Role of transient elastography and controlled attenuation parameter measurements in predicting portal hypertension in Egyptian patients with hepatocellular carcinoma candidate for liver resection

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Received: 23 August 2021
Accepted: 12 September 2021
Published: xx Month 2021

The Egyptian Journal of Surgery 2021, 40:1401–1411

Background and aim
Hepatic resection for hepatocellular carcinoma (HCC) is a main therapy for the treatment of surgical candidate patients. However, careful patient selection is required to balance the risk of postoperative liver failure and the potential benefit of long-term outcomes. We investigated the role of transient elastography and controlled attenuation parameter (CAP) in predicting portal hypertension in those patients, to assess if they could replace an invasive procedure [hepatic venous pressure gradient (HVPG)]. Moreover, their role in prediction of HCC recurrence after surgical resection was assessed.

Patients and methods
The study was performed at Ain Shams University hospitals, Tropical Medicine Department. A total of 30 patients with HCC, being candidate for surgical resection, were included in our study. We divided them into two groups according to the presence or absence of portal hypertension. Assessment of portal hypertension was done by laboratory markers, upper gastrointestinal endoscopy, and HVPG measurements. Transient elastography and CAP measurements were done for all patients. Correlations were done between transient elastography readings and CAP readings with other parameters of portal hypertension. Patients who underwent surgical resection were followed up for 6 months after liver resection to detect HCC recurrence.

Results
A positive correlation between transient elastography, CAP, and HVPG was found. Receiver operating characteristic curves of transient elastography, CAP, and a combination between transient elastography+platelet were drawn to differentiate between the two groups. The best cutoff point for transient elastography to detect significant portal hypertension was more than 18, with sensitivity of 93.75%, specificity of 100.0%, and area under the curve (AUC) of 99.8. Moreover, the cutoff point for CAP to detect significant portal hypertension was more than 217, with sensitivity of 87.5%, specificity of 64.29%, and AUC of 81.2%. However, the cutoff point of the platelet count was 166, with sensitivity of 100%, specificity of 86.67%, and AUC of 100%. The combination between transient elastography and platelets showed sensitivity of 87.5%, specificity of 100.0%, and AUC of 95.5%. Moreover, transient elastography showed a significant role in predicting early recurrence of HCC, with *P* value of 0.011.

Conclusion
Transient elastography and CAP can be used as a useful tool in evaluating portal hypertension and also can be used in predicting early recurrence of HCC after surgery.

Keywords:
controlled attenuation parameter, FibroScan, hepatocellular carcinoma, hepatic venous pressure gradient, portal hypertension, resection, transient elastography

Egyptian J Surgery 40:1401–1411

1110-1121

Introduction

Incidence of hepatocellular carcinoma (HCC) has rapidly increased worldwide. HCC is the sixth most common malignancy and the third most common cause of cancer-related deaths [1]. Since HCC usually develops in a damaged liver, the prognosis of HCC depends not only on tumor progression but also on the degree of liver dysfunction [2]. In Egypt, liver cancer forms 23.81% of the total malignancies. HCC

constitutes 70.48% of all liver tumors among Egyptians [3].

Portal hypertension and esophageal varices are predictors of death in patients with HCC, independent of the severity of liver disease and independent of HCC stage [4].

Portal hypertension is a clinical syndrome, hemodynamically defined as an increase in the pressure gradient across the liver (between portal pressure and inferior vena cava pressure) above the normal value of 5 mmHg. In patients with cirrhosis, this gradient can be estimated by its clinical equivalent – the hepatic venous pressure gradient (HVPG) – which is assessed at hepatic vein catheterization and avoids the need to directly puncture the portal vein. An elevated HVPG between 6 and 9 mmHg defines subclinical portal hypertension, whereas an HVPG more than or equal to 10 mmHg defines clinically significant portal hypertension (CSPH), as all of the potential complications of the syndrome (e.g. varices and ascites) can appear above this threshold. The gold standard for the diagnosis and assessment of portal hypertension is the measurement of the HVPG, which is obtained as the difference between 'wedged' (occluded) and 'free' hepatic venous pressures[5].

Guidelines from European Association for Study of Liver mentioned that patients ideally suited for resection have localized HCC confined to the liver without radiographic evidence of invasion of the vasculature of the liver, preserved hepatic function, and no evidence of portal hypertension.

Liver stiffness (LS) measured by transient elastography (FibroScan) is a well-accepted objective noninvasive method to reliably estimate liver fibrosis. It has been shown that LS and HVPG show a good correlation in patients with compensated cirrhosis. LS cutoff for the detection of CSPH varies across studies, but it is widely accepted that values above 21 kPa have a high specificity for CSPH.

On the contrary, non alcholic fatty liver disease (NAFLD) is considered one of the most common chronic liver diseases worldwide, with increasing disease prevalence in parallel with the obesity and metabolic syndrome epidemic [6], and can potentially progress to cirrhosis and accompanying complications such as HCC [7].

