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LIVER STEATOSIS AND ITS IMPLICATIONS IN PATIENTS WITH CHRONIC VIRAL HEPATITIS C

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Abstract

Introduction. *Hepatic steatosis represents a common pathological feature in patients with chronic viral C infection and can be independently associated with obesity, increased alcohol consumption, type 2 diabetes, and hyperlipidemia. These factors can contribute to the development of hepatic steatosis in patients with chronic HCV (Hepatitis C virus) infection.*

Materials and methods. *64 patients who underwent treatment with oral antivirals were included and evaluated through non-invasive methods for the degree of hepatic steatosis.*

Results. *After at least 3 months of sustained viral response, all patients with advanced hepatic steatosis were categorized into lower classes in the Steatotest evaluation.*

Conclusion. *This study highlights the importance of direct acting antiviral (DAA) treatment in the medical care of patients with chronic viral C infection and hepatic steatosis. Thirty years after the discovery of the hepatitis C virus, treatment with oral antivirals revolutionizes the medical care of patients with this chronic infection.*

Keywords*: Hepatic steatosis, Steatotest, chronic viral C infection.*

Rezumat

Introducere. *Steatoza hepatică reprezintă un aspect patologic comun la pacienții cu infecție cronică virală C și poate fi asociată în mod independent cu obezitatea, consumul crescut de alcool, diabetul zaharat de tip 2 și hiperlipidemia. Acestea pot contribui la apariția steatozei hepatice la pacienții cu infecție cronică VHC (virus hepatitic C).*

Material și metodă. *Au fost incluși 64 de pacienți care au urmat tratament cu antivirale orale și au fost evaluați prin metode noninvazive pentru gradul de steatoză hepatică.*

Rezultate. *După cel puțin 3 luni de la obținerea răspunsului viral susținut, toți pacienții cu steatoză hepatică avansată au prezentat îmbunătățiri semnificative la evaluarea prin Steatotest.*

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Concluzie. *Acest studiu subliniază importanța tratamentului cu antivirale cu acțiune directă (DAA) în îngrijirea medicală a pacienților cu infecție cronică virală C și steatoză hepatică. La 30 de ani dupa descoperirea virusului hepatitic C tratamentul cu antivirale orale revoluționează îngrijirea medicală a pacienților cu această infecție cronică.*
Cuvinte cheie: *steatoză hepatică, Steatotest, infecție cronică virală C.*

Introduction

Patients with hepatitis C virus (HCV) infection have a variable prevalence of hepatic steatosis, ranging from 40 to 86%, with a mean value of 55%[(1)]. The mild form of steatosis is the most common (78%), affecting less than 30% of hepatocytes. Steatosis occurs more frequently in patients with HCV (55%) than in the general adult population in Western countries (20-30%)[(2)].
Several scores for hepatic steatosis have been reported since 2005. Steatotest is the first serum biomarker proposed for evaluating the degree of hepatic steatosis and has been used in a cohort of 884 patients with various causes of chronic liver disease (including chronic HCV infection, HBV, and chronic toxic liver disease), compared with liver biopsy as the reference method[(3)].

Materials and methods

This research represents a single-center, prospective study conducted in a Gastroenterology clinic, which analyzed the degree of liver involvement by non-invasive methods in patients with chronic viral C infection after achieving sustained virologic response to oral antiviral treatment.
The study cohort included 64 patients with chronic viral C infection who were treated with oral antivirals and evaluated 3 months after achieving sustained virologic response post-treatment. 71.9% were female (n=46) and 57.8% were over 60 years old (n=37). Cases of liver disease, both known and newly diagnosed based on clinical, biological, and imaging criteria, were included in the study. Additionally, data from the literature regarding the short- and long-term evolution and treatment of chronic HCV infection were analyzed.
To evaluate the degree of liver damage in patients with hepatitis C virus infection, a non-invasive method called Fibromax (Steatotest) was used. This blood analysis includes five non-invasive tests, including Fibro Test for evaluating the degree of liver fibrosis,

