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ORIGINAL ARTICLE

Observational Study

Transient elastography improves detection of liver cirrhosis compared to routine screening tests

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Abstract

AIM: To investigate the diagnostic significance of transient elastography (TE) in a daily routine clinical setting in comparison to clinical signs, laboratory parameters and ultrasound.

METHODS: TE, ultrasound, laboratory parameters and cutaneous liver signs were assessed in 291 consecutive patients with chronic liver disease of various aetiologies who underwent liver biopsy in daily routine.

RESULTS: Sensitivity of TE for the detection of liver cirrhosis was 90.4%, compared to 80.1% for ultrasound, 58.0% for platelet count and 45.1% for cutaneous liver signs ($P < 0.0001$ for comparisons with histology). AUROC for TE was 0.760 (95%CI: 0.694-0.825). Combination of TE with ultrasound increased sensitivity to 96.1% and AUROC to 0.825 (95%CI: 0.768-0.882). TE correlated with laboratory parameters of cirrhosis progression like albumin ($r = -0.43$), prothrombin time ($r = -0.44$), and bilirubin ($r = 0.34$; $P < 0.001$ for each). Particularly, in patients with Child Pugh score A or normal platelet count TE improved sensitivity for the detection of liver cirrhosis compared to ultrasound by 14.1% ($P < 0.04$) and 16.3% ($P < 0.02$), respectively.

CONCLUSION: Transient elastography is superior to routine diagnostic tests allowing detection of liver cirrhosis in additional 10%-16% of patients with chronic liver disease that would have been missed by clinical examinations.

Key words: Transient elastography; Fibroscan; Liver cirrhosis; Liver disease; Chronic hepatitis

Core tip: Diagnosis of liver cirrhosis is often missed in routine clinical practice. Novel non-invasive tools like transient elastography (TE) are available but their

diagnostic performance for the detection of cirrhosis has only been poorly evaluated in a routine clinical setting, where screening and diagnosis is mainly based on clinical signs, simple laboratory parameters and conventional ultrasound. The present investigation shows that TE is found to be superior to routine diagnostic tests allowing detection of liver cirrhosis in an additional 10%-15% of patients. The highest diagnostic benefit is seen in patients with early cirrhosis or normal platelet count.

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INTRODUCTION

Patients with liver cirrhosis have a significantly reduced life expectancy compared to non-cirrhotic patients due to complications such as ascites, bleeding of oesophageal varices, hepatic encephalopathy, hepatorenal or hepatopulmonary syndrome and hepatocellular carcinoma (HCC)[1]. Particularly the increasing incidence of HCC secondary to hepatic cirrhosis contributes significantly to the high mortality seen in these patients[2]. Hence, most guidelines recommend regular screening for HCC in patients with liver cirrhosis at least every six months[3,4]. However, diagnosis of liver cirrhosis is frequently missed in a routine clinical setting[5]. The limitations of available diagnostic tools for the detection of hepatic cirrhosis (clinical signs, laboratory parameters, imaging techniques and liver biopsy) are currently driving interest towards non-invasive tests.

Transient elastography (TE) is a non-invasive instrument that determines liver stiffness by generating a low frequency elastic wave of 50 Hz and a high frequency ultrasound wave of 1500 m/s, which allows measurement of the transmission of the elastic wave into liver tissue. Liver stiffness correlates with the degree of fibrosis, a higher degree of fibrosis implying greater stiffness. TE is a valid tool for the differentiation of cirrhotic from non-cirrhotic liver with sensitivities of 77%-100%, specificities of 78%-98% and mean AUROCs of 0.94 (95%CI: 0.93-0.95), but has limitations in discriminating lower fibrosis stages[6].

Although cutaneous liver signs are part of the routine physical examination, their diagnostic value for determination of the severity of liver disease has been poorly evaluated[7]. Among them, spider naevi (84%) and palmar erythema (70.4%) have the highest sensitivities for the diagnosis of liver cirrhosis.

