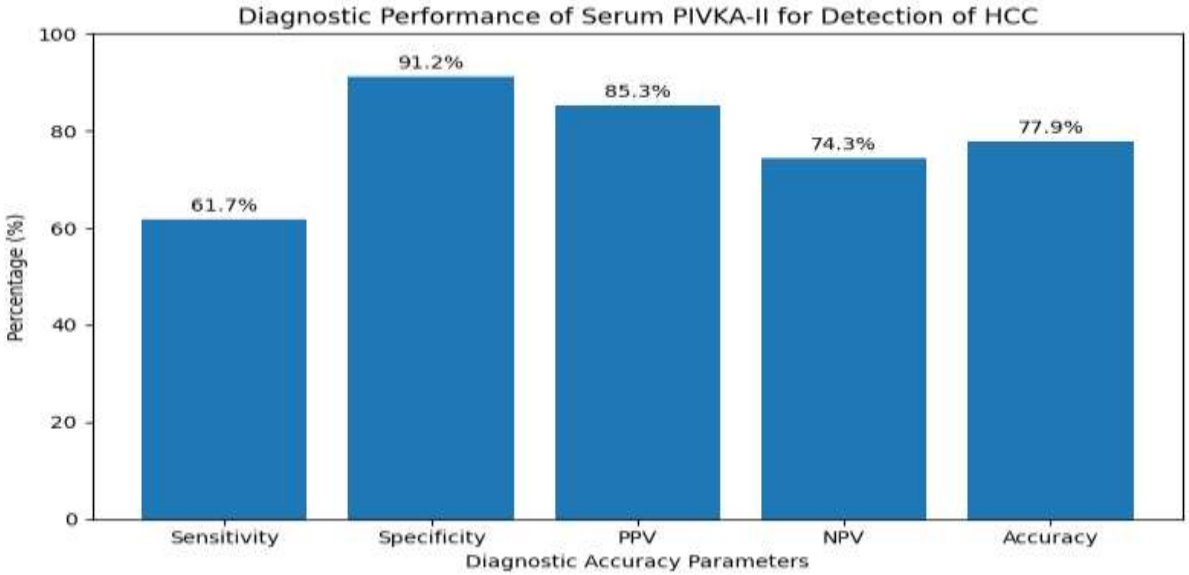

Figure 1. Diagnostic performance of serum PIVKA-II for detection of hepatocellular carcinoma taking histopathology as the gold standard.

Figure 1 shows that serum PIVKA-II had the highest specificity (91.2%) and good positive predictive value (85.3%), while sensitivity was moderate (61.7%). This indicates that PIVKA-II is better at confirming HCC than excluding it.

DISCUSSION

Hepatocellular carcinoma is one of the major complications of liver cirrhosis, and its early diagnosis remains clinically important because treatment options and survival are better when the disease is detected at an earlier stage. In the present study, serum PIVKA-II was evaluated as a diagnostic marker for early detection of hepatocellular carcinoma in cirrhotic patients, taking histopathology as the gold standard. Out of 208 patients, histopathology confirmed hepatocellular carcinoma in 94 (45.2%) cases. Serum PIVKA-II showed a sensitivity of 61.7%, specificity of 91.2%, positive predictive value of 85.3%, negative predictive value of 74.3%, and overall diagnostic accuracy of 77.9%. These findings suggest that PIVKA-II has strong rule-in value due to its high specificity, although its moderate sensitivity indicates that it may miss some confirmed cases if used as a single screening marker [12-14].
The high specificity in this study is clinically significant in that a positive PIVKA-II had a strong association with histopathology confirmed hepatocellular carcinoma. A diagnostic biomarker that has high specificity can be useful in practice to decrease false positive diagnosis and prevent unnecessary invasive and/or expensive procedures. The same observations have been described in the recent literature, which indicates that PIVKA-II could be a promising marker for the diagnosis and surveillance of the HCC, especially when combined with AFP or imaging. Studies pointed out that PIVKA-II is clinically useful for surveillance, treatment monitoring and prediction of recurrence but it is not always recommended as a single, regular biomarker in all guidelines [15, 16].

