

Supplementary materials to:

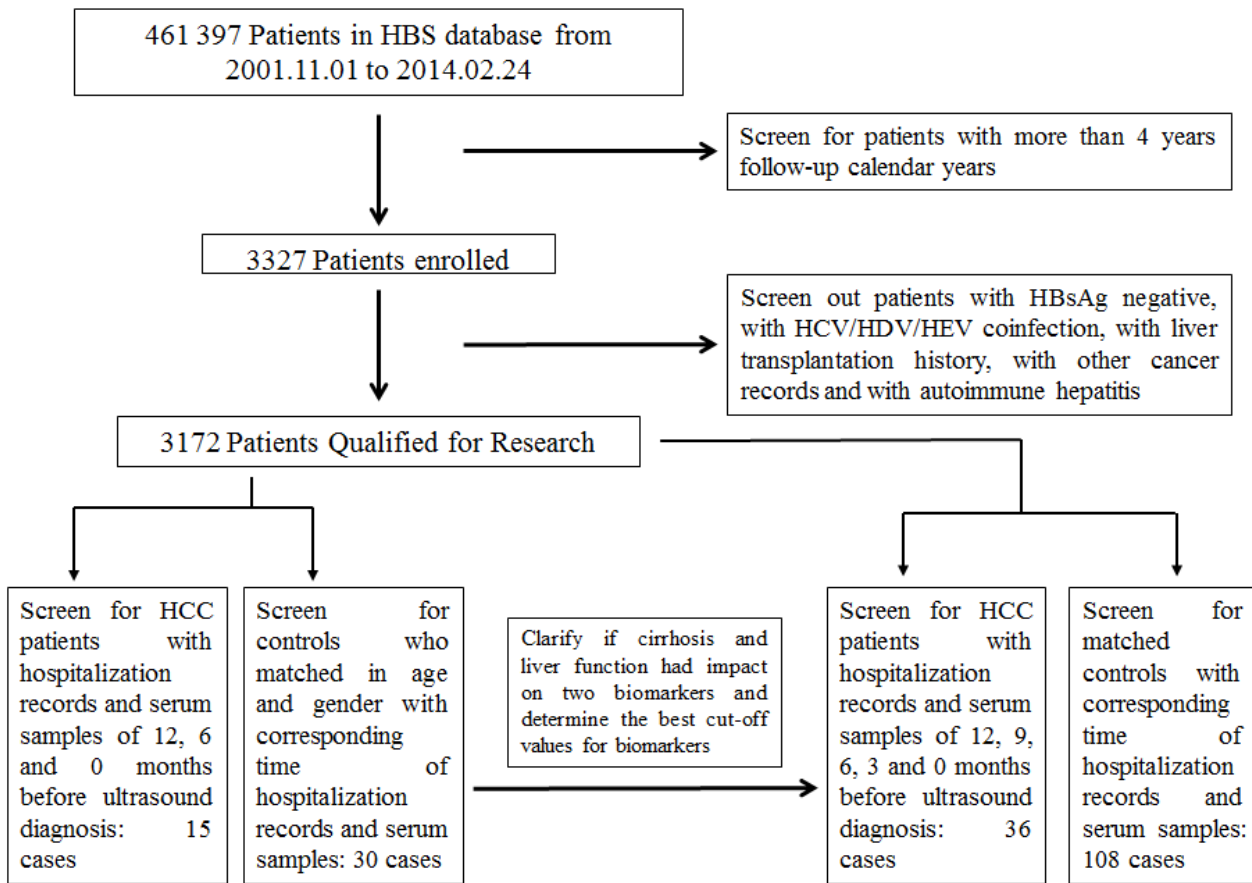
**Efficacy of PIVKA-II in prediction and early detection of hepatocellular carcinoma:  
a nested case-control study in Chinese patients**

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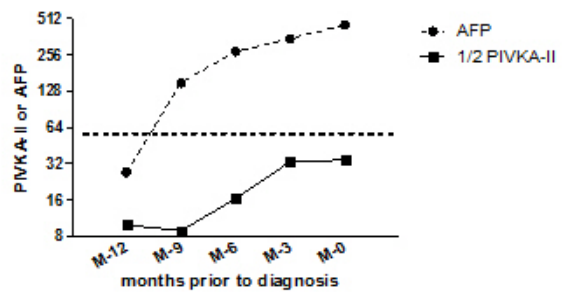
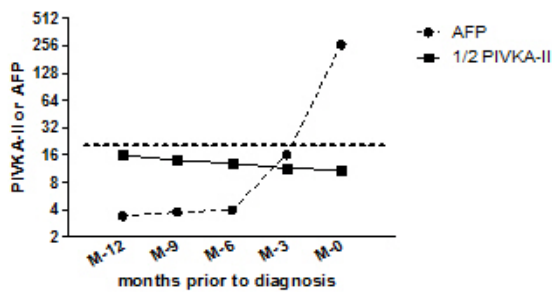
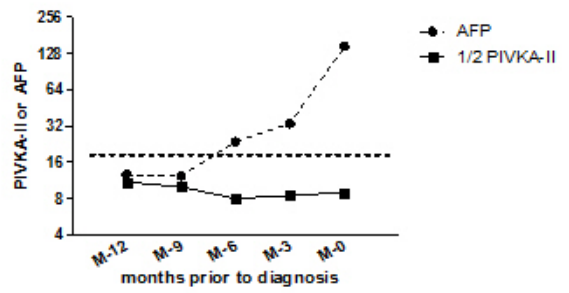
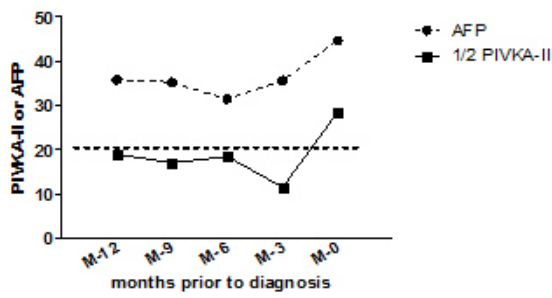
