Effectiveness of APRI score as a non-invasive marker of liver fibrosis in chronic hepatitis C infected patients

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Background

- Establishing the presence of liver fibrosis or cirrhosis is important in the management of Hepatitis C infection.
- Liver biopsy remains the gold standard to assess the degree of liver fibrosis.
- However, the utility of liver biopsy is limited by procedure discomfort, adverse events, sampling error and interpreter variability.
- So evaluation of hepatic fibrosis stage is done non-invasively using transient elastography (TE)/FibroScan, or serum biomarkers, etc.
- Access to FibroScan is limited by resources in many settings including in many places in our country.

Objective

- To evaluate the effectiveness of APRI score as a non-invasive marker of liver fibrosis compared to results of liver fibrosis assessments using FibroScan for chronic hepatitis C infected patients

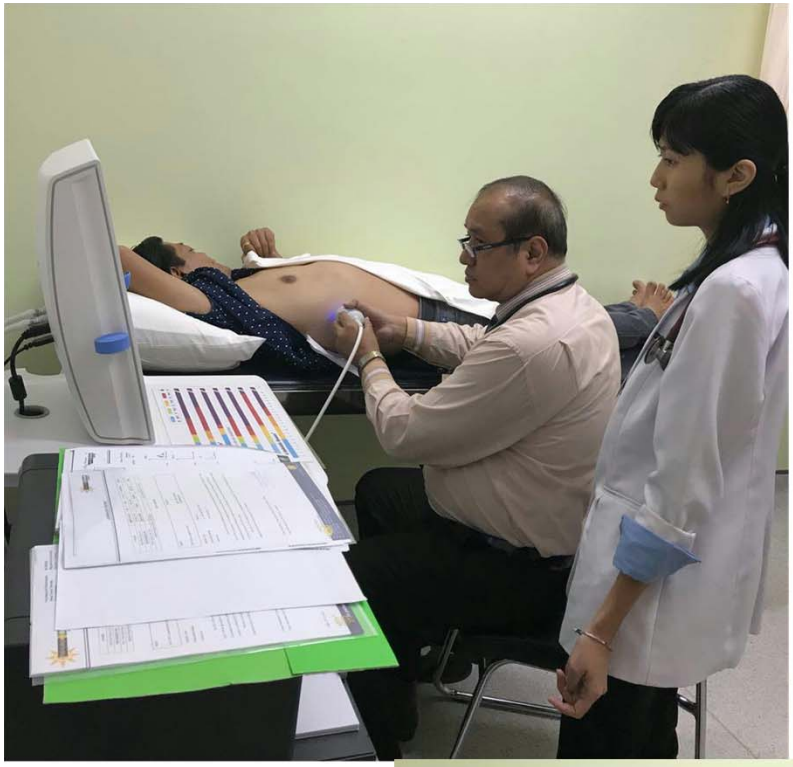
Methods

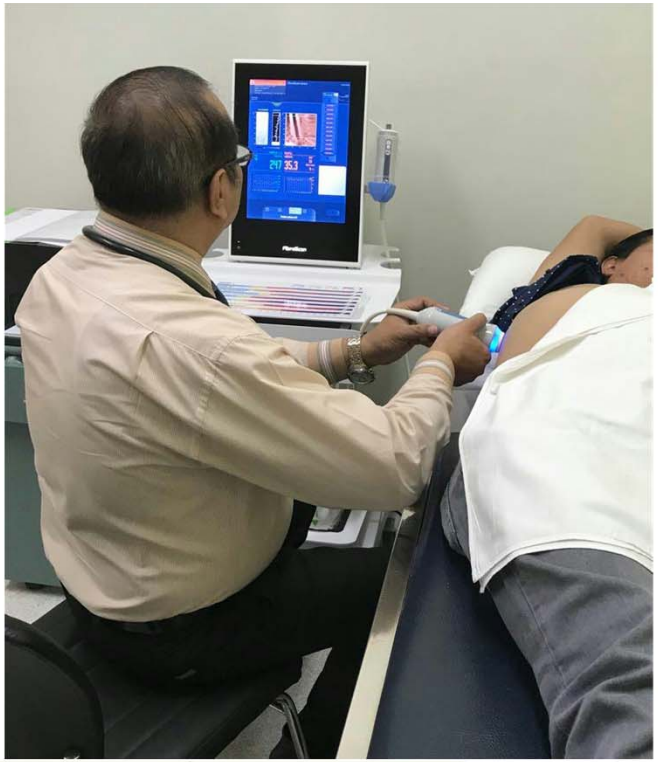
- This is the cross sectional descriptive study
- This study was conducted on Hepatitis C infected patients who underwent FibroScan examination between February 2017 and September 2017 in PunHlaing Siloam Hospital (PHSH), Yangon.
- Demographic data was collected including age, sex, and biochemical and hematological parameters were also determined.
- TE was performed on the FibroScan® (Echosens 530 compact) device according to the manufacturer's guidelines by Consultant Hepatologist Prof Kyaw Soe Tun.
- Participants were requested to fast for at least 2 hours prior to the examination.

