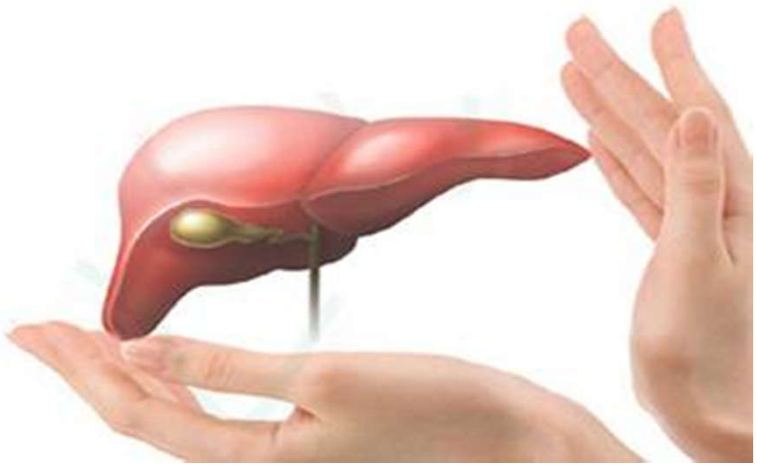
Medic Center

NEW MARKER M2BPGi IN LIVER FIBROSIS EVALUATION-

EXPERIENCE IN CLINICAL PRACTICE



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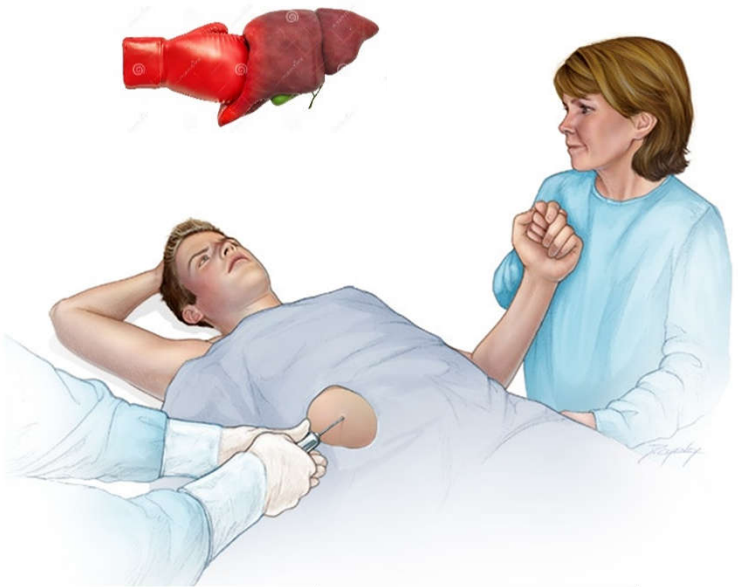
I.Methods of evaluation of liver fibrosis in Vietnam

WHY WE NEED STAGING FOR LIVER FIBROSIS

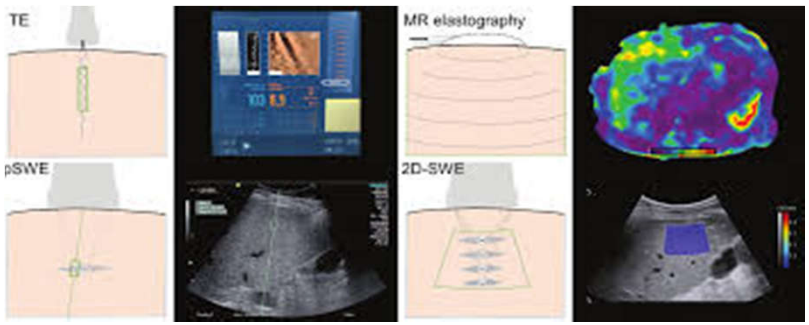
- 1. Assess stage and prognosis of disease
- 2. Decide on treatment (In case the treatment is costly and has many side effects)
- 3. Monitor and assess effectiveness of treatment
- 4. Detect HCC early and make differential diagnosis of liver tumor.

METHODS OF EVALUATION OF LIVER FIBROSIS

Liver Biopsy.



Serum Biomarkers & Elastography.



