Enhanced liver fibrosis test in a group of patients with alcohol abuse

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Abstract

Background: Enhanced Liver Fibrosis (ELF) test is a set of indirect markers of liver fibrosis that can be used for assessing the severity of liver fibrosis. The ELF test includes three biomarkers: hyaluronic acid (a component of the extracellular matrix), TIMP-1 (an inhibitor of matrix metalloproteinases that break down collagen) and PIIINP (a marker of collagen synthesis at the site of disease process). These biomarkers or the ELF test can be used in early diagnostic approaches of liver damage caused by viral infections or alcohol abuse. The main aim of our study was to measure ELF values in three groups of individuals: a control group, a group of alcoholics and a group of patients with acute alcohol intoxication. The results of the ELF test were compared with established biochemical markers of alcoholism.

Methods: The study involved 113 individuals (71 males, 42 females) with a mean age of 43 years. They were divided into three groups: OSM group consisted of individuals (N = 39) who were examined in the Occupational and Sports Medicine Clinic. The AAI group consisted of 31 individuals with acute alcohol intoxication, and the AD group consisted of 43 individuals who were undergoing treatment for alcohol dependence. We assessed the following parameters in the serum samples of all three groups of subjects: mean corpuscular volume (MCV), activity of aspartate amino transferase (AST), alanine amino transferase (ALT), gamma glutamyl transferase (GGT) and the parameters of a novel ELF test for liver fibrosis stage assessment. ELF values are below 7.7 in the early stage of fibrotic process and above 9.8 in severe fibrosis. All statistical tests were conducted by SPSS 21.0 for Windows (SPSS, Inc. Chicago, USA).

Results: Mean values of the established biomarkers of alcoholism in OSM, AAI and AD groups for MCV were 91.9; 90.9 in 95.3, medians of catalytic activity of AST were 0.30; 033 in 0.42 µkat/L, for ALT 0.41; 0.34 in 0.56 µkat/L and for GGT 0.37; 0.34 in 0.92 µkat/L. Kruskal – Walliss test showed a statistical significance between groups for AST, GGT in MCV ($p < 0.002$), while ALT ($p = 0.052$) did not differ significantly. In OSM the median of the ELF test is 7.99 (6.99–10.18), and in AD group 9.47 (6.98–14.73). In the AD group a statistically significant correlation was between AST, ALT, GGT and the ELF test ($r = 0.524$; 0.306 in 0.632), in OSM the significance was proven only for MCV ($r = 0.327$).

Conclusion: The results of the measurements show a statistically significant increase in the established markers of alcoholism (MCV, AST, ALT and GGT) in the AD group as compared to the OSM group. Median ELF test in the AD group indicates moderate liver fibrosis, however, considering the range of 6.98 to 14.73, some individuals in this group have severe fibrosis. The results show that increased values of AST, ALT and GGT and correlations between them indicate liver damage, while the ELF test better predicts developing stage of liver fibrosis. Various scores and indexes are used for liver fibrosis assessment. The ELF test is proposed as a very useful diagnostic test and probably has a high potential of applicability in the primary care of patients with alcoholic and nonalcoholic liver damage.

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1 Introduction

Chronic consumption of excessive amounts of alcohol leads to liver damage, ranging from steatosis, steatohepatitis, progressive degrees of fibrosis, cirrhosis to hepatocellular carcinoma. Most individuals with severe alcohol dependence develop steatosis, while a smaller share of these develop steatohepatitis and liver cirrhosis. Steatosis is usually presented with no symptoms and clears after full abstinence of some duration. Long-term alcohol consumption leads to the inflammation of the liver, infiltration of polymorphonuclear cells, hepatocyte injury and the development of alcohol steatohepatitis, while 20–40% of patients go on to develop liver fibrosis and 10–20 % develop cirrhosis, which is linked to a risk of associated complications, including ascites, liver encephalopathy, renal failure, etc. (1).

