High Prognostic Value of Mini-Laparoscopy for Advanced Liver Disease-Related Complications in Patients with HCV Infection

Eugen Zizer^a Johanna Backhus^a Stephan Bohl^b Anette Braun^a
Irina Baturina^a Dietmar Klass^c Nektarios Dikopoulos^a
Thomas Seufferlein^a Matthias Dollinger^a

^aKlinik für Innere Medizin 1, and ^bKlinik für Innere Medizin 3, University of Ulm, Ulm, and ^cKlinik für Allgemeine und Innere Medizin und Gastroenterologie, Lüneburg, Germany

Key Words

HCV · Mini-laparoscopy · Advanced chronic liver disease · Cirrhosis

Abstract

Background/Aim: The assessment of advanced chronic liver disease (ACLD) is a prerequisite for therapy and surveillance in patients with chronic hepatitis C infection. Mini-laparoscopy-assisted liver biopsies facilitate both histological and macroscopical evaluation of liver fibrosis. This study is aimed at investigating the prognostic significance of the laparoscopic assessment for the cumulative incidence of ACLD-related events. **Patients and Methods:** We performed a single center, retrospective analysis of 94 patients with either macroscopically or/and microscopically assessed advanced fibrosis/cirrhosis caused by chronic hepatitis C infection. The patients' data, the respective laboratory results, and follow-up period were evaluated in the outpatient clinic. **Results:** The group with both macro- and microscopic diagnosed ACLD showed a significantly higher number of decompensating events ($n = 7$) compared with the other 2 groups ($n = 0$ in the group with only histological and $n = 1$ in the group with only laparoscopic diagnosis of advanced liver disease). The results were not affected by the successful treatment of

the hepatitis C virus. In the Cox-regression analysis, the spleen size (>120 mm) was significantly associated with the incidence of ACLD-related events. **Conclusions:** Assessment of ACLD in chronic hepatitis C by mini-laparoscopy-assisted liver biopsies may facilitate the selection of patients with a poor prognosis, irrespective of achieving a sustained virological response following treatment. Follow-up of these patients should be intensified to treat decompensation early.

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Introduction

The diagnosis of cirrhosis or an advanced stage of fibrosis in patients with chronic HCV infection is a prerequisite for planning therapeutic regimens and surveillance investigations [1]. Even after successful antiviral therapy, patients with high-grade fibrosis or cirrhosis continue to be at risk of developing liver disease-related complications such as variceal bleeding or hepatocellular carcinoma (HCC) [2, 3]. The gold standard for diagnosing advanced chronic liver disease (ACLD) is the histological assessment by liver biopsy; however, sampling errors are a well-recognized limitation of the method [4]. Thus, other invasive (e.g. hepato-venous pressure gradient

Table 1. Assessment by mini-laparoscopy, histology, and APRI score: range for grading liver fibrosis/description of advanced liver disease

Grade of fibrosis	No fibrosis	Beginning to moderate fibrosis		Advanced liver disease	
		mild fibrosis	moderate fibrosis	severe fibrosis	cirrhosis
Histological grading	No histologic features of fibrosis, F0	Enlarged, fibrotic portal tracts, F1	Periportal or portal-portal septa, but intact architecture, F2	Fibrosis with architectural distortion, but no obvious cirrhosis, F3	Probable or definite cirrhosis, F4
Laparoscopic assessment	Even liver surface without pathologic features	A few to moderate number of pale fibrosis marks, healthy liver surface is visible to predominant, no nodules on liver surface		Liver surface completely covered by pale fibrosis marks, no healthy liver surface detectable, no nodules on liver surface	Irregular nodular liver surface with fibrosis septations
APRI score	<0.7	0.7–1.5		>1.5	>2.0

(HVPG)) and non-invasive (Fibroscan, AST to platelet ratio index (APRI) score) techniques have been extensively evaluated for distinguishing various stages of liver disease and the probability of related complications [5, 6]. Their prognostic value and reliability varies depending on a number of factors, not at least the stage of the liver disease [7, 8]. Detection of a pre-cirrhotic liver or compensated state of cirrhosis, in particular, can be challenging with clinically characteristic signs usually lacking. Diagnostic markers for future decompensation of the liver are even more elusive [8].

Elevated portal venous pressure and hypersplenism have been shown to play a major part in the development of adverse events related to advanced liver disease [9, 10]. The laparoscopically performed assessment of the liver surface reliably complements the histological evaluation of advanced liver disease in the clinically compensated state and detects up to 37% more patients with cirrhosis [11] compared with the histological assessment alone. The prognostic benefit resulting from this additional information has not been evaluated yet.