There are numerous laboratory markers which can be used individually or in combination to determine the extent of fibrosis. However, most of these markers and scores have no causal relationship with fibrogenesis[8]. Among the individual measures, the platelet count is the most convenient rough guide for the evaluation of the fibrosis stage and correlates moderately with the histologically determined stage of fibrosis (r = -0.46 to -0.50)[9]. Another frequently used measure of serum fibrosis is the APRI ("aspartate aminotransferase to platelet ratio") index, which is calculated from the AST level and the platelet count. The APRI score has so far only been evaluated in patients with viral hepatitis. A threshold level for significant fibrosis has been defined (Ishak score F3 to F6) at a score of > 1.5, liver cirrhosis at a score of > 2, whereas a score of < 0.5 is said to rule out significant fibrosis[10].

Conventional ultrasound allows accurate diagnosis of liver cirrhosis in 82%-88 % of cases[11]. However, its value depends on the experience of the operator and the quality of the ultrasound instrument. Furthermore, diagnosis of hepatic cirrhosis by ultrasound relies to a significant extent on indirect parameters of liver cirrhosis such as evidence of portal hypertension.

Despite the increasing propagation of transient elastography no studies have investigated the diagnostic performance of transient elastography compared to clinical signs and only one in comparison to ultrasound including only a limited number of cirrhotic patients[12]. Therefore, the present investigation evaluated the benefit of transient elastography for the assessment of liver cirrhosis in a large cohort of patients with chronic liver disease compared to diagnostic tools available in the daily routine like cutaneous liver signs, laboratory parameters and ultrasound.

MATERIALS AND METHODS

Between 2005 and 2008 a total of 291 patients with chronic liver disease of different aetiologies who underwent liver biopsy in a tertiary care centre were additionally investigated by transient elastography, ultrasound, biochemical parameters and cutaneous liver signs within 12 mo after liver biopsy. Ultrasound examination, blood sampling, physical examination and transient elastography were performed on the same day. Ultrasound examination was done unaware of the results of transient elastography and of liver biopsy.

Inclusion was restricted to patients with chronic liver disease (duration of liver disease > 6 mo) and absence of acute flares defined as acute ALT elevation higher than 5 times the upper limit of the patient's individual baseline level. In four out of 291 patients liver stiffness could not be assessed by transient elastography due to morbid obesity. Histologically confirmed liver cirrhosis was present in 182 patients.

Liver histology and quantification of liver fibrosis

Liver biopsy was performed percutaneously by the Menghini technique using a 1.6-mm-diameter needle. Liver fibrosis was evaluated semiquantitatively according to the scoring system of Desmet *et al*[13] or Bondini *et al*[14]. All liver specimens were stained with HE, Elastica-van-

Table 1 Baseline clinical and biochemical characteristics of all patients

	All (n = 291)	HCV (n = 92)	ASH/NASH (n = 109)	HBV (n = 35)	Cryptogenic (n = 13)	HDV (n = 10)	Other causes (n = 32)
Age, yr	54 ± 15	59 ± 13[b]	53 ± 15	51 ± 13[b]	59 ± 15	43 ± 9[a]	50 ± 17[a]
Gender,%							
Female	39.9	41.3	36.7	28.6	38.5	30	59.4[a]
Male	60.1	58.7	63.3	71.4	61.5	70	40.6
Cirrhosis, %	62.5	76.1	56	68.6	100[b]	70	25.0[d]
BMI, kg/m²	25.5 ± 4.2	24.6 ± 3.9[a]	25.8 ± 4.8	27.2 ± 3.3	25.3 ± 3.0	23.2 ± 4.9	25.2 ± 3.6
Bilirubin, mg/dL	2.7± 4.8	1.5 ± 2.5[b]	4.3 ± 7.0	1.5 ± 1.5[b]	1.8 ± 1.3	2.0 ± 1.6	4.1 ± 5.8
Albumin, g/dL	3.6 ± 0.7	3.8 ± 0.6[b]	3.4 ± 0.7[a]	3.8 ± 0.7	3.4 ± 0.7	3.4 ± 0.6	3.7 ± 0.4
Immunoglobulins, g/dL	1.7 ± 0.7	1.8 ± 0.7	1.5 ± 0.7	1.7 ± 0.8	1.5 ± 0.4	2.6 ± 0.7[b]	1.7 ± 0.5
AST, U/L	116 ± 175	100 ± 54	113 ± 187	76 ± 51	70 ± 55	155 ± 94	243 ± 400
ALT, U/L	106 ± 176	102 ± 71	73 ± 100[b]	72 ± 52	43 ± 20	131 ± 62	300 ± 462[a]
AFP, μg/L[1]	6.2	9.7	5.8	3.4	5.9	7.2	2.9
Platelets, [a]1000/μL	170 ± 83	152 ± 82	181 ± 79	165 ± 78	168 ± 77	127 ± 74	208 ± 96
Prothrombin time, %	83 ± 18	88 ± 16[b]	78 ± 21[b]	85 ± 13	81 ± 23	73 ± 14	86 ± 15