In the early stage of development, alcohol liver disorder (ALD) may be symptom-less. Different imaging diagnostics (UZ, CT, MRI, FibroTest, FibroMeter, Hepascore, elastography, etc.) is used to discover the disease, as well as indirect and direct laboratory tests (2,3). With these methods, we can distinguish between mild and severe liver fibrosis but not the intermediate stage. Laboratory testing has the same limitations. While indirect tests (gamma-glutamyl transferase, transaminases, platelet count, albumin …) reflect liver function and potential inflammatory processes, they do not point to changes in the matrix and the process of fibrogenesis. Prognostic biological markers are based on extracellular degradation during fibrogenesis, which is characterised by a rise in cytokines (tumour growth factor-β), a rise in the extracellular matrix components (hyaluronic acid), breakdown shares in % to products (procollagen NC peptide) and enzymes (tissue inhibitor of metalloproteinase 1). They have a high level of specificity and sensitivity (4,5). Traditionally, evaluation and discovery of liver fibrosis and cirrhosis were confirmed with a liver biopsy, which is not considered a suitable method to be the golden standard anymore due to invasiveness and unrepeatable results (6,7). Despite different evaluation scales and forms non-invasive methods are considered more acceptable, safer, more accessible and appropriate for following the development of fibrosis in the longer-term. However, they have still not been validated for a full diagnostic range to discover different stages of development of liver fibrosis and cirrhosis (2).

Likewise, imaging methods and the use of biological markers have limitations, particularly with regard to discovering the initial stages of fibrosis. In ALD, determining the hyaluronic acid has worked the best (8). In his study, Liber (9) assessed the use of extracellular matrix component in 247 patients with ALD, while Rosenburg (10) performed the ELF test on 1,021 patients. The ELF (enhanced liver fibrosis) test has provided promising results (10,11,12). It is a combination of direct markers of fibrosis that form an algorithm that can be used to evaluate the presence and stage of fibrosis. The test includes three indicators: hyaluronic acid (HA), ami-

no-terminal propeptide of procollagen type III (PIIINP) and procollagen type II (PIINP), and tissue inhibitor of metalloproteinase-1 (TIMP-1). HA, PIINP and PIIINP are markers of the formation matrix deposits – fibrogenesis, while TIMP-1 points to decomposition of the matrix – fibrolysis. Other researcher (13,14,15) have demonstrated that the ELF test is a suitable prognostic test of fibrosis development in chronic hepatic disease and has been confirmed as a useful supplemental test for liver biopsy. Studies' results show that the ELF test is useful for early discovery of hepatic damage when liver biopsy is not yet necessary. According to the findings of Parkers et al (16), it would be necessary to study its suitability to establish the risk of developing chronic liver disease in patients with pathological values of hepatic tests due to excessive consumption of alcohol.

Because excessive consumption of alcohol is common in Slovenia, laboratory test for discovering biochemical injury of the liver are used at both primary and secondary health care levels. The established markers of alcoholism are as follows: gamma–glutamyltransferase (GGT), aspartate–aminotransferase (AST), alanine–aminotransferase (ALT) and mean corpuscular volume (MCV) in the blood samples. Therefore, the purpose of our study was to measure the values of the more novel ELT test in three different groups of subjects: the control group, the group with confirmed diagnosed alcoholism and the group with acute alcohol consumption. We wanted to test laboratory measu rements of three biological markers of hepatic fibrosis, i.e. HA, PIIINP and TIMP-1, and then compare them to GGT, AST, ALT and MCV measurements. As the procedure is invasive, liver biopsy was not performed, so diagnostic applicability of the ELF test was not evaluated.