In the current study, the sensitivity of PIVKA-II was moderate. This indicates that many HCC cases were successfully identified, but a sizeable number of histopathology-positive cases were missed by serum PIVKA-II alone. This is not unexpected given that the levels of the biomarkers can fluctuate with the size of the tumour, the biology of the tumour, the stage of the disease, the underlying liver function, and the assay cut-off value. PIVKA-II sensitivity can be lower in very small tumors, particularly when the diameter of the tumor is less than 2 cm, with reported sensitivity of 30%-53%. The result of the present study confirms that in cases of suspicion, PIVKA-II should not be used as a substitute for histopathology or imaging, particularly when the lesion is small, or if the clinical suspicion persists despite a negative biomarker result [17].

Our outcome is also similar to the local evidence. Study concluded that PIVKA-II with a cut-off value of 62.5mAU/ml was sensitive 62%, specific 91%, had a PPV of 81% and an NPV of 74% in the diagnosis of hepatocellular carcinoma in patients with liver nodules and cirrhosis. The values of the present study are very close to the above values as in the present study, sensitivity is 61.7%, specificity is 91.2%, PPV is 85.3% and NPV is 74.3% [18]. This similarity increases the value of PIVKA-II in a local population of Pakistani cirrhosis patients with possible liver lesions [19].

In this study, lesion size was significantly associated with histopathological confirmation of HCC; that is, HCC was more likely to occur in patients with lesions > 3 cm. This is biologically plausible: the larger the lesion, the more likely that it will develop into a malignancy and the more likely it is to have elevated levels of the biomarkers. Recent studies also indicated that PIVKA-II is associated not just with the diagnosis, but also with the tumor burden and more aggressive tumor behavior. In addition to diagnosis, some studies have shown PIVKA-II to be related to vascular invasion, tumor progression, and to the risk of recurrence [9, 20].

PIVKA-II was found to be quite sensitive in this study, but moderate and should therefore be used with caution. Patients with a negative PIVKA-II may still have HCC, although this is relatively rare, especially if the lesion is radiologically suspicious and the patient has cirrhosis. Recently, the combined use of biomarkers has been increasingly stressed, as it may enhance diagnostic yield. There are several studies demonstrating the superior performance of PIVKA-II in combination with AFP, AFP-L3, GP73 or clinical prediction models as compared to respective single biomarkers. Hence, PIVKA-II may be best used in conjunction with other tests rather than as a single test.

There are some limitations in the present study. It was carried out in one center, so the results do not necessarily reflect the situation of all cirrhotic patients in other hospitals or geographical areas. A fixed cut off value for PIVKA-II was also used in the study, which may not be optimal for various populations and various assay methods. Furthermore, the study primarily evaluated the accuracy of the diagnosis and failed to explore outcomes of interest including recurrence, survival, treatment response, and liver disease progression. Future multicenter studies with a larger number of patients should assess the usefulness of PIVKA-II along with AFP, AFP-L3, imaging findings and clinical scoring systems to achieve better early diagnosis of HCC in Pakistani patients.

CONCLUSION

Serum PIVKA-II showed good diagnostic performance for the detection of hepatocellular carcinoma in patients with liver cirrhosis, with high specificity, good positive predictive value, and acceptable overall diagnostic accuracy. The

high specificity indicates that a positive PIVKA-II result strongly supports the diagnosis of hepatocellular carcinoma. However, the moderate sensitivity suggests that a negative result cannot safely exclude HCC. Therefore, serum PIVKA-II may be used as a useful supportive diagnostic marker, but it should be interpreted along with clinical assessment, imaging findings, and histopathological confirmation where required. Further multicenter studies are recommended to validate its role in routine HCC diagnostic protocols in Pakistan.