[1]Median value. [a]$P \leq 0.05$; [b]$P \leq 0.01$ *vs* all other patients. HCV: Hepatitis C virus; HBV: Hepatitis B virus; HDV: Hepatitis D virus; ASH: Alcoholic steatohepatitis; NASH: Non-alcoholic steatohepatitis.

Gieson (EvG), Gomori, PAS-Diastase and iron stain and analysed by experienced pathologists blinded to the results of transient elastography and ultrasound.

Liver stiffness measurement

Liver stiffness was assessed by transient elastography (Fibroscan®) as described previously[15]. At least 10 measurements were performed. Only procedures with a success rate of 60% were considered reliable. The median value was taken as representative. Liver cirrhosis was assumed in case of a median value ≥ 13 kPa which has been identified in previous studies and a large meta-analysis[15,16].

Conventional ultrasound examination

Liver cirrhosis was suspected if two of the following criteria were present: (1) nodular appearance of the liver surface; (2) inhomogeneous liver texture; (3) rarefaction or tortuosity of hepatic veins; (4) dilatation of portal vein beyond 12 mm; (5) splenomegaly; (6) presence of ascites; (7) collateral circulation and (8) hypertrophy of the quadrate lobe[17].

Cutaneous liver signs

Liver cirrhosis was assumed in patients presenting with at least one of the following cutaneous liver signs: spider angiomata, venectasias of the abdominal wall, glossy tongue, Terry's nails, palmar erythema and gynaecomastia.

Platelet count and APRI index

A platelet count < 150000/μL and an APRI index > 2 were used as a cutoff for the diagnosis of liver cirrhosis. APRI-index was determined only in patients with viral hepatitis. The APRI index was calculated as follows: AST (× upper limit of normal) × 100/ platelet count (10^9/L).

Statistical analysis

A χ^2 was used for comparison of categorical variables. McNemar's test was used on nominal data. Student t test and Mann-Whitney test were used for comparison of continuous variables. The significance level was set at $P < 0.05$, all P values were two tailed. Statistical analysis was performed with the SPSS software 18.0 (SPSS, Munich, Germany).

RESULTS

Among all 291 investigated patients with chronic liver disease 31.6 % had hepatitis C, 37.5 % ASH/NASH, 12% hepatitis B, 3.4% hepatitis D, 11 % had other more rare causes of chronic liver disease (primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis, hereditary haemochromatosis, Wilson's disease) and 4.5% liver disease of unknown cause ("cryptogenic"). Chronic alcohol consumption was defined as daily intake above 20 g in females and 40g in males. 182 of all 291 patients had histologically proven liver cirrhosis. According to the Child Pugh score 58.8% of these patients were classified as A, 20.9% as B and 8.2% of patients as C. A total of 12.1% of patients with liver cirrhosis could not be classified according to Child Pugh score due to missing data. The majority of biochemical and clinical parameters did not differ between the different aetiologies of chronic liver disease (Table 1). Notably, patients with hepatitis D infection displayed higher ALT, AST, immunoglobulin levels, and lower prothrombin time despite a younger age compared to most of the other patient groups (Table 1).