Serum Biomarkers used in Vietnam

1. APRI
2. FiB4
3. Fibrotest & Actitest
4. New: M2BPGi

II. M2BPGi is useful in evaluation of effective treatment

Mak et al. *Clinical and Translational Gastroenterology* (2018)9:163
DOI 10.1038/s41424-018-0020-9

Clinical and Translational Gastroenterology

ARTICLE Open Access

Role of serum M2BPGi levels on diagnosing significant liver fibrosis and cirrhosis in treated patients with chronic hepatitis B virus infection

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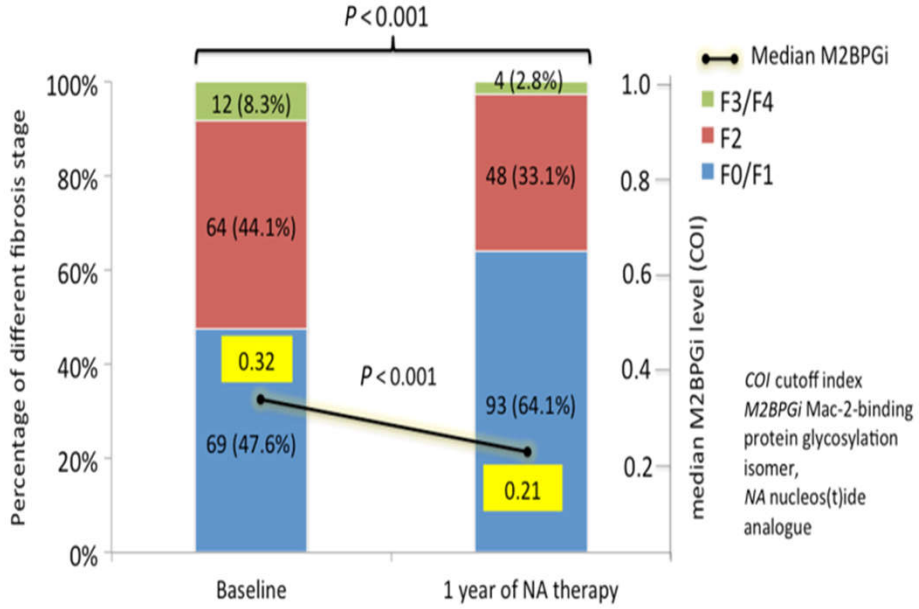
Retrospective
Patients: 327 HBV, NA-treated
1994 – 2013, Hong Kong

Identify fibrosis : Biopsy
(All samples of biopsy: pos+ staining for HBsAg)

Evaluate fibrosis: Ishak Score



Median M2BPGi levels (COI) according to fibrosis stage at baseline and year 1

Fig. 4 Distribution of fibrosis stage and median serum M2BPGi level at baseline and after 1 year of nucleos(t)ide analogue therapy

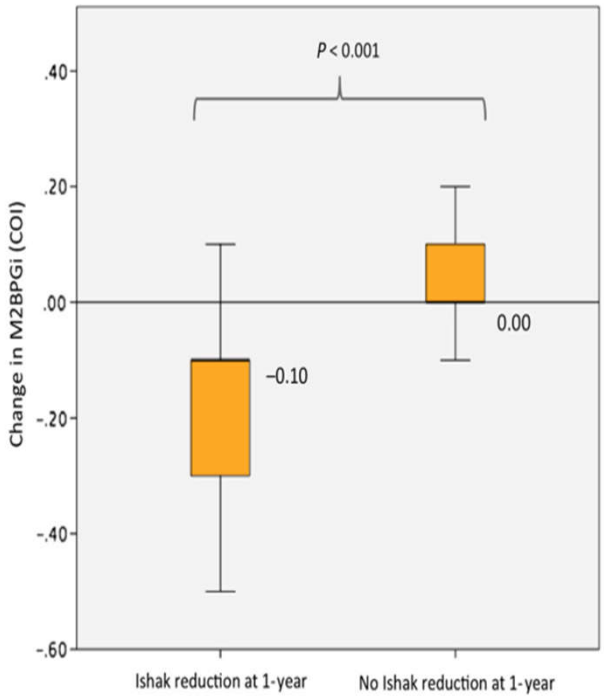


Fig. 5 Change of serum M2BPGi levels after 1 year of nucleos(t)ide analogue therapy with respect to change in histological fibrosis stage

Case 1: Chronic hepatitis C- Patient monitoring

- 76 year-old man
- Significant alcohol consumption (>30 years)
- To quit alcohol after being diagnosed with hepatitis C (HCV) in 2010- No HBV
- No operation in the past
- Brother: HCV
- Stable hypertension
- Refused anti- viral treatment due to financial reason.