2 Materials and methods

2.1 Subjects

113 subjects were included in the study (71 male and 42 female) and divided into three groups (OSM, AAI and AD). The mean age of all subjects was 43 ± 13 years. There were 39 subjects (25 males, 14 females, with mean age of 38 ± 11 years) in the control group (OSM). This group consisted of random subjects who were examined at the department of Occupational and Sports Medicine at the Domžale Community Health Centre. All subjects gave consent and completed a questionnaire. In order to ensure total anonymity of the obtained data, the completed questionnaire was then submitted into a box prepared for this purpose. The second group (AD) consisted of 43 subjects (33 males, 10 females, mean age 46 years) diagnosed with alcohol dependence. They were treated at Begunje Psychiatric Hospital. The third group (AAI) comprised 31 subjects (13 men, 18 women, mean age 52 years) who sought treatment at the Emergency Room Department of Jesenice General Hospital due to a single alcoholic intoxication. In these subjects, serum ethanol concentrations in the range of 1.58 to 4.78 g/L were determined (normal values: 0.00 to 0.50 g/L). The study was conducted in 2012. Prior to commencing the study, permission from the Ethics Committee at the Jesenice General Hospital was obtained on 6 April 2012 (No. 0305-30/2012/2). The subjects signed an informed consent form. All the samples we handled were double-coded, ensuring data confidentiality.

2.2 Samples

Venous blood samples were taken between 7am and 10am from all subjects while fasted. This guaranteed equal sampling conditions for all subjects included in the study. We used excess biological material that remained after routine laboratory tests were performed on individual subjects (OSM), ordered by a specialist at the department of occupational, traffic and sports medicine, or a treating physician for subjects (AD) from Begunje Psychiatric Hospital and subjects (AAI) from Jesenice General Hospital. After 20 minutes, at the end of the coagulation phase, the blood samples for serum biochemical assays were subjected to centrifuge for 10 minutes at 1500 × g and 21 °C. Serum samples intended for liver fibrosis assessment using the ELF test were kept at –20 °C until analysis.

2.3 Laboratory results

The concentrations of the following markers of alcohol dependence were measured: mean corpuscular volume (MCV) in blood and the serum catalytic activity of AST, ALT and GGT enzymes. The analyses were performed at the Department of Laboratory Diagnostics at Jesenice General Hospital and at the Diagnostic Laboratory of Domžale Community Health Centre. MCV was determined using a combined haematological method combining impedance and laser detection of blood cell size. The catalytic activities of all three enzymes (AST, ALT, GGT) were determined using the recommended IFCC laboratory methods. ELF test parameters (HA, PIIINP and TIMP-1) were measured on an ADVIA Centaur® Siemens device with an *invitro*diagnostic multivariate test, which allows a uniform assessment of the presence or progression of liver fibrosis in patients with signs of chronic liver disease. This estimate is based on a mathematical equation (Table 1) that combines the logarithms of the measured serum concentrations of HA, PIIINP and TIMP-1. The concentration of all parameters is expressed in ng / ml, whereas the final ELF values are absolute numbers without units.

An interpretation of the stage of hepatic fibrosis assessed using the ELF test is given in comparison with the Ishak Rating Scale, which was formed on the basis of liver biopsy results of 1.021 patients (aged 18 to 75 years) with chronic liver disease of different etiologies (10). Samples were divided into three group considering the stage of liver fibrosis in accordance with the Ishak scale. No fibrosis to mild fibrosis corresponds to stage 0–2 on Ishak scale, moderate fibrosis to stage 3–4 and severe fibrosis to stage 5–6 Using descriptive statistics, two limit values were set – the low and the high one. Low limit value separates the stage of liver fibrosis on Ishak scale between 0–2 from 3–6 stage with a sensitivity of 88.6 % and specificity of 34.6%. High limit value separates stages 0–4 from 5 and 6 on Ishak scale with a specificity of 89.7% and a sensitivity of 65.4%. According to the manufacturer of the reagent kit, the precision of the ELF method is set by the variation coefficient in

Table 1: Evaluation equation
$ELF = 2.278 + 0.851 \ln(c_{HA}) + 0.735 \ln(c_{PIIINP}) + 0.394 \ln(c_{TIMP\text{-}1})$.

