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Utility of PIVKA-II in Non-hepatocellular Carcinoma Patients with Elevated Alpha-fetoprotein.

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Background & Objective

- Serum alpha-fetoprotein (AFP) is the most used biomarker for hepatocellular carcinoma (HCC) surveillance.
- Benign elevation of AFP can occur in situations such as necroinflammation of the liver.
- False elevation of AFP may lead to unwarranted evaluations for HCC, causing unnecessary stress in the patients.
- Protein induced by vitamin K absence of antagonist-II (PIVKA-II) is a newer biomarker for HCC. It is an abnormal prothrombin precursor found in the presence of HCC.
- We studied and compared the utility of PIVKA-II to confirm false elevation of AFP in patients without HCC, by using three different commercially available assays.

Methods

- Patients undergoing HCC surveillance at Singapore General Hospital were recruited between December 2017 and October 2018.
- Baseline serum specimens were collected at the time of surveillance together with routine ultrasound imaging.
- The serum specimens were tested using Abbott ARCHITECT®, Roche Elecsys® and Fujifilm µTASWako® assays for AFP and PIVKA-II respectively.
- Cut-off AFP assay for Abbott, Roche, and Fujifilm was 8.78ng/ml, 7.0ng/ml, and 10.0ng/ml respectively.
- Cut-off PIVKA-II assay for Abbott, Roche, and Fujifilm was 40mAu/ml, 28.5ng/ml, and 40mAu/ml respectively.
- Patients with conditions associated with false elevations of PIVKA-II were excluded from the analysis.

Results

- In the Abbott ARCHITECT® cohort, 20 patients had high AFP with only 1 of these patients having high PIVKA-II.
- In the Roche Elecsys® cohort, 12 patients had high AFP of which only 1 patient had concomitant high PIVKA-II.
- In the Fujifilm µTASWako® cohort, there were 6 patients with high AFP but none of them had elevated PIVKA-II.
- Thus, the sensitivity of a normal PIVKA-II assay in refuting an elevated AFP was 95.0%, 91.7% and 100% using the Abbott ARCHITECT®, Roche Elecsys® and Fujifilm µTASWako® assays respectively.

	Abbott (n=597)	Roche (n=279)	Fujifilm (n=187)
Gender, male(%)	362 (60.6)	162 (58.1)	100 (53.5)
Age, median (IQR)	65 (14)	57 (14)	57 (14)
Aetiology, HBV(%)	542 (90.7)	256 (91.8)	137 (73.3)
No. of patients with abnormal AFP (%)	20 (3.4)	12 (4.3)	6 (3.2)
No of patients with abnormal AFP but normal PIVKA-II (%)	19 (95.0)	11 (91.7)	6 (100)

Conclusion

- Inclusion of a PIVKA-II measurement using any of the commercially available assays was shown to be useful in confirming false positive AFP in our study cohort.
- PIVKA-II measurement can be considered in patients with raised AFP to minimise unwarranted extensive investigations.