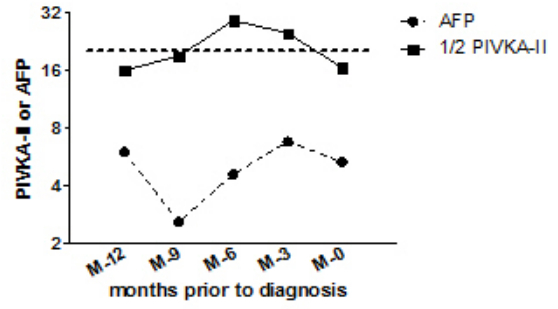
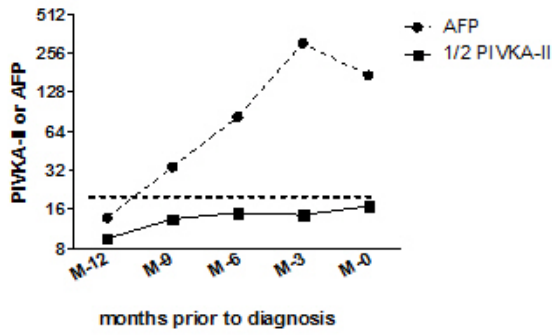
**Supplementary Fig. 1 Flow chart representing the selection procedure based on the HBS cohort**

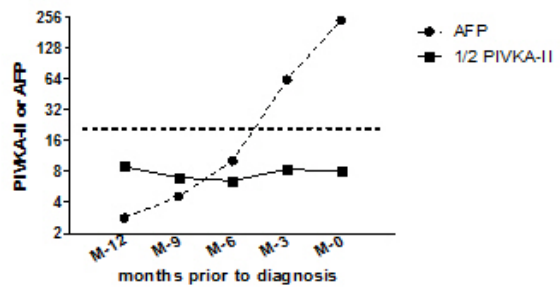
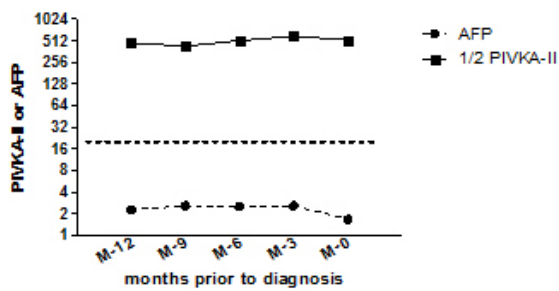
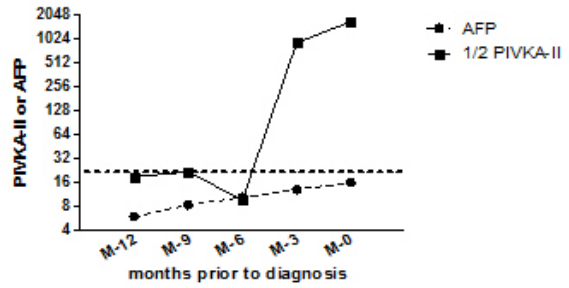
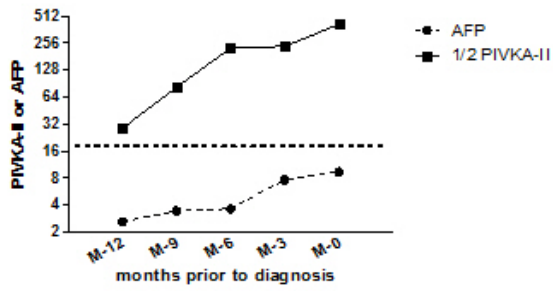
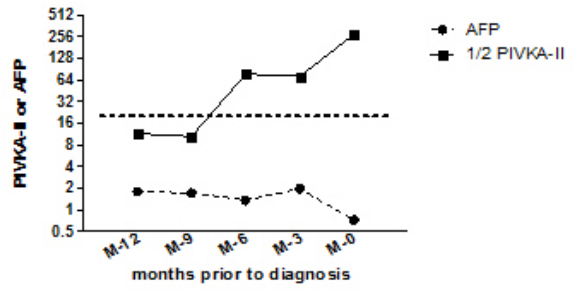
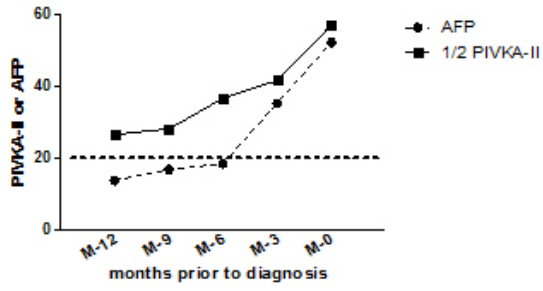
**dataset.** All HCC patients were checked for hospitalization records and sera samples and patients with regular follow-up records were selected for use. Totally, 51 cases (most were early-stage HCC) were qualified. In the end, 15 cases with -12, -6 and 0 months before diagnosis were classified into discovery stage and for each case, 2 controls were selected from the same cohort dataset for matching. So did the validation stage, but there were 1:3 matched controls in validation stage.