Case 1: Chronic hepatitis C- Patient monitoring

- Received anti-viral treatment for HCV in 2020

Treatment regime: 12 weeks

Sofosbuvir 400mg

Velpatasvir 100mg

Case 1: Chronic hepatitis C- Patient monitoring

Diagnosed with HCV	Treatment initiation (August 2020)	End of treatment (EOT)	12 weeks after EOT (SVR 12)
Liver enzymes AST(U/L)	74	30	27
ALT (U/L)	78	32	28
Tumor marker AFP (ng/mL)	3.2	2.5	2.1
Viral load HCVRNA (IU/mL)	19,300,000	Negative	Negative
Genotype 1			
Fibrosis Marker : M2BPGi	3.24	1.50	1.14
Ultrasound : Doppler	Cirrhosis	Chronic hepatitis	Chronic hepatitis
Elastography: FibroScan(kPa)	17.3	16.9	16.5

Case 1: Chronic hepatitis C- Patient monitoring FibroScan

3 months of treatment

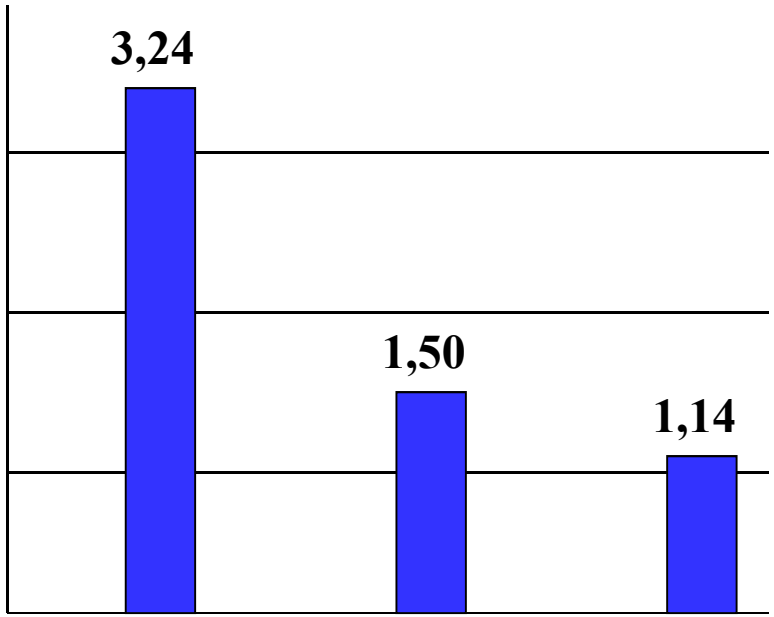
3 months of follow up

F4: 17.3 kPa

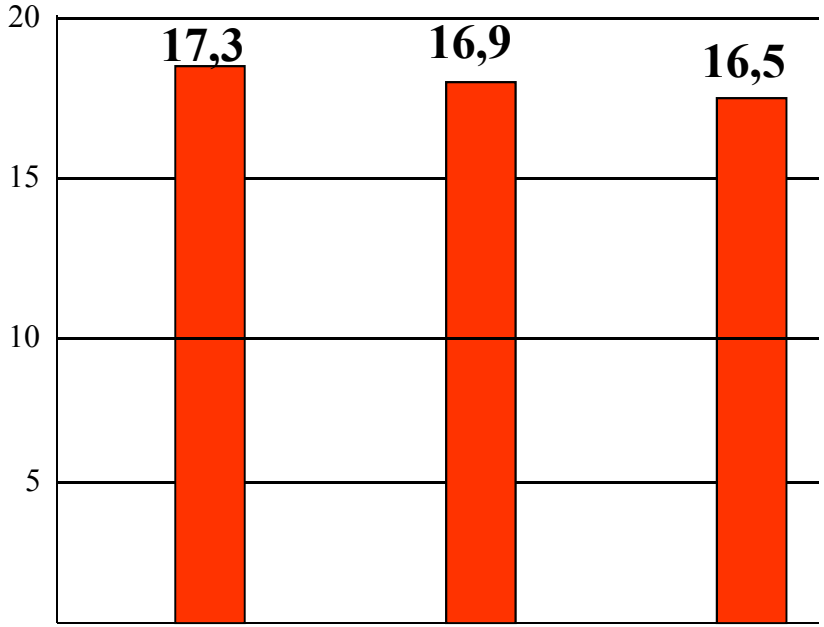
F4: 16.9 kPa

F4: 16.5 kPa

Evaluation improvement of liver fibrosis after 3 months of treatment- Comparison between M2BPGi & FibroScan



M2BPGi every 3 months



FibroScan every 3 months

Case 1: Chronic hepatitis C- Patient monitoring

Comments:

- M2BPGi is a dynamic test that can reflect the liver fibrosis progression . M2BPGi levels can be more reflective liver fibrosis activation process, while imaging methods measure liver stiffness which is not dynamic and might be not changing.