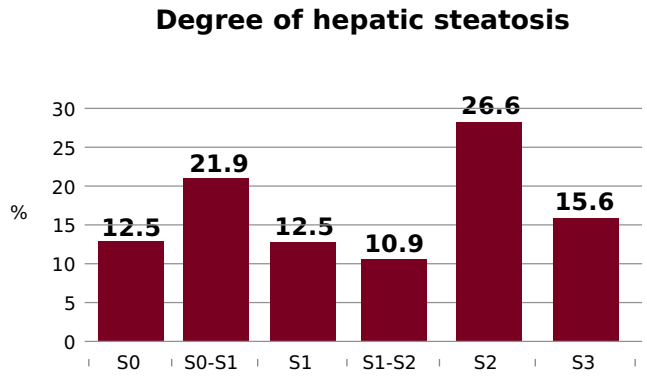

Figure 1. *Study population structure according to steatosis stage before treatment*

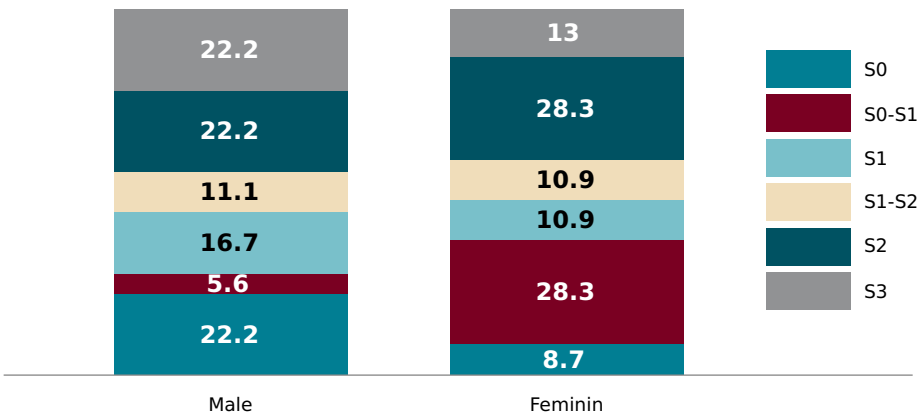

Figure 2. *Correlation between steatosis staging and gender at study baseline*

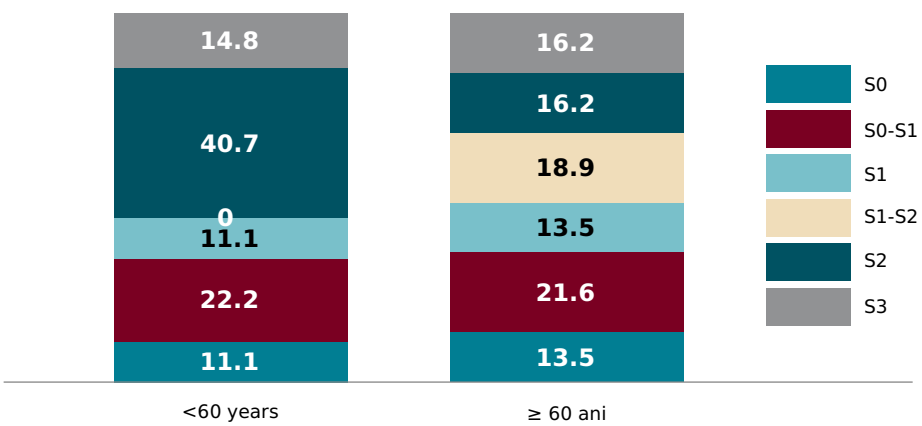

Figure 3. *Correlation of steatosis staging with age group at study baseline*

Acti Test for determining necroinflammatory activity, SteatoTest for evaluating the degree of liver fat accumulation, NashTest for determining the presence of nonalcoholic steatohepatitis (NASH) in patients with metabolic syndrome, and AshTest for determining the degree of liver damage in chronic alcohol consumers.

The study used specific reference values for SteatoTest, which were S0 ≤ 0.25, 0.25 < S1 ≤ 0.5, 0.5 < S2 ≤ 0.75, and S3 > 0.75. This test was performed both before oral antiviral treatment and at 3 months or more after sustained viral response was achieved.

Results

Before treatment, the degree of steatosis was as follows:

- 15.6% (n=10) of patients had stage S3 steatosis;
- 26.6% (n=17) had stage S2;
- in 21.9% (n=14) the staging was S0-S1, in 12.5% (n=8) the staging was S1, and in 10.9% (n=7) of the total study group the staging was S1-S2 (Figure 1).