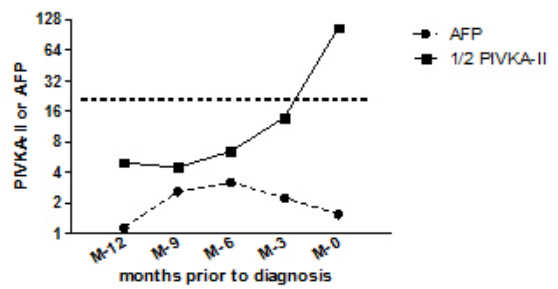
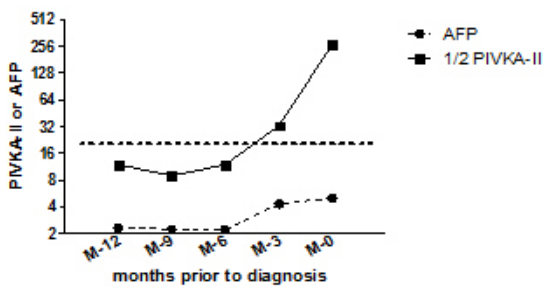
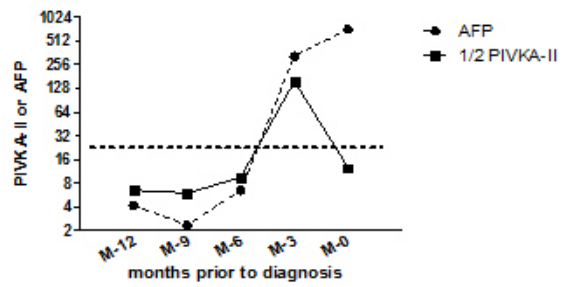
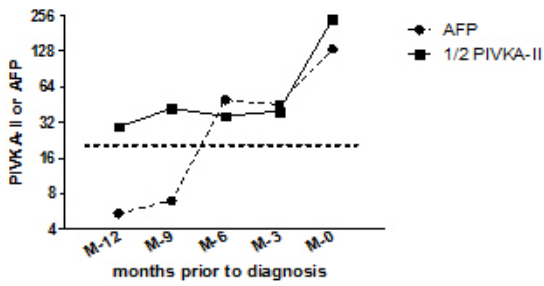
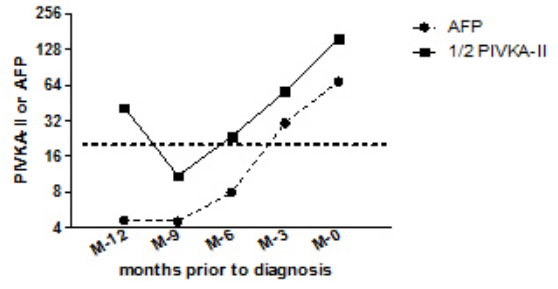
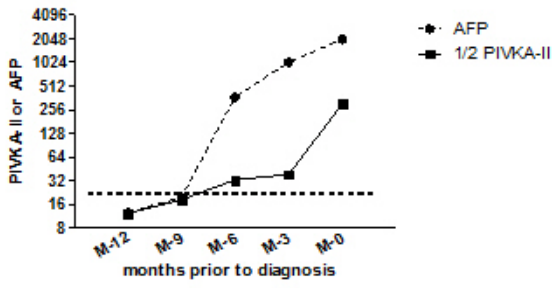
**Supplementary Table 1** Multivariable analysis of HCC in discovery stage.

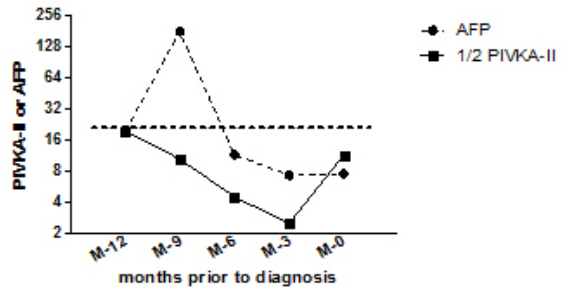
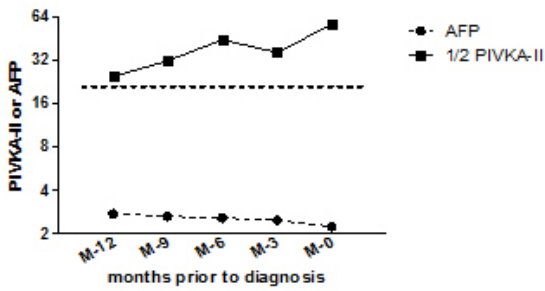
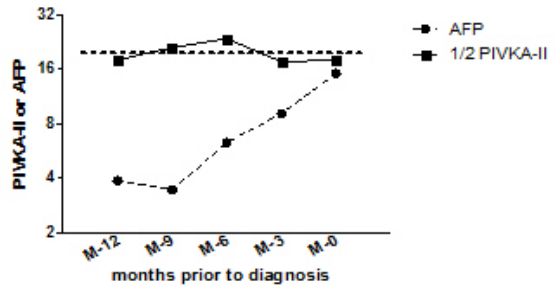
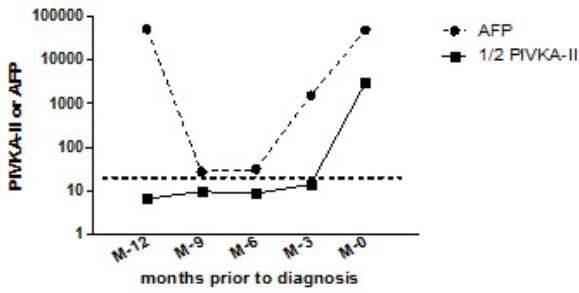
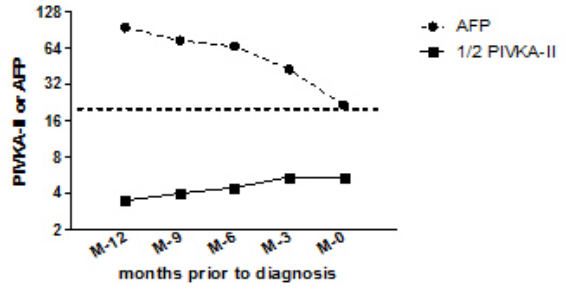
