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# Non-invasive diagnostic methods of the liver fibrosis in patients with overweigh and obesity

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## Abstract

One of the biggest problems of modern medicine is the difficulty in early diagnostic and effective treatment of HCV infection due to its wide distribution, latent form and terrible consequences as a formation of liver cirrhosis (CP) and hepatocellular carcinoma (HCC). It is important to mention, that the rate of progression of liver fibrosis. It is an important medical and social problem that the number of patients with NAFLD, overweight and obesity is constantly increases [9]. Due to the high prevalence of NAFLD and CHC, these two pathologies will progress and contribute to the progression of fibrosis, and depending on the genome of the virus and metabolic syndrome. There is a high risk of developing CP and HCC even after achieving a stable virological response.

The main aim of our investigation was to assess the stages of fibrosis by using non-invasive methods for patients with overweight and obesity who being treated for HCV infection (with posthepatic fibrosis).

**Keywords: posthepatic fibrosis; overweight; elastography; FibroTest; FIB-4 index.**

**Topicality.** One of the biggest problems of modern medicine is the difficulty in early diagnostic and effective treatment of HCV infection due to its wide distribution, latent form and terrible consequences as a formation of liver cirrhosis (CP) and hepatocellular carcinoma (HCC) [1-3]. The WHO estimates that 1.75 million new HCV infections were reported worldwide in 2015 (23.7 new HCV infections per 100,000 people) [4, 5].

It is important to mention, that the rate of progression of liver fibrosis, liver failure and potential mediators of this process effects on the progression of liver disease. The fibrosis is reversible in the initial stages, but after the formation of fibrous septa that do not contain liver cells, the process becomes irreversible. New studies about fibrosis shows that adequate treatment of fibrosis is reversible at later stages of fibrosis [6-8].

It is an important medical and social problem that the number of patients with NAFLD, overweight and obesity is constantly increases [9]. Due to the high prevalence of NAFLD and CHC, these two pathologies will progress and contribute to the progression of fibrosis, and depending on the genome of the virus and metabolic syndrome. There is a high risk of developing CP and HCC even after achieving a stable virological response [10].

Modern development of new technologies contributes to the improvement of methods of diagnosis of liver diseases and fibrosis. The method of elastography is used as an addition to the widely used FibroMax tests (FibroTest, ActiTest, SteatoTest, AshTest, NashTest), is used [11, 12]. Elastography is a new method of ultrasound diagnosis and is considered as a non-invasive alternative method of diagnosis of liver fibrosis. The essence of the method is to reflect the elastic properties of soft tissues, which depend and change on the existing pathological processes. A diffuse decrease in elasticity (increased stiffness) is characteristic of fibrous changes in the liver [13-16].

Nowadays, the diagnosis of liver fibrosis by elastography is very important because this method allows to use non-invasive way of assessment to determine the degree of liver damage at the period of treatment, dynamics, effectiveness of treatment and prognosis, as well as narrow the indications for biopsy in patients [17, 18].

The main aim of our investigation was to assess the stages of fibrosis by using non-invasive methods for patients with overweight and obesity who being treated for HCV infection (with posthepatic fibrosis).

**Materials and Methods**

The research was conducted in Ternopil University Hospital at the Gastroenterology Department. There were examined 56 patients with posthepatic fibrosis after HCV infection without other diseases. All patients were re-examined by PCR to confirm a stable virological response and recovery from HCV infection. According to the WHO classification (1997), patients were divided according to their BMI. The first group consisted of 17 patients with normal body weight (BMI = 18.5 – 24.9 kg/m2), the second group included 18 patients with overweigh (BMI = 25 – 29.9 kg/m2), the third – 21 obese people I degree (BMI = 30 – 34.9 kg/m2). The control group included 20 healthy people. All patients were assessed by using Elastograph to determine the stage of fibrosis therefore FibroTest index and Fib-4 index was calculated. Elastography was done by using an ultrasound system Acuson S2000 (Simens). Liver parenchymal fibrosis was measured by using shear wave velocity (m/s) and was classified by using the METAVIR scale depending on the shear wave velocity. Indices were calculated by these formulas:

