

Real-life Perception and Practice Patterns of NAFLD/NASH in Romania: Results of a Survey Completed by 102 Board-certified Gastroenterologists

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ABSTRACT

Introduction: Nonalcoholic fatty liver disease (NAFLD) has an increasing incidence worldwide, reflecting the epidemics of obesity and metabolic syndrome. Data on knowledge, attitude and management by the Romanian gastroenterologists with regard to NAFLD are lacking.

Methods: We assessed current diagnostic and treatment patterns of the management of NAFLD among 102 Romanian board certified gastroenterologists using a survey developed to collect information regarding participants' clinical practice, diagnostic tools and usage of medication in patients with NAFLD.

Results: 71.6% of the surveyed gastroenterologists (SG) had more than 5 years of gastroenterology practice, were university affiliated and 37.3% had predominant activity in hepatology (>60%). In Romania, 60.8% of the SG would diagnose NAFLD only if all other causes of liver disease were absent. All practitioners use a noninvasive tool for staging NAFLD, 45.1% use both serum markers and transient elastography. Liver biopsy is performed by 61.8% of the SG in the presence of a discordant result in two noninvasive methods of fibrosis evaluation. The most frequently prescribed drugs are: silymarin (88.2%), vitamin E (78.4%) and ursodeoxycholic acid (77.4%).

Conclusion: The results of this survey suggest that clinical practice patterns among Romanian gastroenterologists for the diagnosis (mainly liver biopsy) and management of NAFLD frequently diverge from published practice guidelines. Nonalcoholic steatohepatitis is probably underdiagnosed, especially in patients with normal transaminase levels and is also overtreated with drugs that are not recommended in the guidelines.

Key words: nonalcoholic fatty liver disease – survey – clinical practice.

Abbreviations: ALT: alanine aminotransferase; BMI: body mass index; CLD: chronic liver disease; CAP: controlled attenuation parameter; ESLD: end-stage liver disease; HBV: hepatitis B virus; HCV: hepatitis C virus; HDV: hepatitis delta virus; HCC: hepatocellular carcinoma; HOMA: Homeostasis Model Assessment of Insulin Resistance; LC: liver cirrhosis; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; NASH: non-alcoholic steatohepatitis; PCP: primary care practitioners; SG: surveyed gastroenterologists; UDCA: Ursodeoxycholic acid.

INTRODUCTION

Over the last three decades, prevalence of nonalcoholic fatty liver disease (NAFLD) has risen to become the most prominent cause of chronic liver disease (CLD) in most countries worldwide with an increasing contribution to the burden of liver cirrhosis (LC), hepatocellular carcinoma (HCC), and end-stage liver disease (ESLD) requiring liver transplantation (LT). In

most cases, NAFLD is closely related to the metabolic syndrome, which is highly prevalent in industrialized Western countries from North America and Europe, but is also a growing health problem in Eastern countries (Eastern Europe, Asia) [1-3]. The prevalence rate of NAFLD is 25% in the general adult world population [4]. There are complex and intertwined relationships among age (prevalence of 36% between 60-85 years), sex (males 40% >females 23%), ethnicity (Hispanics 45%>Whites 33%>African-Americans 24%) and metabolic syndrome features (more prevalent in patients with hypertriglyceridemia 50%, hypertension 50%, diabetes mellitus 68-71%, obesity 98%) which heavily affect the risk of development and progression of NAFLD/non-alcoholic steatohepatitis (NASH) [5]. In a recent meta-analysis [4], the

global prevalence of NASH among biopsied NAFLD patients was 59.1%. The overall prevalence of NASH is between 1.5% and 6.45% [4].

Although the real prevalence of NAFLD/NASH in the population of Romania is not known, it is worth mentioning that its prevalence in a hospitalized population (3,005 subjects) is 20% [6] and that in type 2 diabetes mellitus patients it is 87.1% [7]. The perceived deleterious consequences of NAFLD are also probably lower among Romanian gastroenterology specialists, as compared to the widespread chronic HBV, HDV or HCV infections.

On the other hand, there is a need to develop better diagnostic and therapeutic strategies for patients with NASH, the progressive form of NAFLD, eventually leading to LC and HCC, targeting both those with early-stage disease as well as those with advanced liver fibrosis, in order to improve the detection and the prognosis of these patients and thus to increase the awareness of hepatologists/gastroenterologists, nutritionists, endocrinologists and cardiologists regarding the long term outcome.