Epidemiological characteristics correlated with steatosis staging at the initial timepoint highlighted the following aspects: the percentage distribution of steatosis degrees by gender did not differ significantly from a statistical point of view (p=0.237), however, it should be noted that a percentage of 22.2% of men had S3 or S2 steatosis, while among women, 28.3% were in stages S2 and S0-S1 (figure 2).

The percentage distribution of the degree of steatosis compared by age groups showed significant differences (p=0.045): cases of S2 steatosis predominate in patients under 60 years old (40.7%), while in the group over 60 years old the distribution is similar, with variations ranging from 13.5% to 21.6% (figure 3).

At the beginning of the study, among patients with cirrhosis (F4), 33.3% had stage S2 steatosis and 23.8% had stage S3 steatosis (p=0.486) (figure 4).

After treatment, three months after sustained viral response, the degree of steatosis was as follows:

- 6.3% (n=4) of patients still had stage S2 steatosis;
- 10.9% (n=7) had stage S1-S2, 18.8% (n=12) had stage S1, and 26.6% (n=17) of the total study group had stage S0-S1 (figure 5).

The epidemiological characteristics correlated with the staging of steatosis three months after sustained viral response highlighted the following aspects:

- the percentage distribution of the degree of steatosis compared

S1 * F1 Crosstabulation

			F1					Total
			F1-F2	F2	F3	F3-F4	F4	
S1	S0	Count	4	2	1	0	1	8
		% within F1	28,6%	20,0%	6,7%	,0%	4,8%	12,5%
	S0-S1	Count	4	3	2	1	4	14
		% within F1	28,6%	30,0%	13,3%	25,0%	19,0%	21,9%
	S1	Count	2	1	2	1	2	8
		% within F1	14,3%	10,0%	13,3%	25,0%	9,5%	12,5%
	S1-S2	Count	0	2	2	1	2	7
		% within F1	,0%	20,0%	13,3%	25,0%	9,5%	10,9%
	S2	Count	3	2	5	0	7	17
		% within F1	21,4%	20,0%	33,3%	,0%	33,3%	26,6%
	S3	Count	1	0	3	1	5	10
		% within F1	7,1%	,0%	20,0%	25,0%	23,8%	15,6%
Total		Count	14	10	15	4	21	64
		% within F1	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

Figure 4. *Correlation between steatosis staging and fibrosis before treatment*

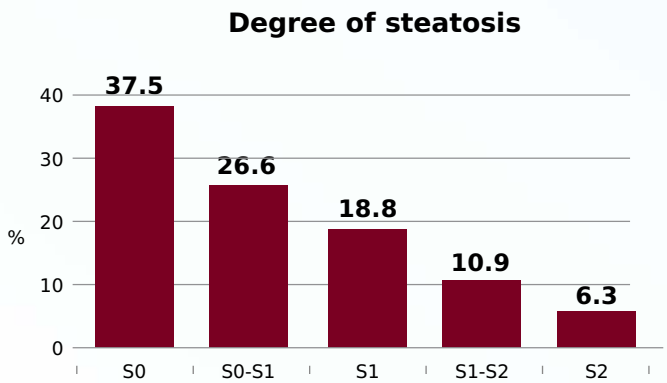

Figure 5. *Group structure three months after sustained viral response based on the degree of steatosis*

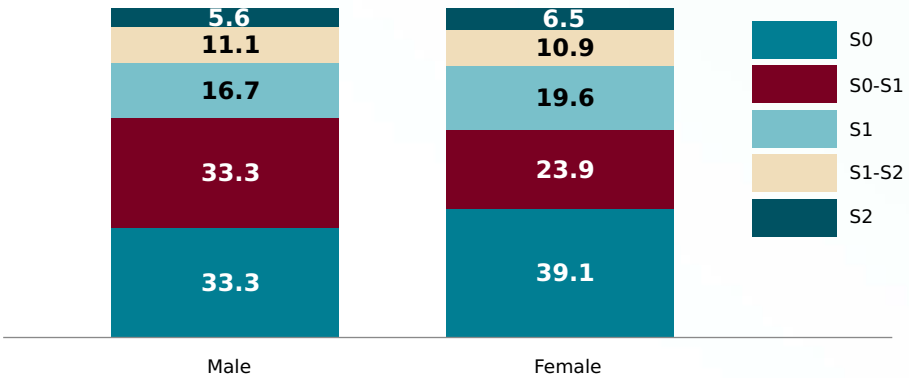

Figure 6. *Correlation between steatosis staging and gender three months after sustained viral response*