Sensitivity of transient elastography for the detection of liver cirrhosis was 90.4 % (Table 2). TE could not be performed in 4 patients due to morbid obesity, these patients were nevertheless included in the calculation of sensitivity. The positive predictive value was 75.2%. Specificity was 51.2% and the negative predictive value was 76.7%. Sensitivity for the detection of liver cirrhosis by transient elastography was about 10% higher compared to ultrasound and exceeded that of platelet

Table 2 Sensitivity, specificity, positive and negative predictive value of the different non-invasive examinations for detection of liver cirrhosis

	All					Viral hepatitis[1]				
	Sensitivity	Specificity	PPV	NPV	*P* value[3]	Sensitivity	Specificity	PPV	NPV	*P* value[3]
Liver stiffness ≥ 13 kPa	90.4	51.4	75.2	76.7		91.3	44.4	82.5	64.0	
Ultrasound[2]	80.1	82.4	88.7	70.6	0.02	96.6	61.2	81.4	90.9	0.04
Platelets < 150.000/μL	58.0	80.2	83.3	52.8	0.03	63.1	72.2	86.7	40.6	0.05
Cutaneous liver signs[2]	45.1	72.1	70.4	47.2	0.0001	42.7	64.7	77.4	28.6	0.01
APRI-Score ≥ 2	NA	NA	NA	NA	NA	56.1	63.3	87.7	24.1	

[1]*n* = 139; only patients with chronic hepatitis B, C and D were included; [2]According to the definitions in the patients and methods section; available for 257 patients; [3]For comparison of sensitivities with liver stiffness as reference. NA: Not applicable; PPV: Positive predictive value; NPV: Negative predictive value.

Table 3 Sensitivities for detection of liver cirrhosis by different combinations of non-invasive examinations

	All patients (*n* = 182)				
	Sensitivity	Specificity	PPV	NPV	*P* value[1]
Liver stiffness ≥ 13 kPa and/or ultrasound cirrhosis	96.1%	50.5%	76.5%	88.5%	
Liver stiffness ≥ 13 kPa and/or platelets < 150.000/μL	93.9%	49.1%	75.4%	82.8%	< 0.0001
Ultrasound and/or platelets < 150.000/μL	88.2%	68.0%	82.6%	76.9%	< 0.0001
Ultrasound and/or cutaneous liver signs	87.6%	62.0%	79.7%	74.7%	< 0.0001
Platelets < 150000/μL and/or cutaneous liver signs	79.4%	63.7%	78.5%	65%	< 0.004

[1]Sensitivity compared to the combination of liver stiffness and/or ultrasound. NS: Not significant; PPV: Positive predictive value; NPV: Negative predictive value.

count, APRI index and cutaneous liver signs by more than 30% (Table 2). In the subgroup of patients with viral hepatitis, sensitivity and specificity of ultrasound was slightly superior to that of transient elastography (Table 2). The highest liver stiffness values were found in patients with cryptogenic cirrhosis, although these patients had the lowest ALT levels (data not shown). The combination of liver stiffness with ultrasound or platelet count allowed detection of liver cirrhosis at a slightly higher rate (96.1% and 93.9% respectively) than transient elastography alone (90.4%). Combinations of screening tests including transient elastography were superior to combinations of ultrasound with cutaneous liver signs or platelet counts (Table 3). Area under the receiver operating characteristic curve (AUROC) for detection of liver cirrhosis by transient elastography was 0.760 (95%CI: 0.694-0.825) compared to an AUROC of 0.796 (95%CI: 0.740-0.863) for detection of liver cirrhosis by conventional ultrasound. The combination of transient elastography with ultrasound resulted in an AUROC of 0.825 (95%CI: 0.768-0.882).

Transient elastography correlated with the severity of liver cirrhosis, like presence of ascites, cutaneous liver signs and particularly with biochemical parameters included in the Child-Pugh score (Table 4). The correlation coefficient of transient elastography with bilirubin was $r = 0.34$ ($P < 0.0001$), with albumin $r = -0.43$ ($P < 0.0001$), with prothrombin time $r = -0.44$ ($P < 0.001$) and immunoglobulins $r = 0.34$ ($P < 0.001$). No correlation was seen between transient elastography and AFP, platelets, ALT or BMI.