*FIB-4 = (age (yers) × AST (оð. / L))/ ( platlets (×$10^9$/L) × ALT (оð. /l)$^{½}$).*

*FibroTest = 4.467×Log [α2-macroglobulin (g/l)]-1.357× Log [Haptoglobin (g/l)] + 1.017×Log [GGT (IU/l)] + 0.0281× [Age (in years)] + 1.737×Log [Bilirubin (umol/l)] - 1.184× [ApoA1 (g/l)] + 0.301×Sex (female=0, male=1)-5.540.*

To all patients also calculated height, body weight, determined waist circumference (WC), hip circumference (HC) and WC/HC index were also determined.

The obtained data was processed by using Microsoft Office Excel 2007 (Microsoft Corp., USA), SPSS for Windows 20.0 (SPSS Inc., USA) Statistica 10.0 (StatSoftInc., USA) program. Quantitative data was presented in the amount (number) of the observations (n), the mean (M), standard error of the mean (m); qualitative data – in the form of relative indicators (%). The Kraskei-Wallis criterion was used to differentiate normal and abnormal data in the case of multiple compassion. Correlation analysis between individual indicators was obtained by using the Spearman correlation coefficient for nonparametric data.

**Result and Discussion**

The range of patient age was from 22-74. The age range of occulated (predominated) patients was 45-59 years (45.22%). The surveyed contained of 29 (25.22%) men and 27 (23.48%) women. The mean age for woman 45.62 ± 2.00 years and for men 53.41 ±1.91 years

**Table 1 - Distribution of patients into subgroups depending on BMI**

| I group | II group | III group |
|---|---|---|
| BMI 18,5—24,9 kg /m$^2$ | BMI 25-29,9 kg /m$^2$ | BMI 30-34,9 kg /m$^2$ |
| 17 (30,36 %) | 18 (32,14 %) | 21 (37,5 %) |

There were signs of asthenovegetative syndrome which was manifested as general weakness, increased fatigue and reduced efficiency (observed in 26,08%) admitted among all subgroups of patients. Dyspeptic syndrome was minimally expressed and was manifested mainly by bitterness in the mouth and loss of appetite.