The introduction and widespread adoption of the XL probe has resolved issues with transient elastography failure in obese patients with NAFLD. Apart from fibrosis assessment, the recent introduction of the novel controlled attenuation parameter (CAP) function allows for the noninvasive measurement of hepatic steatosis [8].

The aim of our study was to assess the role of transient elastography and CAP measurement as a noninvasive tool to assess portal hypertension in patients with HCC undergoing liver resection and their role in decision making in patients with HCC undergoing liver resection.

Patients and methods

This prospective cohort study was conducted at Tropical Medicine Department and Ain Shams HCC Unit, Ain Shams University Hospitals, Cairo, Egypt. A total of 30 patients with HCC potentially candidate for surgical resection were included in our study during the interval from March 2019 till March 2021.

We included all patients above 18 years old with documented diagnosis of HCC according to AASLD 2018 and candidate for liver resection.

The exclusion criteria from the study were obese patient (failure to obtain 10 valid results with the XL probe) and elevated liver enzymes more than three folds.

Patients not candidate for liver resection (owing to presence of ascites, performance grade above 1, HFL not accessible for surgery, or cases with Child class B or C) were excluded from the study.

A written informed consent was obtained from all of the study participants. The study was approved by the ethical committee of Ain Shams University Hospitals.

All enrolled patients with HCC were subjected to full history taking and thorough clinical examination. In addition, complete blood count, alanine aminotransferase, aspartate aminotransferase, serum total bilirubin, serum albumin, international normalized ratio, serum creatinine and alpha-fetoprotein, abdominal ultrasound, and triphasic pelvi-abdomen computed tomography were done.

Portal hypertension was assessed by the following: performing upper gastrointestinal tract endoscopy to detect the presence of varices and HVPG, which was carried out under local anesthesia, and noninvasive vital

sign monitoring. With ultrasound assistance, the right jugular vein (or the femoral or antecubital vein) was catheterized, a venous introducer placed, and a balloon-tipped catheter was guided under fluoroscopic control through the right atrium and IVC into the main right hepatic vein, and the difference between WHVP and FHVP was calculated [9].

Transient elastography was done for all the patients to detect the degree of LS, and CAP measurement was done to detect the degree of steatosis.

Transient elastography was performed on the right lobe of the liver, through intercostal spaces, with the patient lying in dorsal decubitus with the right arm in maximal abduction. A total of 10 valid measurements were performed to examine a patient with transient elastography. Examinations with a success rate higher than 60% were considered reliable. The results were immediately obtained after performance of transient elastography and expressed in kilopascals (kPa), corresponding to the median value of 10 validated measurements (range, 2.5–75 kPa). An interquartile range, which represents the intrinsic variability of transient elastography, less than 30% of the median indicates a high-quality result [10].

According to clinical data, based on the results of upper GIT endoscopy, that is, HVPG, patients were classified into two groups:

Group I included patients with evidence of portal hypertension (excluded from surgery).
Group II included patients with no evidence of portal hypertension (underwent surgery).

Correlations were done between transient elastography readings, CAP readings with HVPG, endoscopy findings, and scores of fibrosis and steatosis to detect the best method to detect portal hypertension in patients with HCC candidates for hepatic resection.

Then, patients were followed after surgery with triphasic CT scans at 1, 3, and 6 months to assess the recurrence of any HCC nodules.

Statistical analysis

The collected data were revised, coded, tabulated, and introduced to a computer using the Statistical Package for the Social Sciences (SPSS 23). Data were presented as mean/median, ±SD, and range for parametric numerical data; median and interquartile range for nonparametric numerical data; and frequency and percentage for nonnumerical data. Student *t* test was used to assess the statistical significance of the difference between the means of two study groups. Mann–Whitney *U* test was used to assess the statistical significance of the difference of a nonparametric variable between two study groups. χ^2 test and Fisher's exact test were used to examine the relationship between two qualitative variables. All statistical analyses were based on two-tailed hypothesis tests, with a significance level of *P* value less than 0.05.

Results

The present prospective cohort study enrolled 30 Egyptian patients with potentially respectable HCC referred to Tropical Medicine Department and HCC Unit, Ain Shams University Hospitals, Cairo, Egypt. There were 20 males and 10 females. The mean age was 57.73±6.79 years (range, 43–71 years). Diabetes mellitus was present in 13 patients. The mean BMI was 26.07±3.71. All patients were Child class A. Five (16.7%) patients had hypertension, 13 (43.3%) patients were smokers, and splenomegaly was detected in 50% of the patients. There were no cases of ascites, jaundice, abdominal wall collaterals, or lower limb edema (Table 1).