between gender did not differ significantly statistically (p=0.962), 5.6% of men and 6.5% of women were still in stage S2 (figure 6);
- the percentage distribution of the degree of steatosis compared between age groups did not differ significantly statistically (p=0.463), however, it should be noted that only 7.4% of patients under 60 years old and 5.4% of those over 60 years old still had S2 steatosis (figure 7).

The evolution of steatosis post-treatment (p=0.004) (figure 8):
- 12.5% of patients who had an initial staging of S0 at the beginning of the study, after three months of sustained viral response, regressed to the S0-S1 class;
- among patients with an initial staging of S1-S2, 14.3% changed to grade S1, but 28.6% remained in the same stage, and 57.1% changed to grade S0;
- only 12.5% of patients with an initial staging of S1 changed to stage S1-S2, while 25% changed into S0-S1 stage and 62.5% changed into stage S0;
- among patients with an initial staging of S1-S2, three months after sustained viral response, 14.3% were classified as S2, 28.6% remained in the same stage, and 14.3% changed to stage S1 or 28.6% to stage S0-S1;
- in 5.9% of patients who had an initial staging of S2 before treatment, the same staging was maintained after three months of sustained viral response, and the rest were classified in lower grades, most frequently in the S0-S1 (35.3%) and S1 (29.4%) classes;
- all patients with steatosis S3, upon re-evaluation, changed into lower classes, most frequently in grade S1 (40%).

Discussions

The factors that contribute to the development of hepatic steatosis in HCV-infected patients are similar to those encountered in patients without HCV, among which metabolic syndrome, increased body mass index, hypertriglyceridemia, chronic alcohol consumption, exposure to certain medications or other infections can be mentioned[4].

However, in the case of hepatic steatosis caused by metabolic syndrome or insulin resistance, unlike that caused by HCV genotype 3, an accelerated progression of fibrosis, a decrease in treatment response, and an increased risk of HCC can be observed[5].

Many patients develop hepatic steatosis as a result of a combination of viral and non-viral

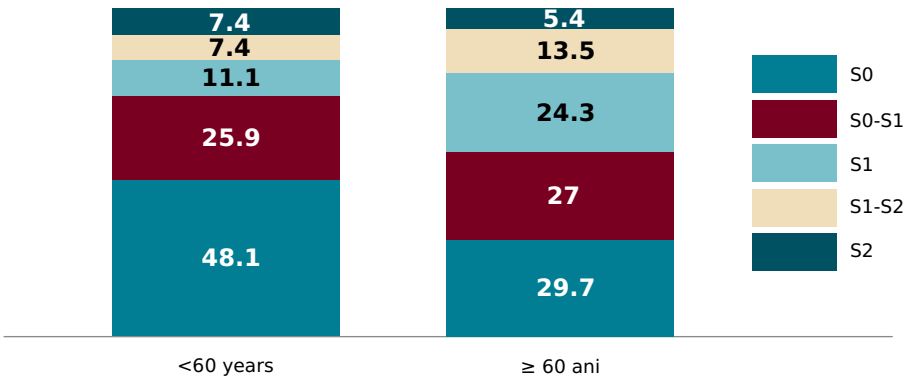

Figure 7. *Correlation between steatosis staging and age three months after sustained viral response*