In the current retrospective study, we present the results of a long-term follow-up of HCV-positive patients with laparoscopically obtained liver biopsies. The prognostic value of the macroscopic evaluation of the liver surface was compared with the histological assessment of the liver parenchyma and biochemical markers of fibrosis. In our cohort, we were able to demonstrate that only the combined macroscopic and microscopic diagnosis of advanced liver disease was associated with decompensation over the next 5 years, irrespective of a sustained virological response (SVR) following antiviral treatment.

Patients and Methods

Patients

Between 2005 and 2011, we performed a mini-laparoscopy-assisted liver biopsy in 368 consecutive patients with chronic HCV infection prior to antiviral therapy. Other causes of liver disease were excluded using laboratory parameters in combination with histology. Fibrosis and/or cirrhosis were graded both macroscopically and microscopically. For the purpose of the study, advanced liver disease was defined as advanced liver fibrosis or liver cirrhosis with the respective laparoscopic and histological criteria listed in table 1.

Follow-Up and Follow-Up Endpoints

Following laparoscopic assessment, patients were seen regularly at variable intervals ranging from 3 to 12 months. The last follow-up was completed in 2008/2015. Surveillance visits included a complete medical history, physical examination, laboratory results, and an ultrasound examination. Patients with the diagnosis of cirrhosis were regularly screened for varices in the upper gastrointestinal tract [8]. Progress or decompensation of liver disease was defined as:

- Development of ascites,
- Hepatorenal syndrome (HRS),
- Hepatic encephalopathy >I° (West Haven criteria),
- Varices bleeding in the upper gastrointestinal tract or varices ≥II° with indication for endoscopic treatment,
- HCC (histological confirmation or 2 coincident imaging methods),
- Liver transplantation.

Histology Assessment

H&E routinely stained liver specimens were evaluated by liver pathologists in the local Institute of Pathology, University of Ulm. The stage of fibrosis (F0–F4) was assessed according to the score by Desmet et al. [12]. Advanced liver disease was defined as fibrosis stages F3 and F4, respectively. All the biopsies were of appropriate size and included enough specimen material for a proper pathological staging of liver fibrosis.

Fig. 1. Picture samples of laparoscopically assessed normal liver surface without fibrosis (a), beginning to moderate fibrosis (b), severe fibrosis (c), and cirrhosis (d).

Liver Fibrosis/Cirrhosis Evaluation by Mini-Laparoscopy

Mini-laparoscopy was performed as described before [13, 14]. Briefly, analgesedation was achieved by i.v.-application of 3–5 mg midazolam, 7.5–15 mg pethidine, and 20–50 mg propofol p.r.n. A Veress needle was inserted into the abdominal cavity guided by a 2.75 mm trocar, and 2–3 liters CO₂ were insufflated for a pneumoperitoneum. A 2.5-mm optical device was inserted through a 2.75 mm trocar, and the 2 investigators evaluated the surface of the liver (size, color, signs of fibrosis or cirrhosis, superficial lesions). The assistant investigator inserted the second trocar in the subcostal area for guiding the semiautomatic tru-cut biopsy needle. A 20-mm long biopsy was taken. In case of bleeding, the biopsy spot was sealed by coagulation. After a successful biopsy, the insufflated CO₂ was aspirated and the sedation terminated. The macroscopically evaluated stage of fibrosis was defined as reported [11]. For a better macroscopic discrimination between beginning and severe fibrosis, a macroscopic graduation was defined as presented in table 1 and figure 1.

APRI Score

The APRI score [15] was assessed within 30 days prior to the mini-laparoscopy. The test value of >1.5 was considered as the cut-off for advanced fibrosis/cirrhosis (histological grading F3/F4).

Ultrasound Assessment

All patients underwent an ultrasound investigation of the abdominal cavity, with assessment of the spleen size. Splenic size measurement (the maximum distance between the dome of the spleen and the splenic tip) was done on the longitudinal section through the splenic hilum. The cut-off for a normal spleen size was set at 120 mm [16, 17]. Patients with ascites were excluded from the study.

Complication Assessment

Peri-interventional complications were recorded and graded as presented in table 2. In detail, a minor complication was defined as an adverse event that does not lead to an interruption of the investigation (e.g. sedation-related AE without interruption of the investigation or skin wound bleeding that needed suturing) and is not associated with a prolonged hospital stay (>24 h) or monitoring, respectively. A major AE was defined as a peri-interventional complication that leads to an interruption of the investigation or prolonged hospital stay (>24 h) with monitoring longer than as scheduled initially.