In the subgroup of patients with normal platelet count ($n = 161$) of the present population transient elastography showed the highest sensitivities for the detection of cirrhosis compared to other screening methods like ultrasound, platelet count, cutaneous liver signs (Table 5). Among patients with Child-Pugh A liver cirrhosis TE was superior with respect to sensitivity compared to other tests by more than 15% (Table 5). In advanced liver cirrhosis (*i.e.*, Child-Pugh B and C patients) gain in sensitivity of transient elastography compared to ultrasound was only small (98.1% *vs* 96.2%). Performance of platelet count (sensitivity 74.1 %) and cutaneous liver signs (sensitivity 64.3%) improved with more advanced cirrhosis but were still worse than corresponding results of conventional ultrasound or transient elastography.

DISCUSSION

Diagnosis of liver cirrhosis and especially early stages of liver cirrhosis with its important clinical implications is often difficult and detection might be missed in daily clinical practice. Autopsy studies in Western populations revealed that one third of patients with liver cirrhosis are not identified during their lifetime[5,18]. This dissatisfying misclassification of liver cirrhosis and the fact that an invasive liver biopsy is supposed to be the "gold standard" has led to the development of several non-invasive technologies.

Transient elastography has been extensively evaluated with more or less complex fibrosis scores and other diagnostic tools[19] but a comparison with routinely available markers in a large series of patients with histologically confirmed liver cirrhosis is still lacking. Therefore, the present study was explicitly designed to reflect a routine clinical setting and investigated the

Table 4 Comparison of transient elastography with clinical and biochemical parameters

	⩾ 13 kPa (*n* = 161)	⩾ 27.5 kPa[1] (*n* = 94)	⩾ 54 kPa[1] (*n* = 48)	⩾ 27.5kPa *vs* < 27.5 kPa *P* value	⩾ 54 kPa *vs* < 54 kPa *P* value	⩾ 54 kPa *vs* 27.5-54 kPa *P* value
Age, yr	60 ± 14	56 ± 13	55 ± 13	NS	NS	NS
BMI, kg/m²	26.2 ± 3.7	25.5 ± 4.0	24.8 ± 3.7	NS	0.05	NS
Bilirubin, mg/dL	1.1 ± 1.0	3.2 ± 5.6	4.4 ± 6.9	0.0001	0.007	0.04
Albumin, g/dL	3.9 ± 0.4	3.4 ± 0.7	3.2 ± 0.7	0.0001	0.0001	0.02
Immunoglobulins, g/dL	1.6 ± 0.7	2.0 ± 0.7	2.1 ± 0.8	0.02	0.007	0.03
AST, U/L	79 ± 49	102 ± 71	115 ± 83	0.02	0.015	0.07
ALT, U/L	79 ± 56	71 ± 51	69 ± 54	NS	NS	NS
AFP, μg/L[2]	7.6	7.7	7.8	NS	NS	NS
Platelets, 1000/μL	145 ± 68	144 ± 82	151 ± 77	NS	NS	NS
Prothrombin time, %	88 ± 13	76 ± 19	70 ± 18	0.0001	0.0001	0.02
APRI-Score[3]	2.4 ± 1.8	3.6 ± 3.1	4.3 ± 3.6	0.03	NS	NS
Platelets < 150.000/μL, %	59.7	60.6	56.3	NS	NS	NS
Ultrasound cirrhosis, %	73.1	88.9	93.6	0.02	0.01	NS
Splenomegaly, %	57.8	71.4	72.3	0.09	NS	NS
Ascites, %	16.4	35.5	52.1	0.01	0.0001	0.01
Cutaneous liver signs, %	43.3	55.3	63.2	NS	0.09	NS

[1]Cut-off values in accordance to Foucher *et al*[30]; [2]AFP is given as median value; [3]APRI-Score was only applied to patients with chronic viral hepatitis. NS: Not significant.