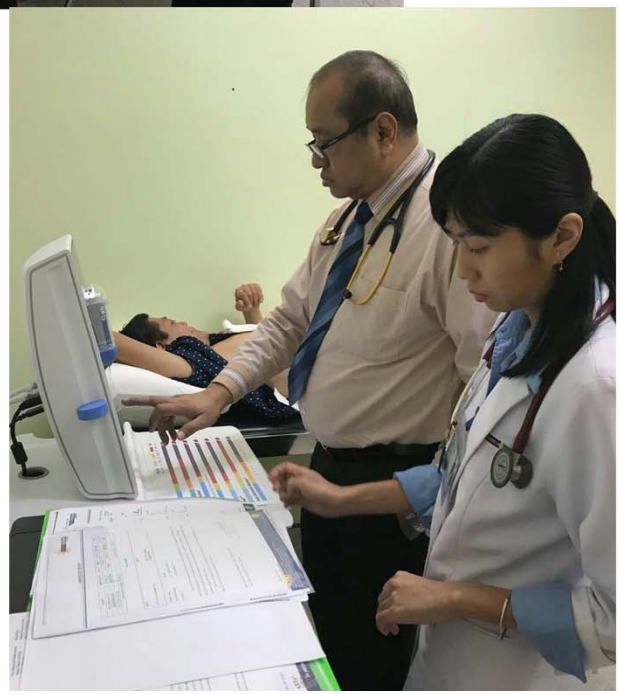
Transient Elastography (FibroScan)

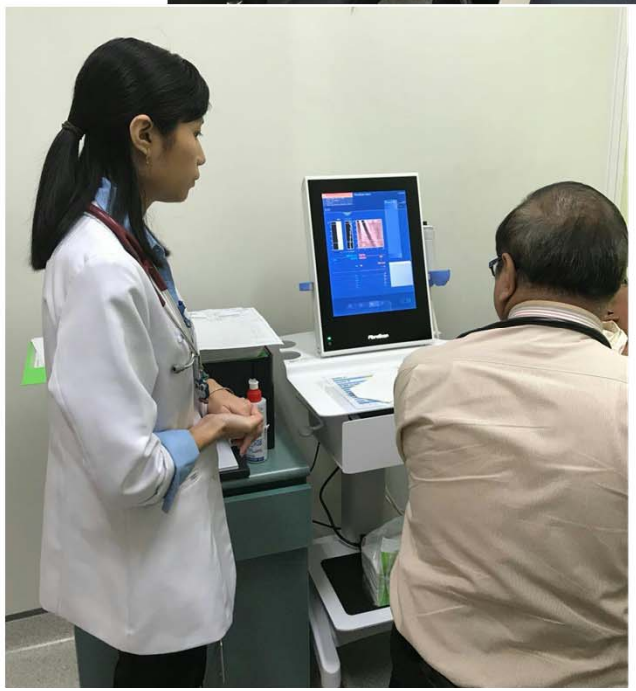
- Non-invasive ultrasound device to assesses Liver stiffness measurement (LSM) by measuring how quickly waves pass through the liver
- Most widely used non invasive method in Europe not only chronic hepatitis C but also other liver diseases with good diagnostic accuracy (sensitivity and specificity is more than 90%)[1]
- It is simple, painless and it takes less than ten minutes and produces immediate results
- LSM was performed in the right lobe of liver through the intercostal spaces, with the patient lying in the dorsal decubitus position, right arm in maximal abduction
- The results were expressed in kilopascals (kPa)

[1]Ref : Ann Gastroenterol. 2012; 25(3): 218–231.