- M2BPGi can represent the liver fibrosis of the whole liver rather than a specific area of liver fibrosis.

III. M2BPGi can predict HCC developments

Reference	Etiology	Treatment status	Threshold of M2BPGi for HCC risk	HR (95% CI)
Yamasaki, *et al.* [31]	HCV		≥4	8.3 (1.8–38)
Tamaki, *et al.* [32]	HCV		≥4.2	4.1 (1.1–15)
			≥0.3 increase/yr	5.5 (1.5–19)
Inoue, *et al.* [36]	HCV		≥4 (mortality risk)	
Sasaki, *et al.* [48]	HCV SVR		≥2.0	5.7 (1.7–20)
Nagata, *et al.* [49]	HCV SVR		≥1.8	2.0 (1.4–2.4)
Yasui, *et al.* [50]	HCV SVR		≥1.75	6.0 (1.8–19)
Akuta, *et al.* [51]	HCV SVR		≥1.0	4.9 (1.4–18)
Ichikawa, *et al.* [53]	HBV	Naive	≥0.71	8.3 (1.0–67)
Jun, *et al.* [58]	HBV	Naive	Each 1 increase	1.1 (1.05–1.18)
Liu, *et al.* [62]	HBV	Naive	≥2.0 (1–2 yr HCC)	7.4 (2.4–23)
Kim, *et al.* [63]	HBV	Naive	≥1.8	1.5 (1.1–2.1)
Mak, *et al.* [64]	HBV	NA treatment	≥1.15 before NA treatment	1.2 (1.04–1.5)
Kawaguchi, *et al.* [65]	HBV	NA treatment	≥1.2 after NA treatment	10.5 (3.0–38)
Shinkai, *et al.* [66]	HBV	NA treatment	≥1.2 after NA treatment	5.0 (1.7–15)
Su, *et al.* [67]	HBV	NA treatment	Each 1 increase after NA treatment	1.6 (1.2–2.1)
Heo, *et al.* [68]	HBV	Naive/NA treatment	≥1.8	11.5 (1.4–97)
Mak, *et al.* [69]	HBV	Naive/NA treatment	≥0.68	4.7 (1.3–17)
Kawanaka, *et al.* [79]	NAFLD		≥1.255	1.7 (1.1–2.3)