ELF calculation	Stage of hepatic fibrosis (ELF)	Stage of hepatic fibrosis (Ishak scale)
< 7.7	zero to mild	0–2
> 7.7 – < 9.8	moderate	3–4
> 9.8	severe	5–6

the series for 8,95 ELF test value, which is 0.35%, and 0.45% between series.

2.4 Statistical analysis

The results of biochemical measurements were expressed as the average value with standard deviation (avg; SD) and as the median with a range (min - max) for parameters whose distribution was not normal. The Kruskal-Wallis test and the Spearman correlation were used for statistical analysis of the data. The statistical significance limit (p) was below 0.05. We used the SPSS 21.0 statistical program for the Windows environment (SPSS, Inc. Chicago, USA).

3 Results

The basic demographic data of the subjects of all three groups (OSM, AAI and AD) are presented in Table 2, while Table 3 shows the results of measurements of standard tests (MCV, AST, ALT, GGT) of liver function. The Kruskal-Wallis test compares the measured concentrations of alcohol dependence markers between the OSM, AAI, and AD groups, showing statistically significant differences in all parameters except ALT, where the catalytic activity is borderline statistically significant ($p = 0.052$). The medians for MCV were significantly lower in OSM and AAI subjects than in AD subjects ($p = 0.001$), as were the medians of catalytic activity for AST and GGT ($p = 0.002$; $p < 0.001$). Catalytic

Table 2: Basic characteristics of subjects.

	OSM	AAI	AD	Total
Number (N)	39	31	43	113
Age (years)	38 ± 11	52 ± 18	46 ± 11	43 ± 13
Gender (m/f)	25/14	13/18	33/10	71/42

OSM – the Occupational and Sports Medicine group; AAI – Acute Alcohol Intoxication group; AD – Alcohol Dependence group.

Table 3: Measured values of basic set of alcoholism markers

	OSM	AAI	AD	p
MCV (fL)	91.9 ± 4.2	90.9 ± 5.7	95.3 ± 7.3	0.001
AST (µkat/L)	0.30 (0.17–0.93)	0.33 (0.20–1.95)	0.42 (0.22–1.50)	0.002
ALT (µkat/L)	0.41 (0.16–2.51)	0.34 (0.17–3.36)	0.56 (0.24–4.22)	0.052
GGT (µkat/L)	0.37 (0.19–4.75)	0.34 (0.10–5.52)	0.92 (0.20–16.16)	0.001

OSM – the Occupational and Sports Medicine group; AAI – Acute Alcohol Intoxication group; AD – Alcohol Dependence group.

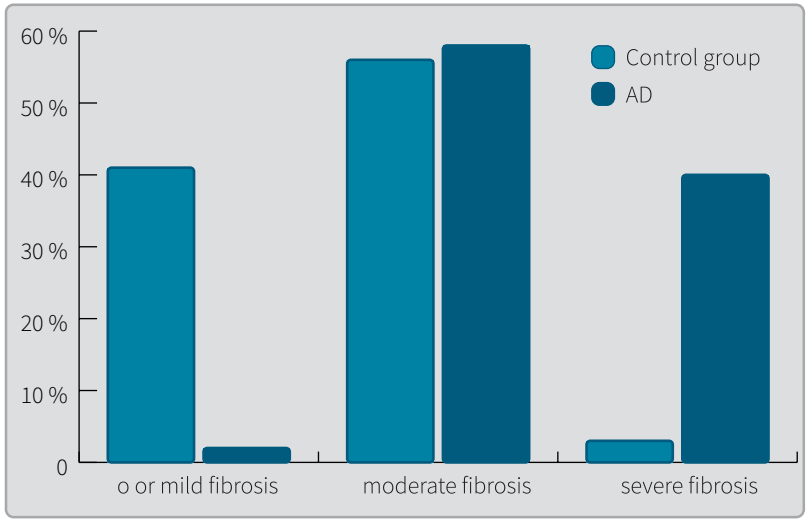

Figure 1: ELF test results in the OSM control group and AD.
Moderate fibrosis defined with values ranging from 7.7 to 9.8 is likewise present in the control group and alcohol dependence group; while the ration between mild fibrosis or no fibrosis (< 7.7) and severe fibrosis (> 9.8) is opposite among groups.

activities range in intervals that are the widest in AD subjects in absolute terms (Table 3).