All our patients were HCV Ab positive. Only one patient had combined HCV and HBV confection. All of the studied patients were child A. Their mean AST/platelets ratio (APRI), model for end stage liver disease (MELD), and ibrosis 4 index (FIB4) scores were 0.61 ±0.39, 8.67±1.32, and 2.42±1.55, respectively. Mean values of HVPG were 12.23±5.46, with a range of 5–22. Three patients had values below 6, whereas two patients had values above 20. Clinically significant HVPG was present in 16 (53.3%) patients of the studied population. The mean transient elastography reading was 27.43±17.13 (range, 14–35), whereas the mean CAP reading was 248.47±60.92 (range, 155–396) (Table 2).

A total of 15 cases underwent surgical resection, whereas the other 15 cases were not candidates for surgical resection owing to the presence of clinically significant portal hypertension.

Comparing the two groups, mean BMI showed a statistically significant difference, where it was 27.53 ±3.48 in the surgical group in comparison with 24.60 ±3.44 in the nonsurgical group (*P*=0.028).

Regarding the scores in the two groups, mean values of APRI score and FIB4 score in the surgical group were

Table 1 Demographic and clinical data of the involved patients

	Total *N*=30 [*n* (%)]
Age	
Mean±SD	57.73±6.79
Range	43–71
Sex	
Female	10 (33.3)
Male	20 (66.7)
BMI	
Mean±SD	26.07±3.71
Range	19–33
HTN	
Negative	25 (83.3)
Positive	5 (16.7)
DM	
Negative	17 (56.7)
Positive	13 (43.3)
Smoking	
Negative	17 (56.7)
Positive	13 (43.3)
Jaundice	
Negative	30 (100.0)
Positive	0
LL edema	
Negative	30 (100.0)
Positive	0
Splenomegaly	
Negative	15 (50.0)
Positive	15 (50.0)
Hepatomegaly	
Negative	21 (70.0)
Positive	9 (30.0)
Ascites	
Negative	30 (100.0)
Positive	0
Abdominal wall collaterals	
Negative	27 (90.0)
Positive	3 (10.0)

DM, diabetes mellitus; HTN, hypertension; LL, lower limb.

Table 2 Baseline APRI, FIB4, HSI score, Child grade, Child score, MELD score, hepatic venous pressure gradient, transient elastography, and controlled attenuation parameter readings of the patients

	Total *N*=30 [*n* (%)]
APRI	
Mean±SD	0.61±0.39
Range	0.14–1.46
HSI score	
Mean±SD	36.51±4.46
Range	29.18–48.18
Child grade	
Child A	30 (100.0)
Child score	
Mean±SD	5.07±0.25
Range	5–6
MELD score	
Mean±SD	8.67±1.32
Range	6–13
FIB4	
Mean±SD	2.42±1.55
Range	0.69–6.34
HVPG	
Mean±SD	12.23±5.46
Range	5–22
Clinically significant HVPG	
Negative	14 (46.7)
Positive	16 (53.3)
Different categories HVPG	
≤5	3 (10.0)
6–9	11 (36.7)
10–12	1 (3.3)
13–20	13 (43.3)
>20	2 (6.7)
Transient elastography	
Mean±SD	27.43±17.13
Range	11–75
CAP	
Mean±SD	248.47±60.92
Range	155–396

APRI, AST/platelets ratio; CAP, controlled attenuation parameter; FIB4, ibrosis 4 index; HVPG, hepatic venous pressure gradient; MELD, model for end stage liver disease.

0.39±0.19 and 1.59±0.71, respectively, whereas they were 0.82±0.43 and 3.25±1.73, respectively, in the other group, with a highly statistically significant difference (*P*=0.003 and 0.004, respectively).

Mean value of the transient elastography readings of the surgery group was 14.73±1.91, showing a highly statistically significant difference (*P*=0.000) in comparison with the other group (40.13±16.09). Moreover, the mean value of the CAP readings of the surgery group was 217.87±41.48 with a highly statistically significant difference (*P*=0.004) in comparison with the other group (mean value of 279.07±62.93) (Table 3 and Fig. 1).

In studying the correlation of transient elastography with the other studied parameters, there was a statistically significant positive correlation between transient elastography and CAP (Fig. 2), alpha-fetoprotein, FIB4, APRI scores, spleen size, and HVPG (Fig. 3), with *P* values of 0.024, 0.027, 0.00, 0.001, 0.001, and 0.00, respectively. There was a positive correlation between transient elastography and BMI, HIS, and child score but it did not reach any statistical significance (Table 4).