Nobuharu Tamaki et al. Annals of Laboratory Medicine 2021

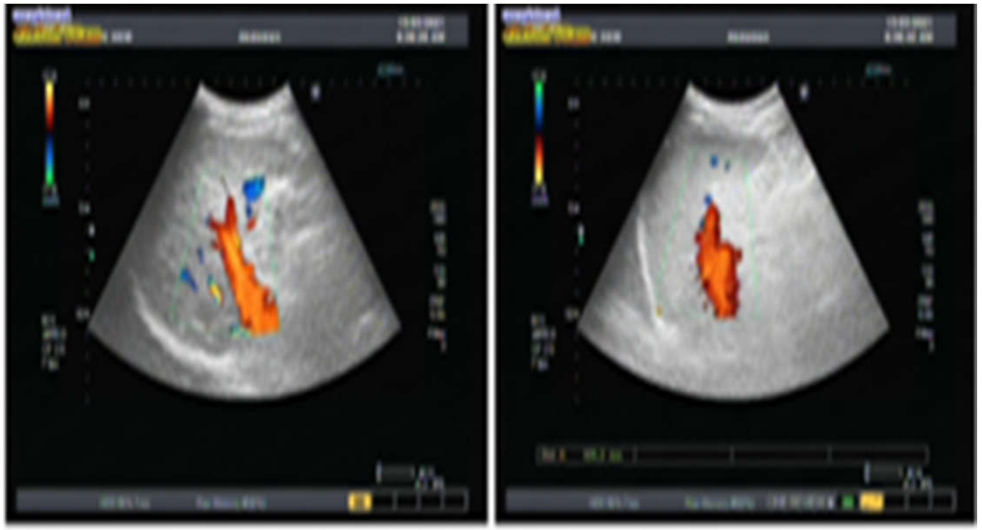
Case 2 :M2BPGi in predicting risk of HCC

- 44 year-old man
- Significant alcohol consumption (>20 years)
- Smoking (> 20 years, 5 cigarettes a day)
- Diabetes is stable
- Parents and two sisters: HBV
- Being diagnosed with hepatitis B in 2000- No HCV
- Refused treatment and visited doctor
- Pain in the right upper quarrant, fatigue----→ Medic Medical Center

Case 2 :M2BPGi in predicting risk of HCC

- HBsAg : Positive
- HBeAg : Positive
- AntiHBcIgM: Negative
- AntiHCV: Negative
- Ultrasound:

Cirrhosis with many regenerative nodules

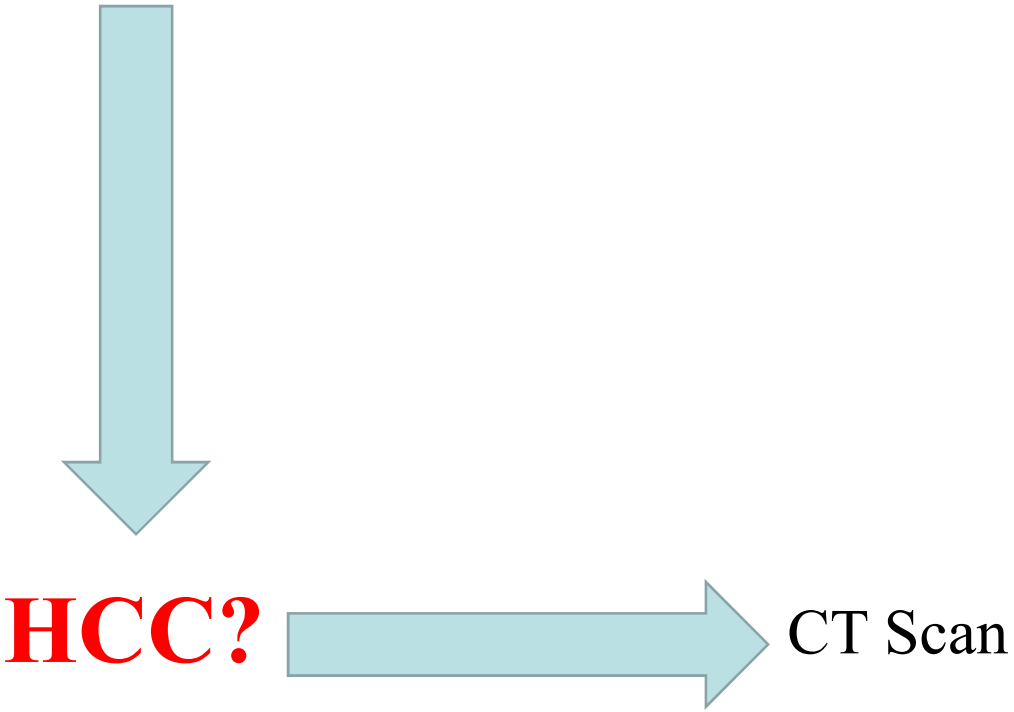


Case 2 :M2BPGi in predicting risk of HCC

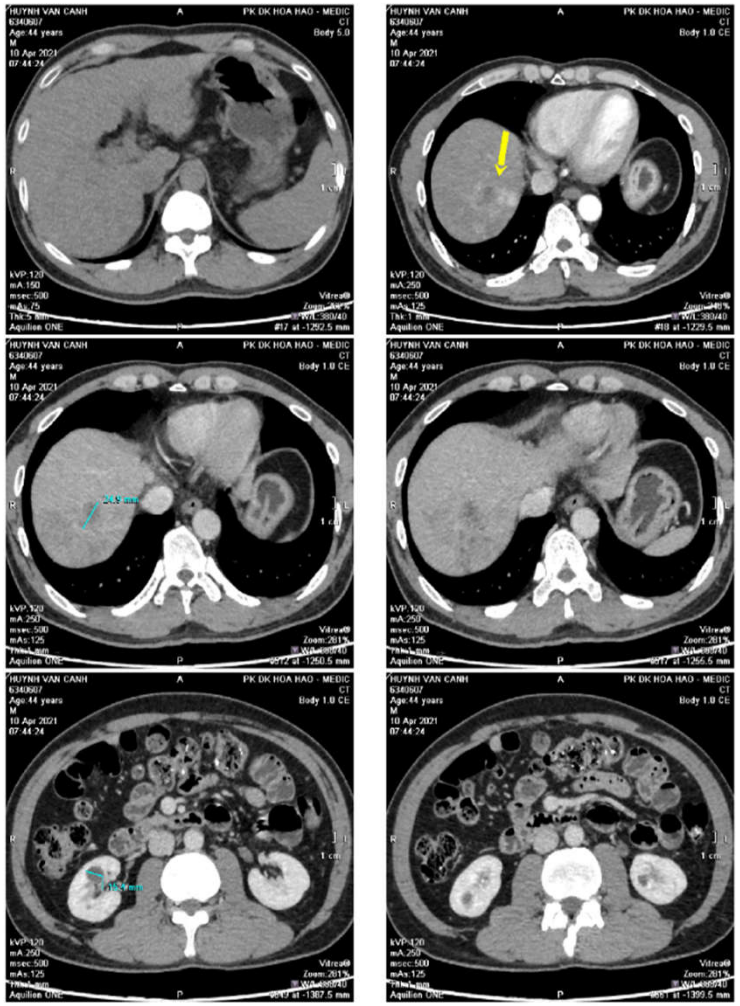
Diagnosed with HBV and cirrhosis	Treatment initiation (TDF)	After one month	
Liver enzymes AST(U/L)	54	52	
ALT (U/L)	57	55	
Tumor marker AFP (ng/mL)	12.4	14.7	???
Viral load HBV DNA (IU/mL)	162,740	Negative	
Fibrosis Marker : M2BPGi	3.21	3.8	???
Ultrasound : Doppler	Cirrhosis	Cirrhosis	???
Elastography: FibroScan (kPa)	18.5		

Case 2 :M2BPGi in predicting risk of HCC

- AFP-L3: 27.3%
- PIVKAII: 342 mAU/mL



Case 2 :M2BPGi in predicting risk of HCC
CT Scan



Some lesions 7-25mm ----HCC/ Chronic hepatitis

Case 2 :M2BPGi in predicting risk of HCC

Comments:

M2BPGi can predict HCC

A patient can have very small tumor which cannot be detected by ultrasound.

Chronic hepatitis + M2BPGGi----→ HCC???

IV. CONCLUSION

- Liver fibrosis progressing to cirrhosis is the leading cause of death in chronic liver diseases. Early evaluation of liver fibrosis is crucial.
- There are non-invasive techniques for evaluation liver fibrosis, each technique has it own advantages and disadvantages
- Clinicians use knowledge, experience and available techniques for suitable patients.
- M2BPGi is a useful and predictive serum marker for evaluating liver fibrosis and predicting HCC.
- M2BPGi has different cutoff points, up to causes, races, countries. Further studies on M2BPGi should apply to have more experiences.


Thank
You