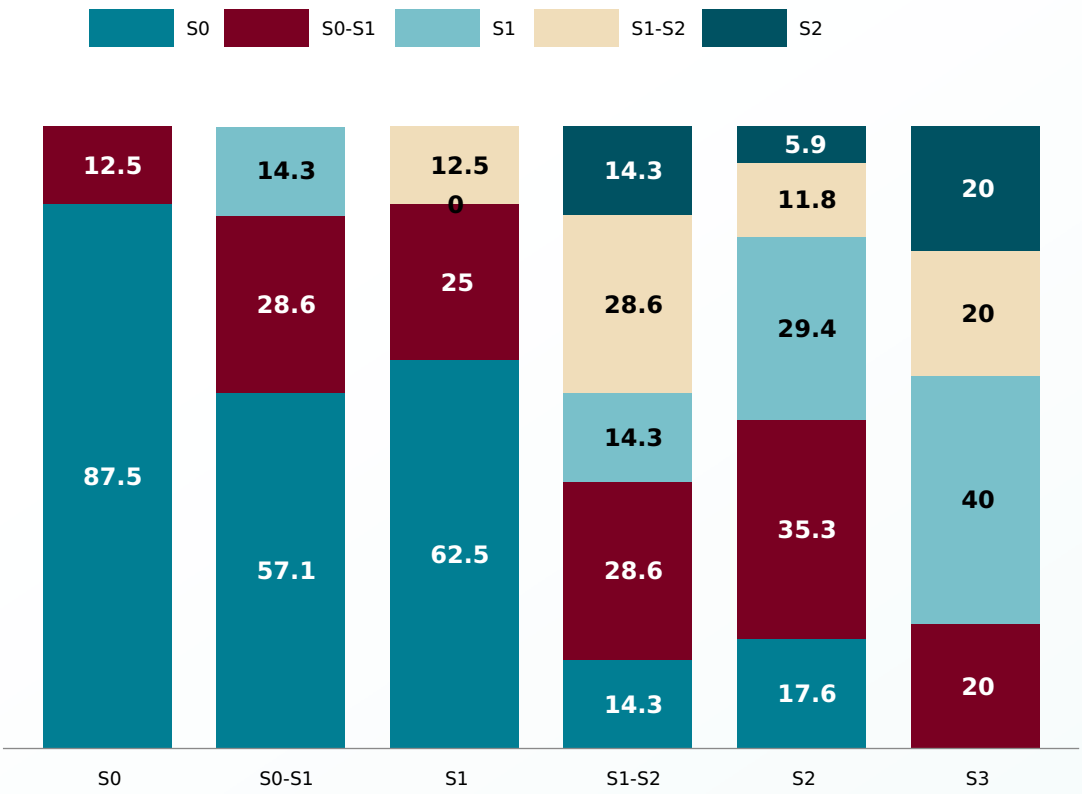

Figure 8. *Evolution of steatosis grade post-treatment according to the pre-treatment staging*

factors. HCV relies on lipid metabolism to replicate, which can lead to hepatic steatosis through various mechanisms, such as increased lipogenesis, altered mitochondrial oxidation of lipids, and decreased activity of microsomal triglyceride transfer protein. Thus, steatosis can favor HCV replication, which, in turn, can affect lipid metabolism[6]. Alcohol, too, can alter lipid metabolism and may be involved in the development of hepatic steatosis[7].

Approximately 40-80% of patients infected with HCV have excessive triglyceride deposits in the liver, called hepatic steatosis[8]. Its prevalence is closely related to the virus genotype[9], and infection with genotype 3 is considered an independent cause of hepatic steatosis.

The severity of hepatic steatosis is related to the higher viral load, but oral antiviral treatment can resolve hepatic steatosis associated with genotype 3 after viral remission[10,11]. Patients with HCV infection of genotype 3 have an increased risk of fibrosis progression and liver cancer development, but these complications are not increased in patients with hepatic steatosis associated with genotype 3[12,13].

While patients with genotype 3 have an increased fibrosis progression and risk of liver cancer development, during DAA treatment, patients with genotype 1 and hepatic steatosis also have an increased risk of negative clinical outcomes.

Hepatic steatosis is not determined solely by HCV infection, and viral remission may not resolve liver injury and fibrosis progression, even though some recent studies have shown improvements in lipid profile after HCV treatment in patients with genotype 1[14,15].

Conclusions

In this study, regression of hepatic steatosis was observed in patients with both mild and severe hepatic steatosis, three months after sustained viral remission was achieved.

It is crucial to correctly use non-invasive evaluations of steatosis and fibrosis in patients who have achieved sustained viral remission, and further research in this area is necessary. The follow-up period for HCV-infected patients after eradication treatment is not yet clearly defined, and current guidelines suggest "indefinite period".

To ensure cost-effective surveillance, easily applicable methods need to be developed for evaluating HCV-infected patients with secondary liver involvement who achieve sustained viral remission, as this is one of the most important determinants of cost-effectiveness of surveillance.

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