We also compared the calculated values for the ELF between OSM and AD groups, which, according to the methods described in the criteria, provides an estimate of the stage of liver fibrosis. There are statistically significant differences between the value of OSM and AD in the ELF test ($p < 0.001$). In OSM subgroup the median of the ELF test is 7.99 (6.99–10.18), which shows moderate fibrosis. In AD group, the median is 9.47 (6.98–14.73), which, while still considered moderate, is close to the borderline value of 9.8 for severe liver fibrosis. ELF values of AD subjects range from 6.98 to 14.73, meaning that subjects include those with moderate fibrosis and those with values above 9.8 who have very severe fibrosis, according to the Ishak scale their fibrosis rates are 5 and 6. Table 4 shows the values of basic liver test and ELF test parameters in OSM and AD subjects. Individual stages of liver fibrosis are also presented with visuals (Figure 1). Moderate fibrosis, determined by the ELF, is represented by values between 7.7 and 9.8. Thus, the median in the OSM subgroup approaches the lower limit for moderate fibrosis and in the DA group the upper one.

Table 5 shows the correlation results between established markers of alcoholism (AST, ALT, GGT, and MCV) and individual ELF test parameters (HA, PIIINP, and TIMP-1) and ELF calculation for liver fibrosis stage. We used the Spearman correlation test for the non-parametric distribution of variables. In the OSM group, AST significantly correlated with HA, PIIINP, and the calculated value of ELF ($p < 0.01$) and TIMP-1

Table 4: Biological markers of alcoholism and ELF test parameters in OSM and AD groups.

Group	MCV (fL)	AST µkat/L	ALT µkat/L	GGT µkat/L	HA ng/mL	PIIINP ng/mL	TIMP – 1 ng/mL	ELF
OSM	91 ± 4.2	0.30 (0.17–0.97)	0.41 (0.16–0.51)	0.37 (0.19–4.57)	11.36 (3.06–86.53)	6.13 (3.06–11.40)	175.9 (117.2–861.7)	7.99 (6.99–10.18)
AD	95.3 ± 7.3	0.42 (0.22–1.50)	0.56 (0.24–4.22)	0.92 (0.20–16.16)	54.30 (5.46–3321)	7.92 (4.25–49.00)	244 (149.9–618)	9.47 (6.98–14.73)
p	0.038	0.001	0.052	0.001	0.001	0.001	0.001	0.001

OSM – Occupational and Sports Medicine group; AD – Alcohol Dependence syndrome

($p < 0.05$). GGT significantly correlates with all three parameters and the ELF calculation ($p < 0.01$) ALT correlates only with TIMP-1 and the calculated ELF value ($p < 0.05$).

The results of Spearman's correlation for OSM group are shown in Table 6. MCV and AST have a statistically significant correlation only with HA ($p < 0.05$), the other correlations between parameters are insignificant.

4 Discussion

Like other studies, the results of our study showed that subjects diagnosed with alcoholism had statistically significantly higher levels of MCV, AST, and GGT, but not ALT, compared to healthy controls. They also have significantly higher values for individual ELF test parameters. As expected, in the OSM group, all three liver enzymes, AST, ALT, and GGT, correlated significantly with the ELF assay, while in the control subjects only AST did.