REFERENCES

1. Feng H, Li B, Li Z, Wei Q, Ren LJBC. PIVKA-II serves as a potential biomarker that complements AFP for the diagnosis of hepatocellular carcinoma. 2021;21(1):401 doi.
2. Suttichaimongkol T, Mitpracha M, Tangvoraphonkchai K, Sadee P, Sawanyawisuth K, Sukeepaisarnjaroen WJJoCB. PIVKA-II or AFP has better diagnostic properties for hepatocellular carcinoma diagnosis in high-risk patients. 2023;12:12 doi.
3. Tian S, Chen Y, Zhang Y, Xu XJJocla. Clinical value of serum AFP and PIVKA-II for diagnosis, treatment and prognosis of hepatocellular carcinoma. 2023;37(1):e24823 doi.
4. Si Y-Q, Wang X-Q, Fan G, Wang C-Y, Zheng Y-W, Song X, et al. Value of AFP and PIVKA-II in diagnosis of HBV-related hepatocellular carcinoma and prediction of vascular invasion and tumor differentiation. 2020;15(1):70 doi.
5. Chan HL, Vogel A, Berg T, De Toni EN, Kudo M, Trojan J, et al. Performance evaluation of the Elecsys PIVKA-II and Elecsys AFP assays for hepatocellular carcinoma diagnosis. 2022;6(5):292-300 doi.
6. Hadi H, Wan Shuaib WMA, Raja Ali RA, Othman HJM. Utility of PIVKA-II and AFP in differentiating hepatocellular carcinoma from non-malignant high-risk patients. 2022;58(8):1015 doi.
7. Kobeissy A, Merza N, Al-Hillan A, Boujemaa S, Ahmed Z, Nawras M, et al. Protein induced by vitamin K absence or antagonist-ii versus alpha-fetoprotein in the diagnosis of hepatocellular carcinoma: a systematic review With Meta-Analysis. 2023;15(7):343 doi.
8. Basile U, Miele L, Napodano C, Ciasca G, Gulli F, Pocino K, et al. The diagnostic performance of PIVKA-II in metabolic and viral hepatocellular carcinoma: a pilot study. 2020;24(24) doi.
9. Hamzah N, Kassim NK, Omar J, Abdullah MS, Lee YYJP. Levels of PIVKA-II and alpha-fetoprotein in unresectable hepatocellular carcinoma compared to healthy controls and predictive values of both markers with radiological responses after loco-regional interventions. 2023;11:e15988 doi.
10. Devillers MJ, Pluimers JK, van Hooff MC, Doukas M, Polak WG, de Man RA, et al. The role of PIVKA-II as a predictor of early hepatocellular carcinoma recurrence-free survival after liver transplantation in a low alpha-fetoprotein population. 2023;16(1):4 doi.
11. Liu S, Sun L, Yao L, Zhu H, Diao Y, Wang M, et al. Diagnostic performance of AFP, AFP-L3, or PIVKA-II for hepatitis C virus-associated hepatocellular carcinoma: a multicenter analysis. 2022;11(17):5075 doi.
12. Xu F, Zhang L, He W, Song D, Ji X, Shao JJDm. The diagnostic value of serum PIVKA-II alone or in combination with AFP in Chinese hepatocellular carcinoma patients. 2021;2021(1):8868370 doi.
13. Lee Q, Yu X, Yu WJJoIM. The value of PIVKA-II versus AFP for the diagnosis and detection of postoperative changes in hepatocellular carcinoma. 2021;4(2):77-81 doi.
14. Degasperi E, Perbellini R, D'Ambrosio R, Uceda Renteria SC, Ceriotti F, Perego A, et al. Prothrombin induced by vitamin K absence or antagonist-II and alpha foetoprotein to predict development of hepatocellular carcinoma in Caucasian patients with hepatitis C-related cirrhosis treated with direct-acting antiviral agents. 2022;55(3):350-9 doi.
15. Zhang S-g, Huang YJLM. Usefulness of AFP, PIVKA-II, and their combination in diagnosing hepatocellular carcinoma based on upconversion luminescence immunochromatography. 2022;53(5):488-94 doi.
16. Toan BN, Tan C-K, Hasan I, Setiawan L, Yu M-L, Izumi N, et al. Utility of combining PIVKA-II and AFP in the surveillance and monitoring of hepatocellular carcinoma in the Asia-Pacific region. 2023;29(2):277 doi.
17. Ji J, Liu L, Jiang F, Wen X, Zhang Y, Li S, et al. The clinical application of PIVKA-II in hepatocellular carcinoma and chronic liver diseases: A multi-center study in China. 2021;35(11):e24013 doi.
18. Husnain F, Khan MD, Chughtai OR, Chughtai AS, Ashraf S, Yar A. Serum PIVKA-II: reference interval of healthy population and establishment of its cutoff value for hepatocellular carcinoma diagnosis in Pakistan. 2021 doi.
19. Chen J, Tang D, Xu C, Niu Z, Li H, Li Y, et al. Evaluation of serum GDF15, AFP, and PIVKA-II as diagnostic markers for HBV-associated hepatocellular carcinoma. 2021;52(4):381-9 doi.
20. Ren T, Hou X, Zhang X, Chen D, Li J, Zhu Y, et al. Validation of combined AFP, AFP-L3, and PIVKA II for diagnosis and monitoring of hepatocellular carcinoma in Chinese patients. 2023;9(11) doi.