Statistics

All data analysis was performed with a statistical software package version 22.0 (SPSS Inc., Chicago, Ill., USA). Statistical significance was evaluated by using the Mann–Whitney U test. A p value <0.05 was considered significant. A Kaplan–Meier curve and Cox regression analysis were used to identify factors significantly affecting the development of cirrhosis-related events.

Results

Patients Data

One hundred twenty one patients showed advanced liver disease (severe fibrosis or cirrhosis). Twenty seven of these were lost to follow-up and excluded from the study. In the remaining 94 patients, advanced liver disease was diagnosed either by macroscopic evaluation only (group A; n = 41), histological evaluation only (group B; n = 17) or concordantly in both methods

Table 2. Grading for peri-interventional complications in mini-laparoscopy investigation

Grade	Characterization of complication
Minor complication	<ul style="list-style-type: none"> – The investigation can be completed as planned initially, no significant interruption necessary – No prolonged monitoring or hospital stay (>24 h) necessary
Major complication	<ul style="list-style-type: none"> – The investigation cannot be completed as scheduled initially – Monitoring and hospital stay >24 h necessary

(group C; n = 36; fig. 2). The baseline data of the 94 patients are presented in table 3. The laboratory results, physical examination, and ultrasound assessment did not show any signs of decompensated advanced liver disease at the time of laparoscopic/histological assessment.

APRI Score Subgroup Analysis in Advanced Liver Disease

The median values for APRI score were 0.5 (range 0.2–2.2) in group A (macroscopic diagnosis), 0.8 (range 0.3–3.8) in group B (microscopic diagnosis), and 1.5 (range 0.3–5.3) in group C (concordant diagnosis) as listed in table 3. Patients of group C with decompensation during follow-up showed a median APRI score of 2.3 (mean value 3.4; SD ± 1.4 ; range 1.6–5.3); the only patient with progression of the liver disease in groups A and B had an APRI score of 0.74. Both groups A and B showed a significant difference in APRI scores compared with group C ($p < 0.001$ and $p = 0.008$, respectively), and there was no significant difference between groups A and B ($p = 0.05$).

Platelets Number Subgroup Analysis in Advanced Liver Disease

The median values for platelets number were 217 g/l (range 110–366) in group A (macroscopic diagnosis), 227 g/l (range 113–320) in group B (microscopic diagnosis), and 169 g/l (range 70–455) in group C (concordant diagnosis) as listed in table 3. Patients of group C with decompensation during follow-up showed a median platelets number of 103 g/l (mean value 110; SD ± 36 ; range 70–184); the only patient with progression of the liver disease in groups A and B had a platelets number of 200 g/l. Group A, but not group B, showed a significant difference in platelets number compared with group C ($p = 0.003$ and $p = 0.092$, respectively), and there was no significant difference between groups A and B ($p = 0.632$).

Fig. 2. Patients' recruitment for follow-up after laparoscopic and histological assessment of cACLD.

Spleen Size Subgroup Analysis in Advanced Liver Disease

The median values for spleen size were 110 mm (range 77–130) in group A (macroscopic diagnosis), 103 mm (range 80–127) in group B (microscopic diagnosis), and 111 mm (range 82–147) in group C (concordant diagnosis) as listed in table 3. Patients of group C with decompensation during follow-up showed a median spleen size of 132 mm (mean value 3.4; SD ± 1.4 ; range 1.6–5.3); the

Table 3. Data of the 94 patients with cACLD; results are presented as mean value $\pm$ SD and (median value; range)