Table 5 Usefulness of transient elastography in cirrhotic patients with Child-Pugh A or normal platelet count

	Child-Pugh A[1]					Normal platelet count[2]				
	Sensitivity	Specificity	PPV	NPV	*P* value[3]	Sensitivity	Specificity	PPV	NPV	*P* value[3]
Liver stiffness ⩾ 13 kPa	91.5%	48.8%	59.5	87.5		85.3%	62.4%	66.7	82.8	
Ultrasound	75.2%	75.2%	72.5	77.8	0.02	71.2%	86.4%	82.5	76.9	0.04
Platelets < 150.000/μL	55.1%	78.6%	68.6	67.3	NS	NA	NA	NA	NA	
Cutaneous liver signs	42.0%	74.8%	59.2	59.7	0.01	46.2%	81.3%	66.7	65.0	0.001

[1]*n* = 107; [2]*n* = 161; Normal platelet count was 150.000-400.000/μL; [3]Values are given for the comparison of sensitivities with transient elastography. NA: Not applicable; NS: Not significant; PPV: Positive predictive value; NPV: Negative predictive value.

additional benefit of transient elastography for the identification of liver cirrhosis compared to clinical signs, simple laboratory parameters and ultrasound. Although measurement of transient elastography requires hardware equipment, it has the potential of a bedside test. High reproducibility of transient elastography for the determination of liver cirrhosis was shown in non-obese persons[20]. In contrast, reproducibility of transient elastography for differentiating fibrosis stages below F3 was poor. Hence, the present study focused on the identification of cirrhosis.

There are many other non-invasive surrogate markers and scores for determination of liver fibrosis and cirrhosis[8]. Recently, magnetic resonance elastography has been evaluated in patients with chronic liver disease[21]. However, these parameters or tests are either not routinely available, expensive or not properly evaluated and were therefore not integrated in the present investigation. Histopathological examination of liver is still considered the gold standard for evaluation of liver fibrosis[22] and was taken as reference in the present study. Liver biopsy has significant diagnostic limitations due the risk of serious complications, sampling and intra- or interobserver errors[23,24]. Error rates of 20%-45% for disease staging have been reported[25]. These limitations of liver biopsy can influence the diagnostic performance of transient elastography.

The major finding of the present study was a significant increase by 10 % of the sensitivity for the detection of liver cirrhosis by the use of transient elastography compared to best routine screening tests available (Table 2). Furthermore, combinations of different tests might improve diagnostic accuracy[26]. In the present investigation the combination of transient elastography with ultrasound allows detection of early stages of liver cirrhosis with the highest sensitivity followed by the combination of transient elastography with a platelet count below 150000/μL (Table 4).

It has to be kept in mind that these findings apply to the selected group of patients in which liver cirrhosis was determined according to the histological evaluation. The present investigation may therefore be biased as patients with advanced and clinically apparent liver cirrhosis might not have been considered for liver biopsy at all. However, if liver cirrhosis can easily be clinically assessed, liver biopsy or non-invasive tests are no longer needed. As expected, patients that were staged Child-Pugh A had greater diagnostic benefit from transient elastography than the overall cohort of patients and especially patients with advanced Child Pugh B or C cirrhosis (Table 5). The

superiority of TE compared to other conventional tests also applied to patients with normal platelet count (Table 5). Unravelling fibrosis in these "unsuspicious" patients with early cirrhosis has important clinical and therapeutic consequences.

Sensitivity of cutaneous liver signs to detect liver cirrhosis varied between 31% and 84% in a recent report[7]. Low sensitivities were found for cutaneous signs like glossy tongue, gynaecomastia and white nails, while presence of spider naevi and palmar erythema showed higher sensitivities. Cutaneous liver signs were not sub-differentiated in the present study as this would have resulted in too small populations. Sensitivities for abdominal ultrasound so far reported were comparable to the present study[11,27]. However, ultrasound largely depends on the quality of the technical equipment used and the operator's skills. Platelet count is often used as a rough estimation for the presence of liver cirrhosis. The present investigation suggests that platelet count and cutaneous liver signs are not useful for the identification of early liver cirrhosis as sensitivities were below 60%. However, there are also several drawbacks of transient elastography. First, in 1%-9% of the cases transient elastography is technically not feasible due to obesity, ascites, scars, narrowing of the intercostal spaces or other reasons[6]. Technical failures of transient elastography were seen in 2% of the present study (n = 4 patients with morbid obesity). These diagnostic failures were still included in the calculations. In addition, acute disease deteriorations with high ALT values and cholestasis can lead to a systematic overestimation of liver stiffness[28,29]. Therefore only patients with chronic liver disease without flares were included in the present study. Misclassification of transient elastography can also occur in the case of macronodular cirrhosis, high body mass index and liver tumors[30].