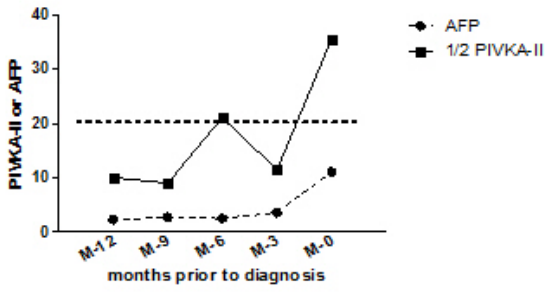
	<b>AFP</b>	<b>PIVKA</b>	<b>gender</b>	<b>age</b>	<b>cirrhosis</b>	<b>AST</b>	<b>ALT</b>	<b>ALP</b>	<b>TBIL</b>	<b>TBA</b>	<b>TP</b>	<b>IgDNA</b>
<b>P</b>	0.019	0.022	0.921	0.261	0.473	0.212	0.296	0.142	0.518	0.632	0.12	0.398
<b>OR</b>	11.086	11.023	0.002	0.912	7.528	0.808	1.327	0.928	1.1	0.93	2.292	0.522
<b>95% CI</b>	0.893	0.986	4.77E-57	0.776	3.55	0.578	0.78	0.84	0.824	0.692	0.805	0.116
	1.321	1.062	8.28E+50	1.071	13.845	1.13	2.258	1.025	1.468	1.25	6.526	2.358