	cACLD		
Mini-laparoscopy	–	+	+
Histology	+	–	+
Number of patients	17	41	36
Age, years	41.7 $\pm$ 11.9 (44; 19–59)	52.8 $\pm$ 10.2 (52; 24–68)	55.1 $\pm$ 5.9 (53; 46–68)
Gender, female/male	5/12	23/18	19/17
Body mass index, kg/m ²	26.7 $\pm$ 4.4 (26.6; 19.2–36.4)	25.3 $\pm$ 4.5 (24.5; 16.6–38.2)	25.7 $\pm$ 3.3 (25.3; 19.8–35.1)
Laboratory results			
Creatinine, μ M/l	93 $\pm$ 57 (81; 45–305)	71 $\pm$ 16 (68; 47–123)	102 $\pm$ 127 (77; 59–783)
Bilirubin, μ M/l	8.7 $\pm$ 3.6 (8; 4–19)	9.7 $\pm$ 3.8 (9; 4–21)	12.0 $\pm$ 6.1 (10; 4–30)
AST, IU/l	79 $\pm$ 47 (67; 30–230)	54 $\pm$ 35 (41; 20–185)	105 $\pm$ 59 (92; 37–317)
ALT, IU/l	132 $\pm$ 76 (113; 33–337)	86 $\pm$ 71 (64; 23–369)	133 $\pm$ 81 (110; 17–400)
GGT, IU/l	105 $\pm$ 95 (84; 15–410)	76 $\pm$ 75 (46; 11–319)	113 $\pm$ 91 (95; 21–484)
AP, IU/l	73 $\pm$ 17 (74; 48–110)	72 $\pm$ 19 (73; 37–119)	86 $\pm$ 37 (82; 41–197)
INR	1.01 $\pm$ 0.09 (1; 0.9–1.2)	1.01 $\pm$ 0.08 (1.00; 0.9–1.2)	1.06 $\pm$ 0.09 (1.05; 0.9–1.4)
Platelets, g/l	206 $\pm$ 55 (227; 113–320)	218 $\pm$ 54 (217; 110–366)	180 $\pm$ 77 (169; 70–455)
APRI score	1.1 $\pm$ 0.9 (0.8; 0.3–3.8)	0.7 $\pm$ 0.5 (0.5; 0.2–2.2)	1.8 $\pm$ 1.3 (1.5; 0.3–5.3)
Ultrasound assessment			
Spleen >120 mm	4	4	13
Spleen size, mm	106 $\pm$ 14 (103; 80–127)	105 $\pm$ 14 (110; 77–130)	114 $\pm$ 19 (111; 82–147)

only patient with progression of liver disease in groups A and B had a spleen size of 116 mm. There was no significant difference between the 3 groups concerning the spleen size (group A vs. B: $p = 0.872$, group A vs. C: $p = 0.072$, and group B vs. C: $p = 0.155$).

Peri-interventional Complications

In the presented 94 patients with ACLD 1, major adverse event was recorded: a 55-year-old patient (laparoscopic diagnosis of advanced liver fibrosis; histological grading 3–4) showed an arterial bleeding from the liver biopsy spot that could not be stopped endoscopically. An abdominal section and operative closure of liver bleeding were necessary. Four days later, the patient could be discharged in good condition. No other adverse events/complications were recorded in the investigated group.

Antiviral Treatment Results

In group A, 33 patients received antiviral treatment achieving 19 SVR (58%). In group B, 8 of 15 patients (SVR 53%) and in group C, 25 of 35 patients (SVR 71%) treated were eradicated successfully. With the recruitment and follow-up period encompassing years 2004–2015, antiviral regimens and agents varied from the combination of ‘pegylated interferon and ribavirin (RBV)’ to the last generation of direct acting agents (DAAs). All data concerning viral load and respective genotype and treatment details are listed in table 4.

Table 4. Data on genotype/viral load and antiviral treatment results in 94 patients with advanced liver disease

	cACLD		
Mini-laparoscopy	–	+	+
Histology	+	–	+
Number of patients	17	41	36
Genotype			
GT1	13	33	27
GT2	1	2	3
GT3	2	5	6
GT4	1	1	0
Viral load (HVL/LVL)	14/3	28/13	22/15
SVR/all treatments	8/15	19/33	25/35
SVR after			
pegIFN/RBV	3	11	10
pegIFN/RBV + TEL or BOC	3	6	5
DAA	2	2	10

GT = Genotype; HVL = high viral load; LVL = low viral load; pegIFN = pegylated interferon; TEL = telaprevir; BOC = boceprevir.