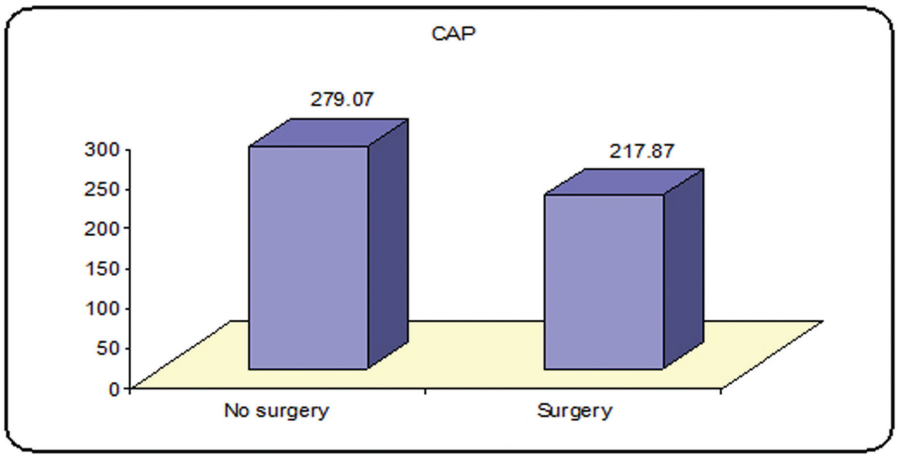
Moreover, there was a statistically significant negative correlation between transient elastography and platelets count, with *P* value of 0.00. A negative correlation was found between transient elastography and MELD score, but it did not reach statistical significance (Table 4).

Table 3 Comparison between the two groups (cases underwent surgery and cases excluded from surgery) regarding APRI, FIB4, HSI score, MELD score, transient elastography readings, and controlled attenuation parameter readings

	No surgery *N*=15	Surgery *N*=15	Test value	*P* value	Significance
BMI					
Mean±SD	27.53±3.48	24.60±3.44	2.321[b]	0.028	S
Range	20–33	19–29			
APRI					
Mean±SD	0.82±0.43	0.39±0.19	−2.966[a]	0.003	HS
Range	0.3–1.46	0.14–0.88			
HSI score					
Mean±SD	38.03±5.02	34.99±3.32	1.953[b]	0.061	NS
Range	29.18–48.18	30–40.13			
MELD score					
Mean±SD	8.40±0.99	8.93±1.58	−1.099[a]	0.272	NS
Range	7–10	6–13			
FIB4					
Mean±SD	3.25±1.73	1.59±0.71	−2.841[a]	0.004	HS
Range	0.9–6.34	0.69–3.48			
Transient elastography					
Mean±SD	40.13±16.09	14.73±1.91	−4.686[a]	0.000	HS
Range	26–75	11–18			
CAP					
Mean±SD	279.07±62.93	217.87±41.48	3.145[b]	0.004	HS
Range	195–396	155–290			

APRI, AST/platelets ratio; CAP, controlled attenuation parameter; FIB4, ibrosis 4 index; MELD, model for end stage liver disease.
[a]Mann–Whitney test. [b]Independent *t* test.

Figure 1

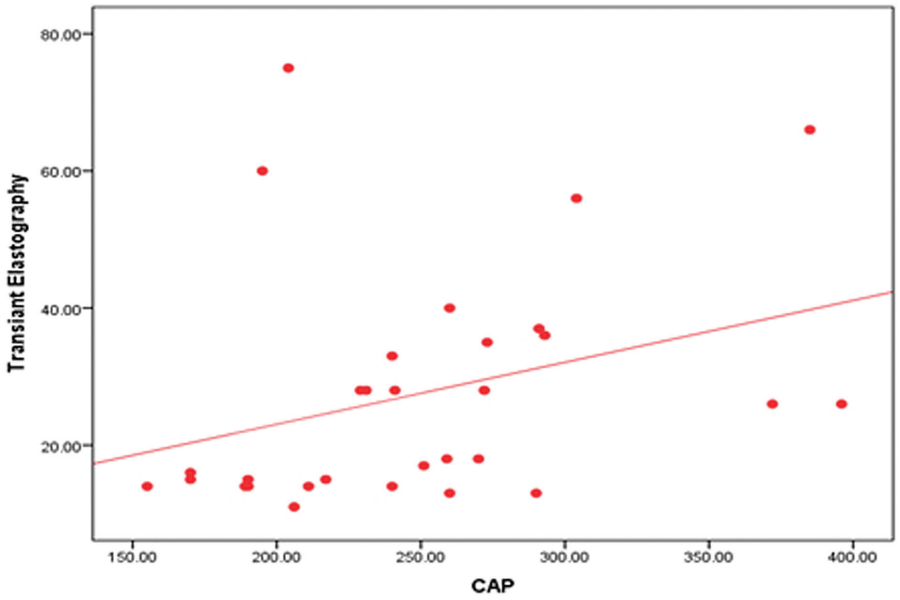


Comparison between nonsurgery and surgery cases regarding CAP readings. CAP, controlled attenuation parameter.