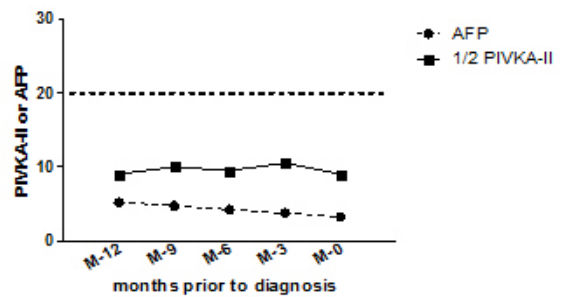
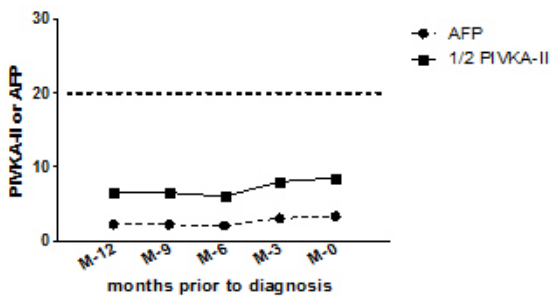
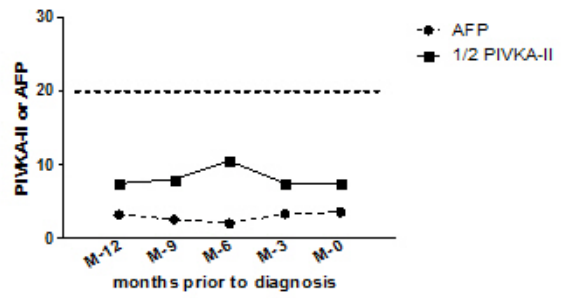
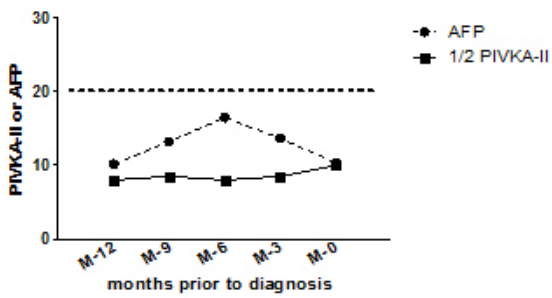
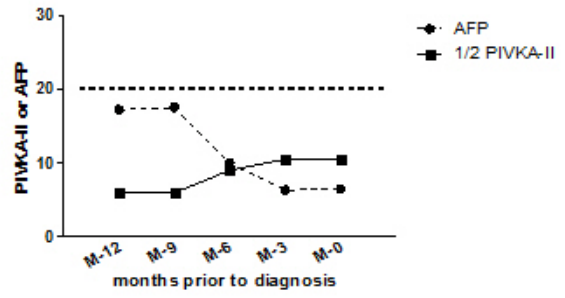
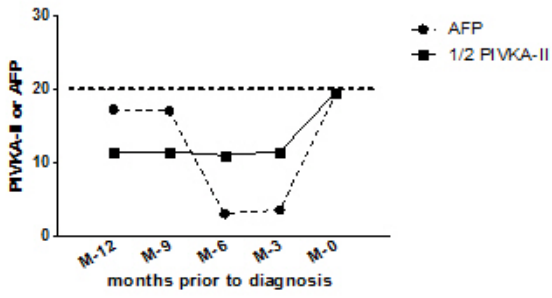
In this binary logistic regression, the state of HCC was set as dependent variable, and biomarkers, cirrhosis basis and bio-parameters reflecting liver function were set as covariates. AFP and PIVKA-II were risk factors for HCC and P values were below 0.05. OR, odds ratio; CI, confidential interval.