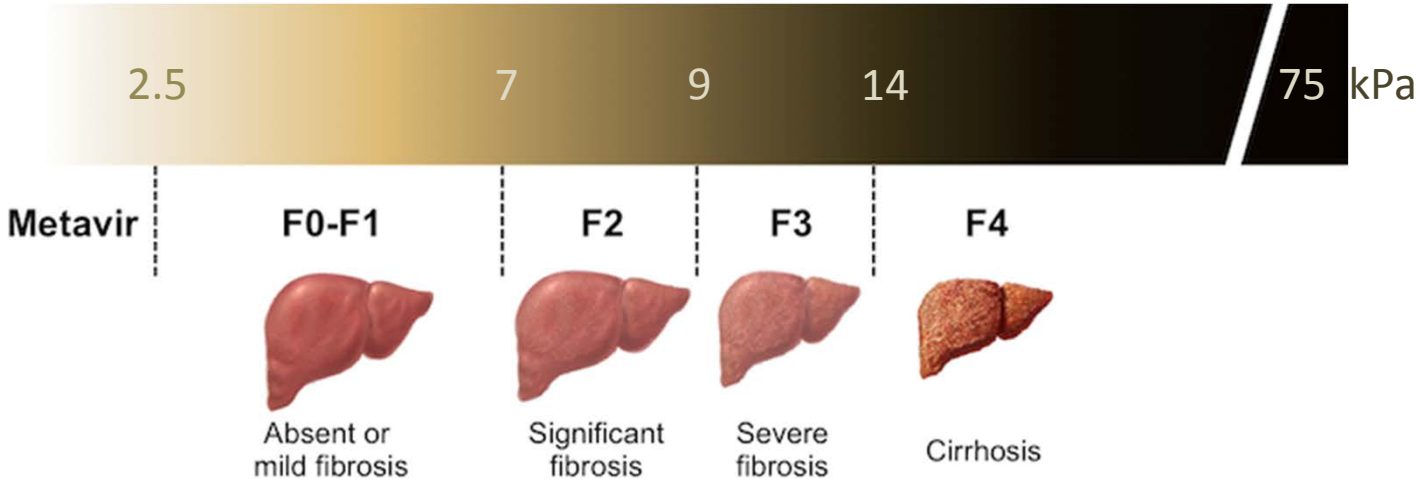


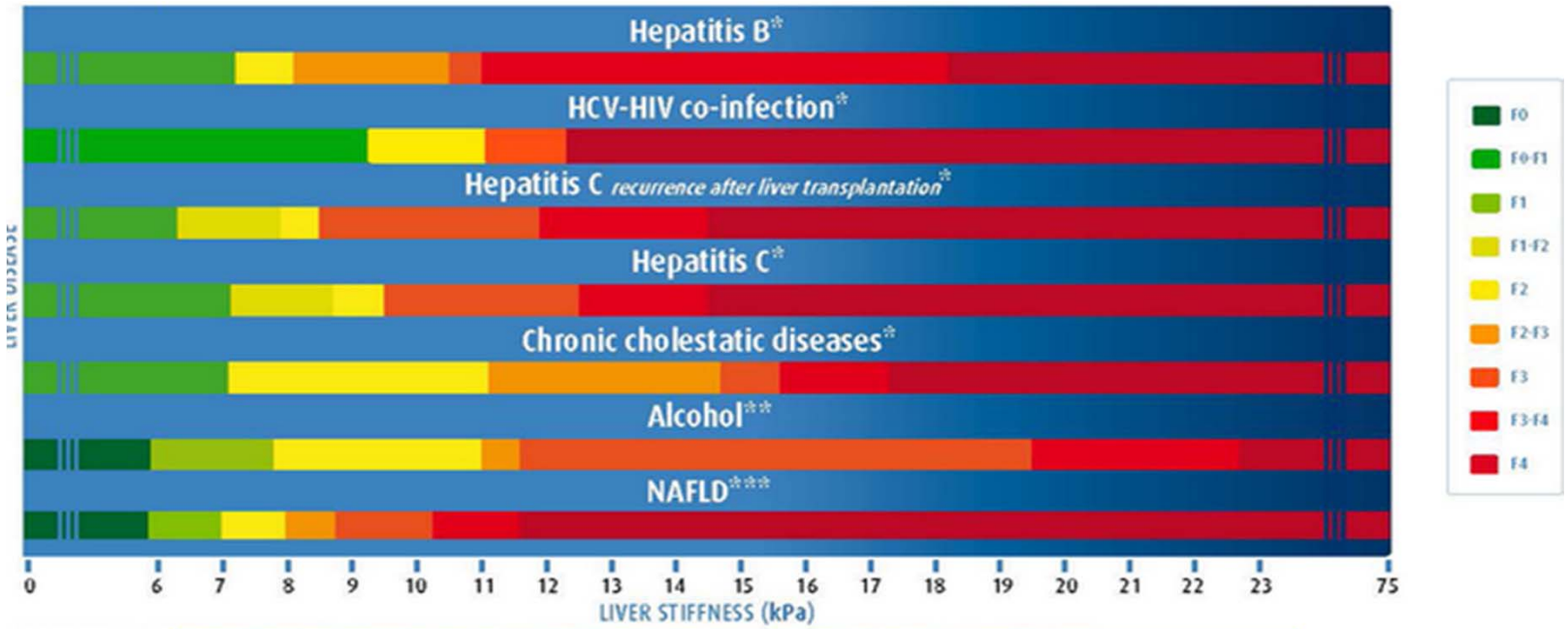




- The following stages of liver fibrosis were defined based on the references provided by manufacturer.
- Fibrosis stage was classified according to Metavia scoring system (F0-F4)

Metavia	Interpretation	kPa
F0-F1	Normal/mild fibrosis	< 7
F2	Significant fibrosis	7 to 8.9
F3	Advanced/ Severe fibrosis	9 to 13.9
F4	Cirhosis	≥ 14





Liver stiffness cut-offs in chronic liver diseases

Matavir	F0-F1	F2	F3	F4
Fibrosis	Mild	Sign	Severe	Cirrhosis

LSM 2.5 – 7 kPa → Mild or absent fibrosis is likely
LSM > 12.5 kPa → Cirrhosis is likely

Castéra L et al. J Hepatol 2008 ; 48 : 835 – 847.

AST to platelet ratio index (APRI) = $\frac{\text{AST/upper limit of normal}}{\text{Platelet count } (10^9/\text{L})} \times 100$

Based on 2011 meta analysis in Hepatology by lin et al:

APRI cutoffs predicted liver fibrosis in patients with hepatitis C as following.

Interpretation	APRI
Significant fibrosis	> 0.7 (77% sensitive and 72% specific)
Severe fibrosis/ cirrhosis	> 1 (76% sensitive and 72% specific)

- After taking informed consent, for each patient, APRI score was calculated from laboratory results of blood drawn within 90 days of TE and the result of APRI was compared with valid FibroScan score (10 readings>60% success; <25% IQR/median).
- XL probe was used for obese patients (BMI ≥ 30) according to the manufacturer guideline

FibroScan® compact 530

Exclusion criteria

- Chronic hepatitis B infection
- HIV infection
- Malignancy