Early detection of biochemical injury to hepatocytes due to excessive alcohol consumption significantly influences the initiation and success of treatment. The use of biological markers and liver tissue imaging techniques has significantly increased over the last decade, with many advantages: non-invasiveness, high repeatability, low cost and relatively easy availability (16,17). Established laboratory testing (AST, ALT, GGT, MCV, albumin, platelet count, etc.) for alcoholic liver injury are not specific because the result may also reflect pathological changes due to inflammatory processes, damage due to toxic factors (legal and illegal drugs) and damage due to infection with hepatitis C, B, and A viruses. While a combination of two or three biological markers improves sensitivity, it decreas-

Table 5: Correlation between biological markers of alcoholism and the ELF test in AD.

	HA	PIIINP	TIMP-1	ELF
MCV	0.241	0.021	0.126	0.200
AST	0.532**	0.491**	0.351*	0.524**
ALT	0.291	0.292	0.342*	0.306*
GGT	0.620**	0.517**	0.517**	0.632**

* $p < 0.05$; ** $p < 0.01$; AD – Alcohol Dependence group

Table 6: Correlation between biological markers and the ELF test in OSM group.

	HA	PIIINP	TIMP-1	ELF
MCV	0.327*	- 0.044	- 0.122	0.311
AST	0.339*	- 0.109	0.024	0.248
ALT	0.045	- 0.010	0.000	- 0.008
GGT	- 0.312	0.013	- 0.039	- 0.277

* $p < 0.05$; OSM – the Occupational and Sports Medicine group

es specificity. Nevertheless, they should be used for liver function screening in patients prone to risky (acute or chronic) consumption of alcohol. Because the liver is the main target of ethanol toxicity, increased GGT and/or AST activity is the first clinical sign of excessive alcohol consumption (18,19,20).

Our subjects diagnosed with alcoholism had significantly higher MCV, AST, and GGT values compared to controls. Likewise, Dinievski et al (21) measured elevated concentrations of indirect biological markers (MCV, GGT, AST, ALT, and glutamate lactate dehydrogenase - GLDH) in alcohol addicts. In continuation, the results of the study were successfully upgraded by calculating the diagnostic use of various combinations of biological markers for diagnosing alcoholism. They demonstrated that GGT and GLDH have the highest diagnostic use (sensitivity of 89.47% and specificity of 78.84%). Due to lack of data, we were not able apply ROC analysis to calculate the sensitivity and specificity of combinations of biological markers. Similarly, in 2015, Gough et al (22) demonstrated in a group of healthy subjects (N = 210) and alcohol addicts (N = 272) that addicts had significantly higher values of MCV, AST and GGT, while ALT may it can also be elevated in a healthy population with higher body mass index. CDT was also determined in both groups of subjects, and, as expected, correlated very well with the amount of alcohol consumed by the addicts. We did not determine CDT, as our study included ELF test parameters (HA, PIIINP in TIMP-1). In 2004, Rosenberg et al (10) demonstrated that ELF tests with a sensitivity of 90% can identify different fibrosis rates of alcoholic and non-alcoholic origin. Therefore, we determined the parameters of the ELF test in the group of alcohol addicts and in the control group, and calculated the stages of fibrosis in both groups using the corresponding algorithm. The results showed moderate fibrosis in the control group as well as severe fibrosis in most subjects diagnosed with alcoholism. We did not validate the performance of the ELF test because measurements were performed using a standardised procedure with a Siemens device, ensuring a high degree of repetition of the results. The diagnostic utility of the ELF assay for assessing the stage of liver fibrosis has not been tested due to low research capacity.

We considered the results of studies conducted by other research groups to calculate different indices of fibrosis in different diseases of the liver. Calibers et al (23) recommend the use of FibroMeters indices to evaluate the stage and extent of liver fibrosis accompanying hepatitis B and C viral infections, liver damage due to alcohol consumption, and non-alcoholic fatty liver disease (NAFLD). The indices are based on blood test results, and index values are based on algorithms supported by the expert system, making them highly diagnostic for specific stages and types of liver damage. Umut Emre Aykut et al (24) compared the results of several scales: NAFLD FibroMeter™ scale, NAFLD Fibrosis scale (NFSA), and elastography to detect fibrosis in subjects with NAFLD. They found that there are no significant differences between the diagnostic utility of NAFLD and the NFSA scales, but was lower than the diagnostic utility of the liver elastometry method. In continuation, Boursier J (25), and Castera L (26) et al used non-invasive indices of biological markers to assess the fibrosis following infection with hepatitis C. According to these researchers, like elastometry of the liver, fibrosis indices have benefits and shortcomings, and they still recommend liver biopsy in case