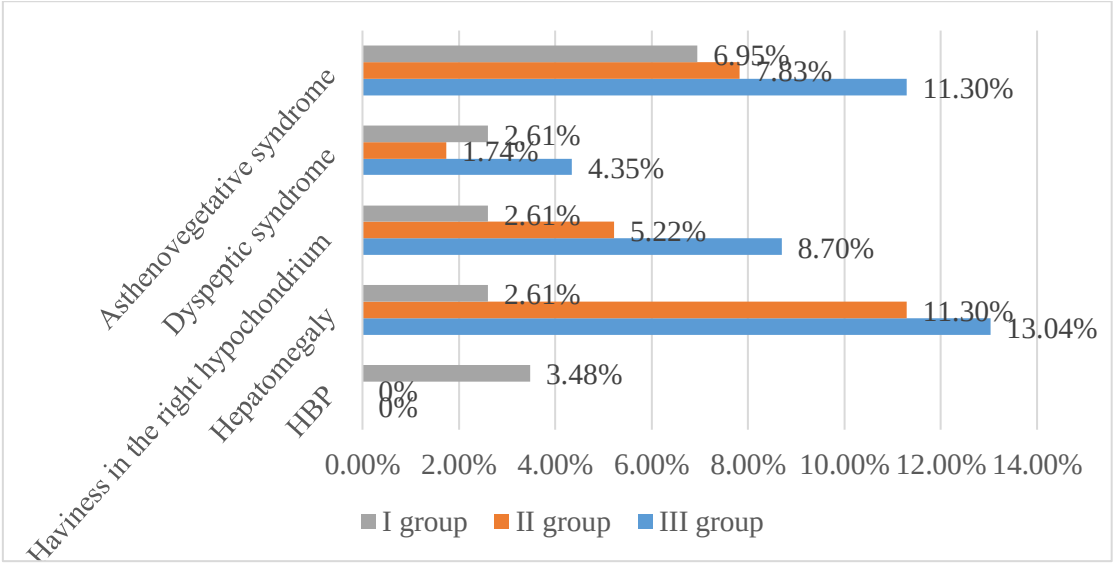


Figure 1. - Frequency of major clinical syndromes in the examined patients

During the objective examination (palpation), most patients showed the increased liver size (26.95%). Hypertension was diagnosed only in group I in 3.48% of patients. The results of the anthropometric analysis are presented in Table 2.

**Table 2. - Anthropometric data depending on BMI, M ± m**

| Indicator | I | II | III |
|---|---|---|---|
| Body weight, kg | 64,47±1,95 | 76,67±2,18* | 94,14±2,64* |
| Height, cm | 169,76±1,8 | 168,61±1,91 | 168,48±1,63 |
| BMI | 22,31±0,4 | 26,99±0,39* | 33,2±0,35* |
| WC, cm | 79,82±2,2 | 87,28±1,91* | 103,38±1,72* |
| HC, cm | 98,18±1,26 | 104,89±1,71* | 114,43±1,76* |
| WC/HC | 0,81±0,02 | 0,84±0,01* | 0,94±0,04* |

*Note. * p <0,05-significance of the difference according to the Kraskel-Wallis test.*

There were only 2 patients (1.74% of all examined) in group I, with an WC/HC index greater than 0.9 which indicated abdominal obesity. In patients with higher body weight (groups II and III) redistribution of adipose tissue increased and was respectively (6 (5.22%) and 11 (9.57%) of patients).

Abdominal obesity ($r = 0.30$, $p < 0.05$) was more common in men than in women (31 (26.96%) and 16 (13.91%)) made a significant difference in results. However, the number of cases of overweight and obesity was more often diagnosed in women than in men ($r = 0.33$, $p < 0.05$).

Thus, in our study, patients with asymptomatic course predominated. Patients with increasing body weight and ITS increased severity of heaviness in the right hypochondrium ($r = 0.21$, $p < 0.05$) and hepatomegaly ($r = 0.51$, $p < 0.05$).

The value of elastography data, FibroTest and FIB-4 had increased with increasing of body weight in patients, and the degree of fibrosis increased from F1 to F3. The average values for each group are shown in Table 3.

**Table 3. Distribution of liver fibrosis data in patients depending on BMI, M ± m**

| group | Elastography, m/s | FibroTest | FIB-4 |
|---|---|---|---|
| BMI ≤ 24,9 | 1,27 ±0,01 | 0,31 ±0,01 | 1,42 ± 0,05 |
| BMI = 25-29,9 | 1,38 ±0,01* | 0,43 ±0,03* | 1,80 ±0,01* |
| BMI = 30-34,9 | 1,49 ±0,04* | 0,52 ± 0,03* | 2,26 ±0,06* |

*Note. * p <0,05- significant difference in the criterion of Kraskel-Wallis,*

Overweight and obesity significantly affect the stage of fibrosis, regardless of its etiology ($p<0.01$).

**Conclusions**

1. It was registered that in patients with posthepatic fibrosis without concomitant pathology after HCV infection asymptomatic course of the disease is dominant, and in patients with increasing body weight and ITS increases the severity of the heaviness in right hypochondrium ($r = 0.21$, $p < 0.05$) and hepatomegaly ($r = 0.51$, $p < 0.05$).

2. It was found that in patients with posthepatic fibrosis in comorbidity with overweight and obesity, the gain of the weight significantly affects the degree of fibrosis ($p<0.01$).

3. It is necessary to use direct and indirect markers of liver fibrosis (FIB-4, Fibrotest indices) and pSWE-elastography to verify the stages of fibrosis depending on body weight, which correlate with each other and avoid false results.

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