- Immunosuppressive therapy
- Clinically significant cardiac and cardiovascular abnormalities
- Other autoimmue liver diseases
- Other causes of thrombocytopenia apart from liver disease

Results

- During the study period (February 2017 to September 2017), approximately 200 successful FibroScan examinations were performed at PHSH, approximately 35% of which are performed on chronic hepatitis C infected patients.
- In the final analysis, 55 patients were included, the mean ± standard deviation of the age of the respondents was 57.67± 11.384 and age group distributions were shown in table 1. Among those, 24 (44%) were male and 31 (56%) were female were shown in table 2 and with the age range of 28 to 81 years old.
- The collected datas were analysed using SPSS software

Demographic data in study population

Characteristics	**Chronic Hepatitis C infected patients (n=55)**
Median age (range), year	58 years (28-81)
Male Female	24 (44%) 31 (56%)
Median BMI (kg/m^2) Male Female	 26.15 25

Table 1. Age group distribution in study population

Age group (year)	Number	Percentage
26-35	2	3.6
36-45	5	9.1
46-55	15	27.3
56-65	21	38.2
66-75	6	10.9
76-85	6	10.9
Total	55	100.0

Table 2. Sex distribution in study population

Sex	Number	Percentage
Male	24	44
Female	31	56

Table 3. Distribution of BMI status in study population

BMI status	Number	Percentage
<18.5 (under weight)	1	1.9
18.5-24.9 (normal weight)	24	43.6
25.0-29.9 (over weight)	19	34.5
≥30.0 (obese)	11	20.0
Total	55	100.0

- BMI status was classified according to WHO criteria.