of unclear assessment of the microarchitecture of the affected liver tissue. Mark CC Cheah et al (27) studied fibrosis indices in NAFLD and non-alcoholic steatohepatitis (NASH). The fibrosis in NAFLD and NASH means poor prognosis of disease outcome, which makes the need for a precise definition of the stage of fibrosis even greater. Among the fibrosis indices, the diagnostic utility of the ELF test has been identified, with area under the curve 0.90 at the rate of over 0.365 for advanced stages of fibrosis. Only Fibrometer has larger area under the curve from the ELF test for advanced fibrosis, while other scales (BARD, BAAT, FIB-4, APRI, FibroTest, NAFLD-NFS) demonstrate smaller areas under the curve and thereby lesser diagnostic utility.

The diagnostic utility of the ELF test has been studied by other researchers in patients with non-alcoholic fatty liver disease (NFLD), and in patients with hepatitis C and/or B infection (28,29,30). A study of patients with chronic hepatitis C, the ELF test was compared with the established AST to platelet ratio index (APRI) to assess the stage of chronic liver disease (10). All patients underwent liver biopsy for histological assessment, which was evaluated on the Ishak scale. Prognostic value for liver cirrhosis was 86% for APRI, and 91% the ELF test. While our subjects did not undergo liver biopsy, we assessed the correlation between established alcoholism markers (AST, ALT, GGT and MCV), individual parameters of the ELF test (HA, PIIINP and TIMP-1) and the ELF calculation for the stage of liver fibrosis. Results indicate that higher or borderline values of liver enzymes AST and GGT in alcohol addicts are a prognostic factor of the development of liver fibrosis. Various fibrosis indices and/or the ELF test can be used to assess the presence of fibrosis at an earlier stage of disease and later to avoid liver biopsy in the continuation of treatment, as it is a significantly more invasive and more expensive procedure for evaluating liver function. The role of the ELF test in distinguishing between patients without liver fibrosis and patients with advanced liver fibrosis has been the focus of many studies (14,15). We confirmed in our study that elevated activity of liver enzymes present a risk of developing liver fibrosis even in the control group. According to Parkes et al (16) the ELF test can predict the clinical outcome of the disease as good as a biopsy and serve as a useful tool for predicting clinical outcome in patients suffering chronic liver disease due to various reasons.

The fibrosis index based on the algorithm developed by researchers led by Paul Angulo (20) has a lower limit (-1.455) with no presence of fibrosis and an upper limit (0.676) that confirms the presence of fibrosis. Slovenian researchers, Joško Osredkar and Monika Nikolić (31), calculated the fibrosis index in 136 patients based on this model and demonstrated that the index' value in the subgroup of patients with cholangitis (N = 17) was –1.46 and 1.94 in the group with liver cirrhosis (N = 89), while the patients wit alcohol hepatitis (N = 6) had 2.73 and patients with undefined cirrhosis (N = 21) had an index of 0.81. As Angulo's fibrosis score was originally meant to assess the stage of fibrosis in non-alcoholic fatty liver, we did not calculate it in our subjects with confirmed diagnosis of alcohol dependence due to a lack of data (body weight).

Various indices and scales are used to assess liver fibrosis, among which ELF has high diagnostic utility according to the findings of foreign researchers. As it is a non-invasive test, it also has every potential to be used at the primary level of medical treatment for persons with al-

coholic and non-alcoholic liver damage. There are additional research opportunities in this area for targeted comparative studies of the ELF test and different fibrosis indices and elastography results in liver damage due to various reasons.

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