A major advantage of transient elastography compared to other non-invasive tests is that it not only indicates the presence or absence but also severity of liver cirrhosis. Different cutoffs have been established that predict or exclude the presence of oesophageal varices, hepatocellular carcinoma, and the Child Pugh score[30,31]. In the present study liver stiffness was positively correlated to parameters of liver function like albumin, prothrombin time and bilirubin (Table 4). In addition, transient elastography correlated to immunoglobulins as further markers of liver cirrhosis stage. Thus, transient elastography like the Child Pugh score should be a valuable tool to estimate progression of liver cirrhosis.

This study also has its limitations: this investigation was performed at a tertiary centre, therefore a high proportion of more advanced stages in patients with chronic liver disease can be expected. This is apparent from the fact that the rate of histologically proven liver cirrhosis in all liver biopsies performed is quite high (n = 182/291; 62.5%). Furthermore, the procedures of the independently prospective performed transient elastography, ultrasound and clinical investigations were compared to liver biopsies which were done in advance with a maximum time range of one year. Usually, the development of chronic liver disease is a continuous, but mostly slow process over many years or decades and therefore rapid changes of liver stiffness or sonographic appearance is generally not expected. Acute flares of chronic disease were excluded as it is already known that measurement of liver stiffness is influenced by acute hepatitis[28]. Investigators of transient elastography and ultrasound were furthermore unaware of the results of liver biopsy to exclude further bias.

Summarising, transient elastography allowed the identification of an additional 10% of cirrhotic patients among patients with chronic liver disease compared to routinely available non-invasive tests and examinations like ultrasound, platelet count, or cutaneous liver signs. Patients with early cirrhosis had the greatest diagnostic benefit from transient elastography. Combination of transient elastography with conventional ultrasound or platelet count further improved diagnostic accuracy.

COMMENTS

Background

The detection of liver cirrhosis is crucial for patients as this condition may lead to complications like hepatocellular carcinoma, variceal bleeding or hepatic decompensation. Autopsy studies reveal that one third of patients with liver cirrhosis are missed during their lifetime. Liver biopsy is thought to be the "gold standard" but non-invasive tools like transient elastography are increasingly available.

Research frontiers

Transient elastography is a valid tool for the differentiation of cirrhotic from non-cirrhotic liver but no studies have investigated the diagnostic performance of transient elastography compared to clinical signs and conventional ultrasound. Therefore, the present investigation evaluated the benefit of transient elastography for the assessment of liver cirrhosis in a large cohort of patients with chronic liver disease compared to diagnostic tools available in the daily routine like cutaneous liver signs, laboratory parameters and conventional ultrasound.

Innovations and breakthroughs

The major finding of the present study was a significant increase by 10% of the sensitivity for the detection of liver cirrhosis by the use of transient elastography compared to routine screening tests. Patients with early cirrhosis had the greatest diagnostic benefit from transient elastography. Furthermore, liver stiffness positively correlated with parameters of liver function like albumin, prothrombin time and bilirubin.

Terminology

Liver cirrhosis: end-stage of chronic liver disease which is characterised by progressive scarring of liver tissue ("fibrosis") while healthy cells are vanishing. This leads to a functional loss of the organ, development of portal hypertension and also represents a precancerosis for liver malignancies; transient elastography: non-invasive method that determines liver stiffness by generating an elastic wave. Liver stiffness correlates with the degree of fibrosis, a higher degree of fibrosis implying greater stiffness.

Peer review

Transient elastography has been compared with routinely available markers (clinical signs, simple laboratory parameters and ultrasound) in a large series of patients with histologically confirmed liver cirrhosis. A major advantage of transient elastography compared to other non-invasive tests is that it not only indicates the presence or absence but also severity of liver cirrhosis. In the present study liver stiffness was positively correlated to parameters of liver function like albumin, prothrombin time and bilirubin.

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