Table 4. Distribution of Metavia group in study population

Metavia group	Number	Percentage
F0-F1 (normal/mild fibrosis)	17	30.9
F2 (significant fibrosis)	8	14.5
F3 (advanced/ severe fibrosis)	7	12.7
F4 (cirrhosis)	23	41.8
Total	55	100.0

- The mean ± standard deviation of Metavia group E(kPa) was 17.22 ±16.2.

Table 5. Distribution of APRI group in study population

APRI group	Number	Percentage
≤0.7 (normal)	35	63.6
0.7 to 1 (significant fibrosis)	5	9.1
>1 (severe fibrosis/ cirrhosis)	15	27.3
Total	55	100.0

- The mean ± standard deviation of APRI score was 1.05 ± 1.27

Table 6. Correlation between Metavia (kPa) and APRI scores among study population

	Mean ± Standard deviation		Correlation value (r value)	p value
E(kPa)	17.22	16.2	0.610	0.000
APRI	1.04	1.26		

Discussion

- After calculating the Pearson's correlation result r value was 0.610 and p value was 0.000 at statistical significant between Metavia (kPa) and APRI scores among study population.
- So the scatter plot was drawn in below, to show the correlation between Metavia (kPa) and APRI scores.
- It means that significant positive correlation and the scores of Metavia (kPa) and APRI increased together.