Regarding CAP, there was a statistically significant positive correlation between CAP readings and transient elastography (Fig. 2), BMI, HSI score, spleen size, and HVPG (Fig. 4), with *P* values of 0.024, 0.00, 0.00, 0.013, and 0.017, respectively. However, a statistically insignificant positive correlation was found between CAP and both FIB4 and APRI scores. There was an insignificant negative correlation between CAP and age, platelet count, MELD, and child scores (Table 5).

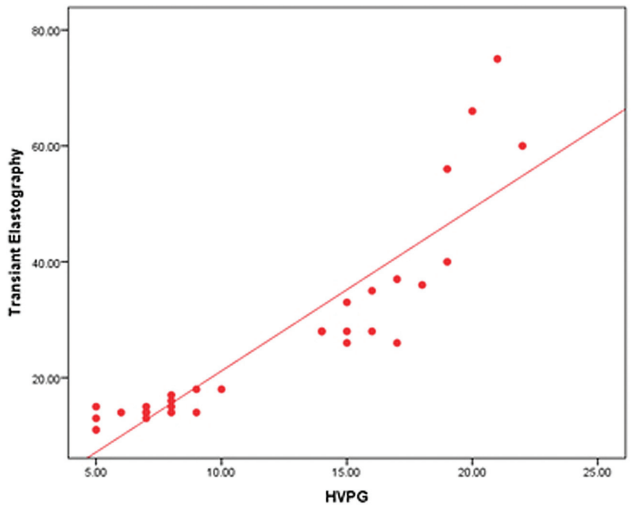
We used receiver operating characteristic curves for transient elastography, CAP, and combination between transient elastography+platelet to differentiate between patients who have clinically significant portal hypertension (HVPG ≥10) and those without clinically significant portal hypertension (HVPG <10). It showed that the best cutoff point for transient elastography to detect significant portal hypertension was more than 18, with a sensitivity of 93.75%, a specificity of 100.0%,

Figure 2



Scatter dot diagram showing a positive correlation between transient elastography and CAP. CAP, controlled attenuation parameter.

Figure 3



Scatter dot diagram showing a positive correlation between transient elastography and HVPG. HVPG, hepatic venous pressure gradient.

and area under the curve (AUC) of 99.8. Moreover, the cutoff point for CAP to detect significant portal hypertension was more than 217, with a sensitivity of 87.5%, a specificity of 64.29%, and AUC of 81.2%.

However, the cutoff point of the platelet count was 166, with a sensitivity of 100%, a specificity of 86.67%, and AUC of 100%. The combination between transient elastography and platelets showed a sensitivity of 87.5%, a specificity of 100.0%, and AUC of 95.5% to detect clinically significant portal hypertension (Table 6 and Fig. 5).

Table 4 Correlation of transient elastography with other studied parameters

	Transient elastography	
	r	*P* value
AFP	0.402	0.027
CAP	0.412	0.024
Age	−0.114	0.548
BMI	0.292	0.117
TLC	−0.072	0.707
HB	0.193	0.308
Platelets	−0.771	0.000
ALT	−0.043	0.820
AST	−0.090	0.636
Bilirubin	−0.215	0.254
INR	−0.073	0.701
Serum creatinine	−0.052	0.786
Serum albumin	−0.036	0.851
FIB4	0.611	0.000
APRI	0.581	0.001
Child score	0.326	0.079
MELD score	−0.181	0.340
Liver size	−0.214	0.256
Spleen size	0.919	0.000
HVPG	0.937	0.000

AFP, alpha-fetoprotein; ALT, alanine aminotransferase; APRI, AST/platelets ratio; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; FIB4, ibrosis 4 index; HB, hemoglobin; HVPG, hepatic venous pressure gradient; INR, international normalized ratio; MELD, model for end stage liver disease; TLC, total leukocyte count.

Only four patients had recurrent HCC after surgical resection in the first 6 months. Comparison between the two groups (recurrence and nonrecurrence) was done to assess the role of transient elastography and

CAP in predicting early (6 months) HCC recurrence. Postresection transient elastography had a significant role in predicting HCC recurrence, with *P* value of 0.011, whereas the CAP role was nonsignificant (Table 7 and Fig. 6).