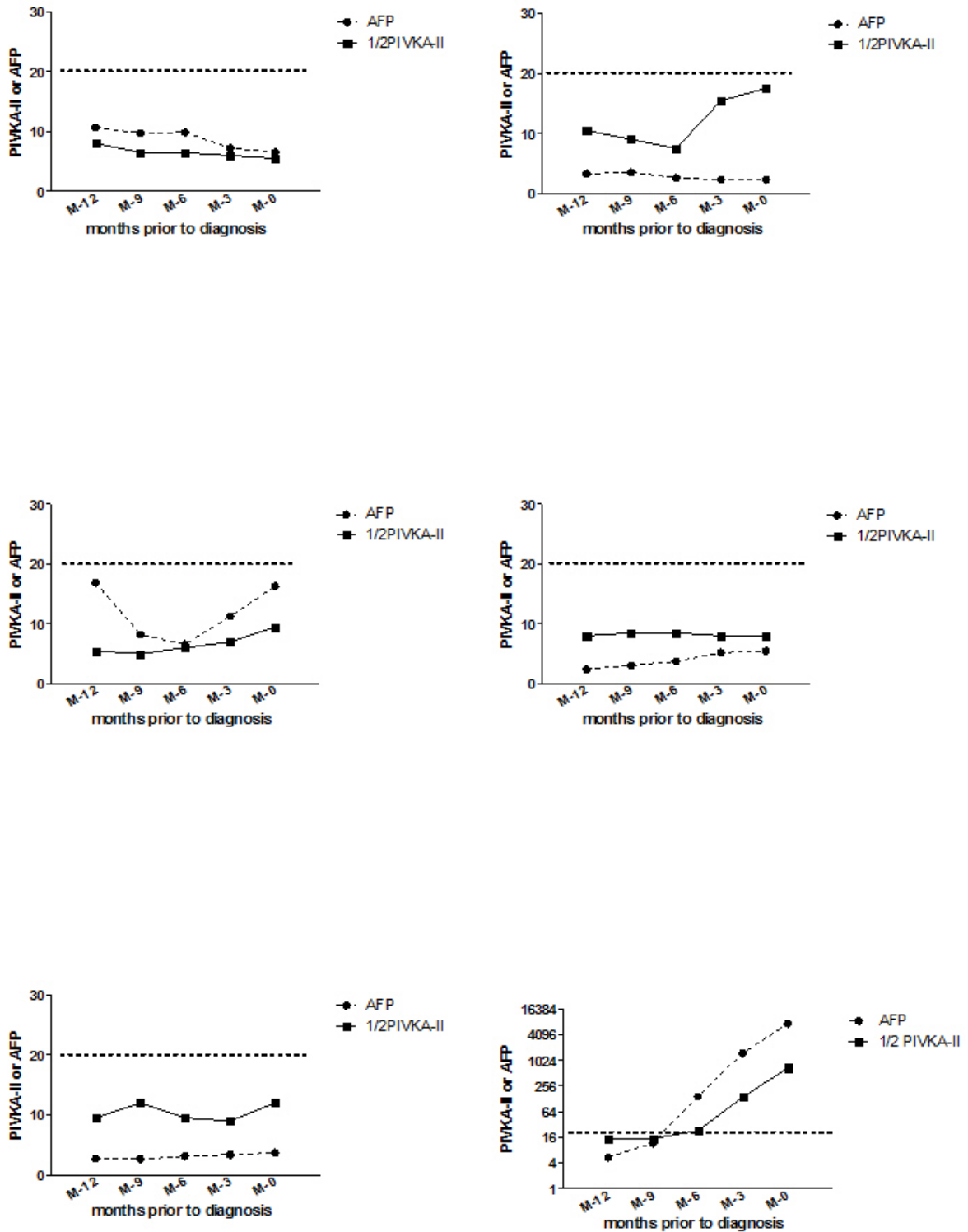












**Supplementary Fig. 2** Chang trends of AFP and PIVKA-II serum level in each HCC patients at **validation stage**. Each figure shows the change trend of biomarkers' trend of a HCC patient from 12 months prior to diagnosis to the diagnosis time. The horizontal dotted line refers to the cut-off value. PIVKA-II levels were reduced to 1/2 so as to keep a same cut-off value as AFP. PIVKA-II: Protein Induced by Vitamin K Absence or Antagonist-II; AFP:  $\alpha$ -fetoprotein.