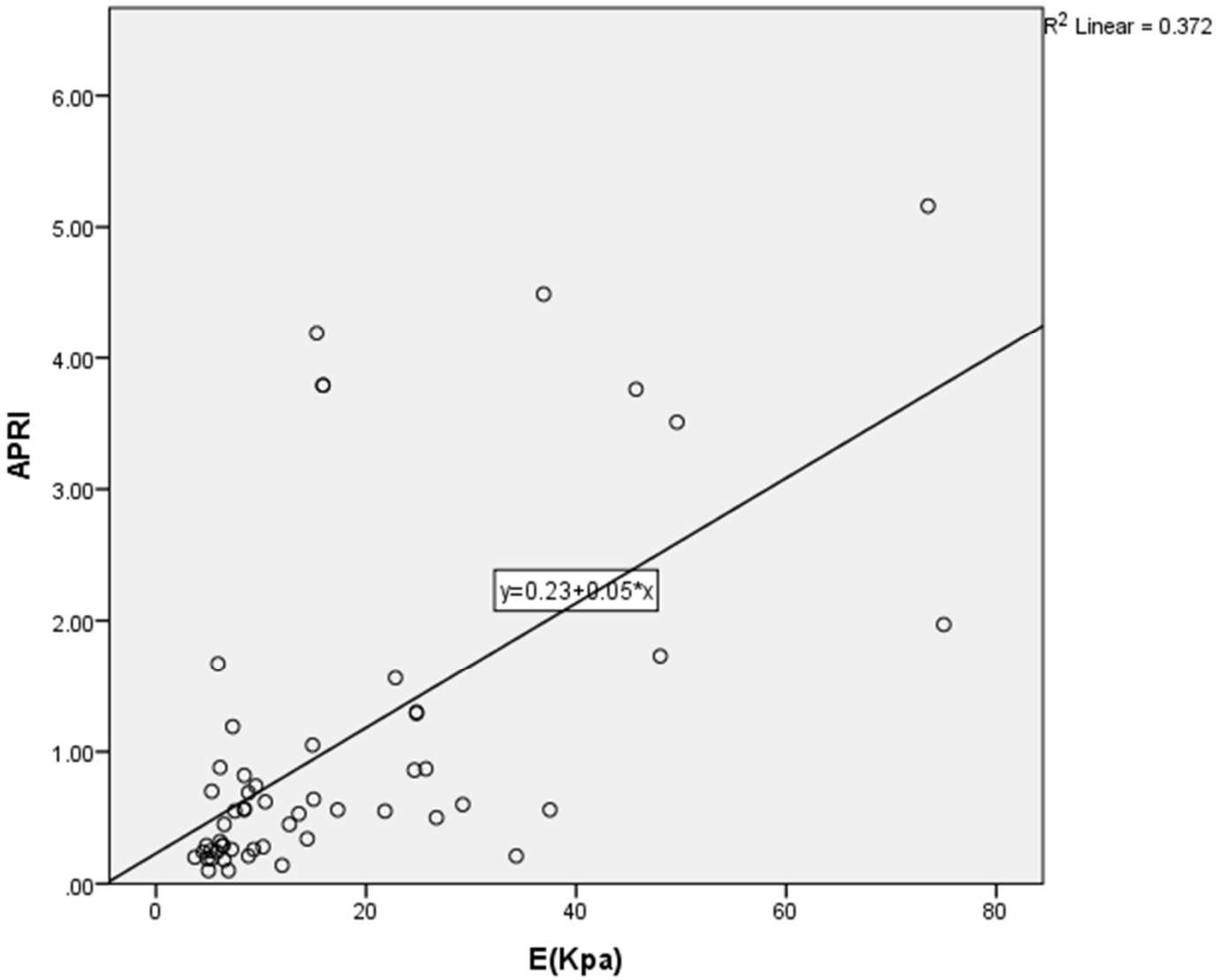

R2 Linear = 0.372
y=0.23+0.05*x
APRI
E(Kpa)
6.00
5.00
4.00
3.00
2.00
1.00
.00
0
20
40
60
80

Table 7. Association between the Metavia (E(kPa)) group and APRI group of study population

Metavia E(kPa)	APRI group				Chi-square value	p -value
	≤0.7	0.7 to 1	>1	Total		
	Number (%)	Number (%)	Number (%)	Number (%)		
F0-F1	15 (88.2%)	1 (5.9%)	1 (5.9%)	17(100.0%)	17.78	0.002
F2	6 (75%)	1 (12.5%)	1 (12.5%)	8 (100.0%)		
F3	6 (85.7%)	1 (14.3%)	0	7 (100.0%)		
F4	8 (34.8%)	2 (8.7%)	13 (56.5%)	23 (100.0%)		
Total	35 (63.6%)	5 (9.1%)	15 (27.3%)	55 (100.0%)		

Discussion

- Regarding the APRI group of among patients with different grades of Metavia, this study revealed that higher scores of APRI group were recorded with the severe grades of Metavia calculated with the Chi–square value of 17.78 and that these higher scores and severe grades were statistically significant between groups ($p=0.002$).

APRI group	TE score high (Metavia F3-F4)	TE score low (Metavia F0-F2)
APRI > 0.7	16	4
APRI ≤ 0.7	14	21
	Sensitivity 53.3%	Specificity 84.0%

APRI group	TE score high (Metavia F4)	TE score low (Metavia F0-F3)
APRI > 1	13	2
APRI ≤ 1	10	30
	Sensitivity 56.5%	Specificity 93.7%

Discussion

- APRI ≤ 0.7 predicted Metavia F0-2 on TE with sensitivity of 53.3% and specificity of 84.0%
- APRI > 1 predicted Metavia F4 on TE with sensitivity of 56.5% and specificity of 93.7%

Limitations

- This study has some limitations. First, the small number of patients recruited. Second, liver biopsy and other non-invasive methods (eg., Fibrotest, MR-elastography, Fibro-CT) did not performed for detection of liver fibrosis.

Conclusion

- In chronic Hepatitis C infected patients there is significant positive correlation between Metavia and APRI.
- The severe the liver fibrosis by FibroScan, the higher the APRI score can be concluded
- When TE/FibroScan is not available, low APRI score (≤0.7) could be considered to exclude cirrhosis.
- Because of limitations, combination of FibroScan, ultrasonography and biochemical parameters showed the best prediction parameters for diagnosis of liver fibrosis in chronic hepatitis C infected patients.

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- Ann Gastroenterol. 2012; 25(3): 218–231.

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