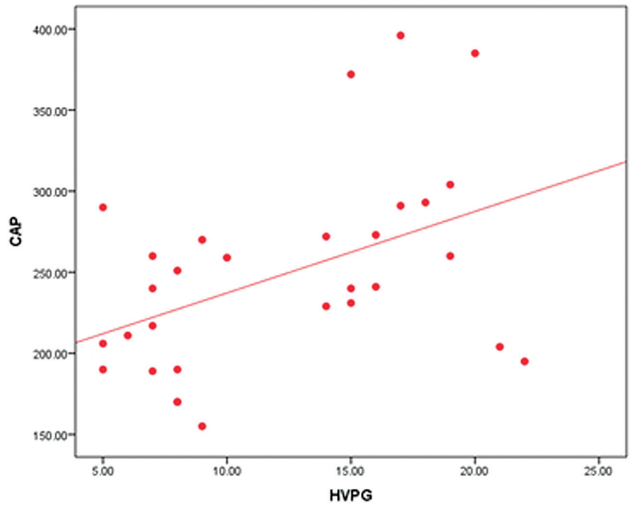
Discussion

HCC is a major health problem worldwide as more than 700 000 cases are diagnosed yearly [11]. HCC is the fourth leading cause of cancer-related death in the world [12]. Liver resection is one of the main curative options for early HCC in patients with cirrhosis and is the treatment of choice in noncirrhotic patients. However, careful patient selection is required to balance the risk of postoperative liver failure and the potential benefit on long-term outcomes. In the past decades, improved surgical techniques and perioperative management, as well as better patient selection, have enabled the indications for liver resection to be expanded [13].

In our study, male patients represented a higher percentage of the study group (66.7%) compared with females (33.3%). This preponderance of men is already known and is even more pronounced in high-incidence regions of HCC and goes hand in hand with Shaker *et al.* [14] who reported that a male to female ratio of 3.7 : 1 was found in their series, which was conducted on 1313 patients with HCC. Although not fully understood, the differences in sex distribution are thought to be owing to variations in hepatitis carrier states, exposure to environmental toxins, the trophic effect of androgens [15], and/or potentially protective effects of estrogen mediated through inhibition of interleukin 6 [16].

The peak age of incidence of HCC was found to be in older population, with a mean age of 57 years, which is in line with published data from Devaki *et al.* [17], which was between 57 and 59 years [17]. However, this is fairly different from the average age as reported in

Figure 4



Scatter dot diagram showing a positive correlation between CAP and HVPG. CAP, controlled attenuation parameter; HVPG, hepatic venous pressure gradient.

Table 5 Correlation of controlled attenuation parameter measurements with other studied parameters

	CAP readings	
	r	*P* value
AFP	0.176	0.352
Age	−0.148	0.436
BMI	0.833	0.000
TLC	−0.038	0.843
HB	0.189	0.318
Platelets	−0.249	0.185
ALT	−0.283	0.130
AST	−0.154	0.416
Bilirubin	−0.152	0.424
INR	−0.054	0.777
Serum creatinine	0.142	0.456
Serum albumin	0.056	0.768
FIB4	0.076	0.688
APRI	0.045	0.814
Child score	−0.131	0.489
MELD score	−0.080	0.675
Size of the lesion	0.082	0.665
Liver size	−0.190	0.314
Spleen size	0.447	0.013
HVPG	0.432	0.017

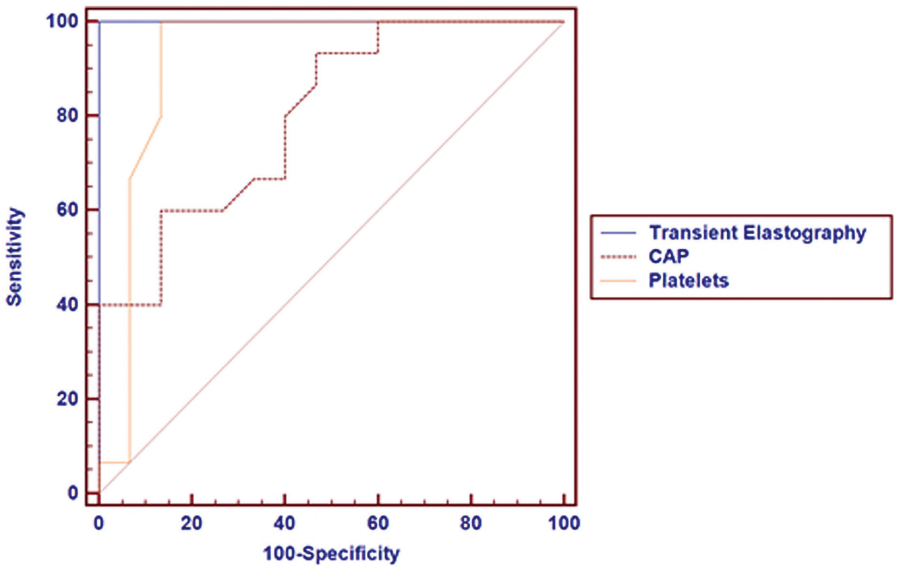
AFP, alpha-fetoprotein; ALT, alanine aminotransferase; APRI, AST/platelets ratio; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; FIB4, ibrosis 4 index; HB, hemoglobin; HVPG, hepatic venous pressure gradient; INR, international normalized ratio; MELD, model for end stage liver disease; TLC, total leukocyte count.