Incidence of Advanced Liver Disease-Related Events

Patients in group A were followed up for (mean) 67 months (range 16–125), group B for (mean) 62 months (range 11–122), and group C for (mean) 71 months (range 11–127), respectively. Group B patients did not experience advanced liver disease-related events in the follow-up period (0/17, 0%). In group A, one patient (1/41, 2%)

Table 5. Time in follow-up and events related to cACLD: event one was recorded for a patient with cACLD assessed by laparoscopy alone; events 2–8 were recorded for patients with cACLD assessed by laparoscopy and histology. The respective patient's data are listed below. Follow-up time is recorded in months (mean $\pm$ SD; range)

cACLD								
Mini-laparoscopy	–	+	+					
Histology	+	–	+					
Follow-up	62 $\pm$ 38; 11–122	67 $\pm$ 34; 16–125	71 $\pm$ 41; 11–127					
Events	0	1	8					
Follow-up time till event	0	93	40 $\pm$ 24; 11–78					

Number of patients	Sex	Age, years	Event	FU till event, m	GT	Spleen size, mm	APRI	Number of platelets
1	Male	60	HCC	124	1a	<120	0.74	200
2	Female	53	HRS	43	1b	>120	4.12	97
3	Female	65	HCC	68	2	>120	4.45	83
4	Male	48	Ascites	11	1b	>120	5.32	70
5	Male	68	HCC, varices III ^o	78	1b	>120	2.41	130
6	Male	49	HCC	48	3	<120	2.14	184
7	Female	66	HCC	32	1b	>120	2.06	109
8	Female	49	Ascites	30	3	>120	1.58	125
9	Male	52	Varices III ^o	13	1b	>120	1.74	85

developed a HCC that was detected 93 months after the staging investigation. In group C, 8 of 36 patients (22%) showed advanced liver disease-related events (HCC in 4, development of ascites in 2, esophageal varices grade III^o requiring ligation and HRS followed by an urgent liver transplantation in one patient each). The incidence of decompensating events was significantly higher in group C compared with the other 2 groups. Decompensation of the liver disease occurred on an average 40 months (range 11–78) following laparoscopic staging (table 5). A Cox regression analysis of patients' data with ACLD-related complications revealed a spleen size greater than 120 mm and/or platelets of less than 150 g/l as the only parameters associated with decompensation (table 6; fig. 3).

Discussion

The diagnosis of advanced liver disease in patients with chronic HCV infection has been essential for the management of antiviral therapy and follow-up in the era of interferon/RBV therapy, and it is still required for determining the choice of the new DAAs and the duration of therapy [18]. While decompensated liver cirrhosis is easy to detect clinically, the diagnosis of compensated stages of ACLD may be more challenging. The combination of macroscopic and microscopic assessments of the liver has

previously been shown to be superior to the histological evaluation alone for the detection of fibrous changes [11, 14, 19], most likely due to the sampling error generated by just one liver biopsy [4]. Accordingly, laparoscopy revealed a significant number of patients in our care suffering from severe fibrosis or cirrhosis, but understaged by histology. Since the APRI score was only validated against histology [15], it failed to improve the sensitivity of the bioptic assessment in this subgroup of patients.

Other than previous studies, however, we were able to relate the macroscopic and/or microscopic changes of the liver to the development of ACLD-associated adverse events within 5–10 years of the investigation. To our knowledge, we are the first to show the relevance of the macroscopic assessment compared with histology in predicting the natural history of ACLD. None of the patients solely diagnosed with ACLD on histology developed decompensated liver cirrhosis, in contrast to 2% of patients with a macroscopic diagnosis only and 22% of patients with the combined diagnosis. Thus, mini-laparoscopy might be a reliable diagnostic tool for selecting patients with compensated ACLD (cACLD) at risk of decompensation within the next 10 years. The predictive value of the assessment was irrespective of successfully treating the virological infection, that is, active liver disease as stated in the recent Baveno guidelines. This issue is even more striking because even in the stage of ACLD (advanced fi-

Table 6.

a Sensitivity, specificity and predictive values (nPV, pPV), likelihood ratios (pLR, nLR) for the prediction of cACLD-related events in patients with laparoscopy and histology assessment or with laparoscopy assessment alone. The calculation of predictive values in the group with histology assessment alone was not possible for histology alone assessed patients showed no cACLD-related events. The used cut-off-values are presented below (number of platelets <150 g/l, spleen-size >120 mm and APRI score >1.5)