Table 6 Receiver operating characteristic curve for transient elastography and controlled attenuation parameter to predict positive hepatic venous pressure gradient

	Cut off point	AUC	Sensitivity	Specificity	PPV	NPV
Transient Elastography (kPa)	>18	0.998	93.75	100.00	100.0	93.3
CAP (dB/m)	>217	0.812	87.50	64.29	73.7	81.8
Platelets per microliter (mcl)	>166	0.920	100.00	86.67	88.2	100.0
Transient elastography+PLT		0.955	87.50	100.00	100.0	87.5

AUC, area under the curve; CAP, controlled attenuation parameter; NPV, negative predictive value; PPV, positive predictive value.

Figure 5



ROC curve for transient elastography and CAP to predict positive HVPG. CAP, controlled attenuation parameter; HVPG, hepatic venous pressure gradient; ROC, receiver operating characteristic.

Table 7 Role of transient elastography and controlled attenuation parameter in predicting early (6 months) hepatocellular carcinoma recurrence after resection

	No recurrence *N*=11	Recurrence *N*=4	Test value	*P* value	Significance
Transient elastography					
Median (IQR)	14 (13?15)	17 (15.5?18)	−2.540	0.011	S
Range	11–17	15–18			
CAP					
Mean±SD	218.09±38.85	217.25±54.74	0.033	0.974	NS
Range	155–290	170–270			

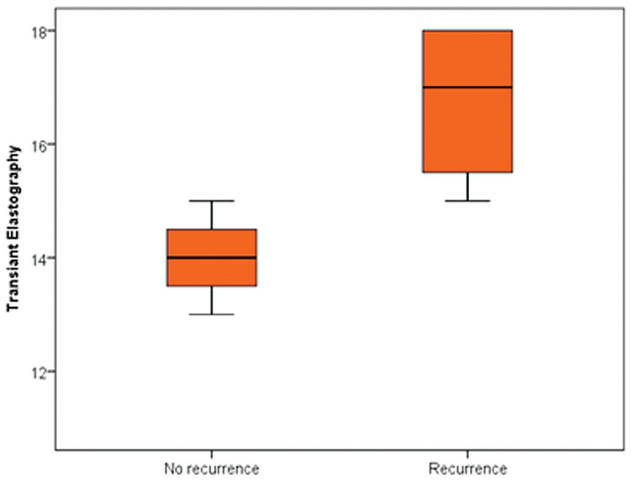
CAP, controlled attenuation parameter; IQR, interquartile range.

Alswat *et al.* [18], in a study done in the Saudi Arabia, which found that the mean age was 65 years.

We found that nearly half of the studied patients [13 (43.3%) patients] had diabetes mellitus. Diabetes mellitus may have a significant role in HCC development. This is consistent with a large population-based cohort study. The study included 19 349 patients with newly diagnosed diabetes and 77 396 patients without diabetes [19]. The incidence of HCC was significantly higher among patients with diabetes compared with those without diabetes (21.0 vs. 10.4 per 10 000 person-years).

In the setting of diagnosed HCC, HVPG measurements assisted in identifying patients who are candidates for surgical resection. Because resistance to blood flow increases following partial hepatectomy, elevated baseline preoperative HVPG can predict hepatic decompensation and poor long-term outcomes in patients with cirrhosis after liver resection for HCC.

Figure 6



Role of transient elastography in predicting early (6 months) HCC recurrence after resection. HCC, hepatocellular carcinoma.

Elevated HVPG has been significantly associated with unresolved decompensation within 3 months after surgery [20].

Fibrosis markers may have a role in predicting the presence of portal hypertension. In the present study, APRI score and FIB4 score were associated with the presence of portal hypertension.

APRI and FIB4 scores were first introduced to evaluate the presence and severity of liver fibrosis in patients with chronic viral hepatitis. A study done by Deng *et al.* [21] stated that APRI and FIB4 scores may be simple and convenient noninvasive diagnostic tests of liver fibrosis because they are based on the regular laboratory tests and demographic data. Serum liver fibrosis indices exhibit modest diagnostic performance in predicting the presence of varices in patients with liver cirrhosis [22]. Based on a systematic review and meta-analysis, APRI and FIB4 scores had low to moderate diagnostic accuracy in predicting the presence of varices in liver cirrhosis. A retrospective study that included 478 patients with cirrhosis who underwent gastroscopy revealed that FIB4 correctly stratified patients with cirrhosis without high-risk varices [23].

A recent study by Jay Freeman *et al.* [24] performed on children with cystic fibrosis found that LS measured by transient elastography was significantly associated with conventional laboratory biomarkers of liver disease (platelet count, APRI, and FIB4) and spleen size by US. Moreover, another study by Fallatah *et al.* [25] concluded that there was a significant positive correlation between LS measurements detected by transient elastography as compared with APRI and FIB4 results ($P<0.001$). All are in agreement with our study where transient elastography readings had a positive correlation with fibrosis markers like APRI and FIB4 results.

While evaluating the relation between transient elastography and portal hypertension, we found that there was a statistically significant difference between the two studied groups regarding transient elastography.

Different previous studies showed the performances of transient elastography in detection of clinically significant portal hypertension. Vizzutti *et al.* [10] found that LS measurement predicts severe portal hypertension in patients with HCV-related cirrhosis with a cutoff value 13.6. Lemoine *et al.* [26] found that LS measurement was a predictive tool of clinically significant portal hypertension in 44 patients with compensated hepatitis C virus or alcohol-related cirrhosis with a cutoff value of 20.5. Moreover, Bureau *et al.* [27] also found that transient elastography accurately predicts presence of significant portal hypertension in patients with chronic liver disease with a cutoff value of 21. Another study of 326 patients from India reported that transient elastography had a fair positive correlation with HVPG and found that transient elastography can be used as a noninvasive modality to assess the degree of portal hypertension. A cutoff transient elastography value of 21.6 kPa identifies CSPH with a PPV of 93% [28].

The Baveno VI consensus workshop proposes that patients with compensated advanced chronic liver disease with a LS less than 20 kPa and a platelet count more than 150 000/mm^3 are at very low risk for high-risk varices and could potentially avoid screening endoscopy. This is slightly different from our study that included only patients with HCC, which could justify the lower threshold of transient elastography in identification of clinically significant portal hypertension (>18). HCC can lead to an increase in HVPG (sinusoidal pressure) through the presence of arteriovenous shunting within the tumor.

The recent introduction of the novel CAP function allows for the noninvasive measurement of hepatic steatosis [8]. Early assessment of extent of hepatic steatosis and monitoring during therapy are important. The gold standard method to detect hepatic steatosis and steatohepatitis is liver biopsy, but it has some limitations like sampling errors, intraobserver and interobserver variability, invasiveness of the procedure, and major complications like bleeding. To avoid these limitations of liver biopsy and to quantify hepatic steatosis, CAP was implemented on FibroScan as a noninvasive method to evaluate both steatosis and fibrosis simultaneously. It is reported to be highly sensitive in detecting low-grade steatosis as fat deposition more than or equal to 10% [29].

While evaluating the relation between CAP and portal hypertension, we found that there was a statistically significant difference between the two studied groups regarding their CAP values. Our results showed that CAP had a statistically significant role in detecting clinically significant portal hypertension. This agrees with an interesting study by Mendes *et al.* [30] on 100 patients with portal hypertension identified from a cohort of 354 cases with biopsy-proven NAFLD. They found that 23 patients with portal hypertension (varices, encephalopathy, ascites, or splenomegaly) had no cirrhosis, including 12 patients with F2 or lesser fibrosis. Steatosis was more severe in those with portal hypertension.

Moreover, Francque *et al* [31] found that portal hypertension (HVPG >5 mmHg) was correlated with the extent of steatosis (P=0.016) but not with inflammation, ballooning, or fibrosis in a prospective cohort study of 50 patients with obesity and biopsy-proven NAFLD with HVPG measurement.

In contrary, most recently, a group from the Medical University of Vienna, Austria, published a retrospective observational study that questioned the link between steatosis and portal hypertension. The authors drew their conclusions from a cohort of 261 patients undergoing simultaneous HVPG measurements and transient liver elastography complemented with liver fat content estimation by CAP. CAP correlated negatively with HVPG in patients with LS [32].

Regarding the role of LS and CAP in predicting recurrence for early-stage hepatoma patients after curative resection, our prospective cohort found that only LS had a significant role in predicting recurrence, with P value of 0.011, unlike CAP measurement. A recent study done by Wang *et al* [33] assessed the predicting factors for early tumor recurrence, including tumor diameter, number, histology grade, microvascular invasion, and nontumor factors including stage of liver disease. They found that LS was the only independent factor associated with recurrence after curative resection in this prospective cohort of patients. We need more studies with larger sample sizes to confirm the value of transient elastography measurements as a predictor of HCC recurrence after liver resection.

Owing to the fact that transient elastography does not allow liver imaging during LS measurement, we cannot exclude that the liver nodules were placed in the measurement area and that it can misleadingly increase the values of LS, at least in some cases. This drawback might be overcome by newer methods for LS measurement in real time, such as Acoustic Radiation Force Impulse, which also allows a concomitant standard real-time ultrasound examination of the liver [34]. Another drawback is the relatively small number of the population study. This was due to the COVID pandemic, as routine elective surgery has been postponed where possible and the number of the patients admitted to hospital was lower than the same periods in the pre-COVID time.

LS measurements by transient elastography is a simple and noninvasive tool and could be used in predicting clinically significant portal hypertension in HCC cases preparing for liver resection. CAP is a simple method for detection of hepatic steatosis. It could be used in detection of clinically significant portal hypertension. However, more studies are needed with larger sample sizes to prove its use.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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