	Laparoscopy and histology	95% CI	Laparoscopy only	95% CI
Platelets number (150 g/l)				
Sensitivity	77.78	39.99–97.19	77.78	39.99–97.19
Specificity	84.71	75.27–91.60	83.82	72.90–91.64
pLR	5.09	2.76–9.36	4.81	2.53–9.15
nLR	0.26	0.08–0.89	0.27	0.08–0.90
pPV	35.00	15.39–59.22	38.89	17.30–64.25
nPV	97.30	90.58–99.67	96.61	88.29–99.59
Spleen size (>120 mm)				
Sensitivity	77.78	39.99–97.19	77.78	39.99–97.19
Specificity	82.89	72.53–90.57	85.00	73.43–92.90
pLR	4.55	2.48–8.33	5.19	2.58–10.40
nLR	0.27	0.08–0.91	0.26	0.08–0.89
pPV	35.00	15.39–59.22	43.75	19.75–70.12
nPV	96.92	89.32–99.63	96.23	87.02–99.54
APRI score (>1.5)				
Sensitivity	88.89	51.75–99.72	88.89	51.75–99.72
Specificity	74.47	64.43–82.91	81.43	70.34–89.72
pLR	3.48	2.30–27	4.79	2.78–8.23
nLR	0.15	0.02–0.95	0.14	0.02–0.87
pPV	25.00	11.46–43.40	38.10	18.11–61.56
nPV	98.59	92.40–99.96	98.28	90.76–99.96

nPV = Negative predictive value; pPV = positive predictive value; pLR = positive likelihood ratio; nLR = negative likelihood ratio.

b The multivariate Cox-regression analysis (94 patients from groups A–C enclosed) showed reduced number of platelets <150 g/l and spleen size >120 mm being the relevant parameters for the development of cACLD-related events

	HR (95% CI)	p value
SVR	2.428 (0.306–19.245)	0.401
Bilirubin, $\mu\text{M/l}$	1.223 (0.961–1.557)	0.102
AST, IU/l	1.009 (0.969–1.051)	0.664
ALT, IU/l	1.005 (0.984–1.027)	0.627
AP, IU/l	1.014 (0.982–1.048)	0.391
Platelets, g/l	0.977 (0.960–0.994)	0.008
Spleen size (>120 mm)	5.251 (1.424–19.365)	0.013

AST = Aspartate aminotransferase; ALT = alanine aminotransferase; AP = alkaline phosphatase.

brosis or beginning of cirrhosis), adequate therapy ameliorates the inflammation activity in the liver. Thereto, the condition of inflammation-related structural changes in the liver can be stopped and the hepatic stellate cells resolve fibrosis significantly. This is also shown in acute liver failure [20]. But the structural changes of the liver, as detected by mini-laparoscopy, appear to be long-term ef-

fective for the macroscopic assessment of ACLD-predicted adverse events in successfully treated patients as well. This issue may present a point of potential interest for further investigations.

In a multivariate analysis, the only other parameters associated with decompensation were spleen size and platelet count, hinting a close relationship between the

Fig. 3. **a** Kaplan–Meier curve for the cACLD-related events in 94 patients with macroscopic or microscopic cACLD or both. **b** Kaplan–Meier curve for the probability of cACLD-related events according to the 3 observed groups: A = macroscopic cACLD, B = microscopic cACLD, C = both macro- and microscopic cACLD.

changes detected by mini-laparoscopy and the development of portal hypertension. Considering no significant difference in the distribution of spleen size values between the 3 groups of patients, this underlines the relevance of complementing laparoscopic assessment for the diagnosis of ACLD. Indeed, portal hypertension has been shown to predict decompensation of liver disease [21]; however, its assessment by measuring the HVPG has been restricted to specialized centers, and transjugular biopsies are limited by size and quality for histological staging and grading of liver disease [22]. In addition, mini-laparoscopy is a low-risk endoscopic procedure: in line with the experience from other endoscopy units [19, 23], a major complication was recorded in only one investigation. The number of 12 minor complications and only 1 major complication (presented above) for the total of 1,120 mini-laparoscopy investigations performed in 2005–2011 in our endoscopy unit highlights the good safety profile of mini-laparoscopy. Thus, mini-laparoscopy offers a valuable and safe alternative diagnostic method for patients at risk of cACLD.

The obvious limitations of our study and the method are the semi-quantitative assessment of fibrosis during laparoscopy and the non-blinded investigators due to the retrospective design. However, a total of 5 hepatologists were involved in the presented investigations with 2 of them having to agree on the macroscopic diagnosis at any given time, strengthening the reliability of results in daily practice. The limited number of patients and the single

center experience are other points to be addressed in future.

In conclusion, our data demonstrates the ability of mini-laparoscopy combined with histology to stage hepatitis C accurately and to predict ACLD-associated complications, thus identifying patients with compensated disease at risk of decompensation within 10 years. Currently, we are analyzing the diagnostic capability of mini-laparoscopy in other liver diseases; however, future studies will have to validate mini-laparoscopy against other methods such as HVPG-measurement and elastography [24].

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