All things considered, increased attention has to be given to NAFLD/NASH in Eastern European countries. We therefore conducted a survey in a representative population of board certified gastroenterologists in Romania in different practice settings in order to gain better insights into the perception of NAFLD/NASH in real life gastroenterological practice. This is similar to a study performed in France and published in 2012 [8] and another more recent one realized in the USA [9]. We believe that the current findings will provide a better understanding of the NAFLD prevalence (which is probably underestimated), severity and treatment in Romania, leading to an improvement of the awareness among hepatologists/gastroenterologists, and to a better longterm follow-up and management of this challenging/complex entity.

METHODS

The survey of patterns of practice was designed and initiated by representatives of the French Association for the Study of the Liver (ASEF) and the Romanian Society of Gastroenterology and Hepatology (SRGH). An anonymous five page questionnaire was sent electronically to participants identified from the SRGH membership list. The questionnaire was divided into several sections: 1) participant information (data on age, sex, place of practice, patterns of recruitment of NASH patients, including collaborative networks with other specialists dealing with NAFLD/NASH patients), as well as perceived severity of NAFLD/NASH; 2) circumstances and criteria of diagnosis of NAFLD/NASH; 3) initial work-up including the use of non-invasive markers; 4) practices of liver biopsy; 5) indications for biopsy and place of biopsy in the diagnostic algorithm; 6) therapeutic management including non-pharmacological vs. pharmacological therapies, patterns of monitoring and follow-up. Requested answers were either oriented (multiple choice), semi-quantitative (e.g. never, rarely, sometimes, frequently), quantitative (e.g. 0-100% scale) or open-ended (choice of words by the participant). Patient profiles explored for NASH were assessed on a scale from 0 to 4 with 0 being never and 4 always. Investigations performed for

the initial diagnosis were scaled: "almost always", "sometimes/frequently" or "rarely/ever". The use of monitoring methods was assessed with a scale including: "in all your patients", "in some of your patients", "never". Pharmacological products were assessed with the following scale: "very often", "sometimes", "rarely" or "never". Results have been expressed as means (SD) or medians for quantitative variables or by the frequency of distribution for qualitative variables. Comparisons were performed using the Student's *t*-test for quantitative variables or the chi-squared test for qualitative variables.

RESULTS

Study participants

One hundred and two out of the 548 board-certified gastroenterologists in Romania completed the questionnaire (response rate 18.6%). Although all nine tertiary/referral centers were invited to participate, only four of them accepted and entered into the survey (Bucharest 54.9%, Iasi 17.6%, Timisoara 12.7%, Craiova 6.8%). The majority of the questionnaires were completed by female physicians (61.8%). The majority of the surveyed gastroenterologists (SG) had more than 5 years of gastroenterology practice (71.6%) and were university affiliated (59.8%), followed by mixed practice 25.4%. Of the SG, 37.3% predominantly practiced in hepatology (spending more than 60% of clinical time taking care of patients with CLD). Female SG had a significantly higher interest and activity in hepatology ($p = 0.03$).

Place of NAFLD in real-life hepatology practice and perceived severity

Patient referral and collaborative networks

Overall, 40% of the NAFLD patients were referred to the SG by general practitioners and only 20% by a specialist in endocrinology, internal medicine or cardiology. Almost one third (30%) of the NAFLD patients had been diagnosed by chance while visiting the SG for other gastroenterological diseases and performed an abdominal ultrasound and/or were detected with increased aminotransferase levels.

In Bucharest, more than 50% of the NAFLD patients were sent to SG in 32.4% of cases by their general practitioner and 3.9% of them were referred to SG by another specialist. The SG working in university hospitals evaluated a significantly higher number of patients with NAFLD compared with SG from other units ($p=0.04$); 30.4% of the SG who diagnosed more than 60 new NAFLD cases yearly were from university centers compared to 11.8% of SG from other centers. The same was true in regard to the HCV patients: SG affiliated with academic centers had seen more than 30 patients with HCV annually as compared to SG from the other regional/community centers (44.2% vs 19.5%, $p=0.01$).

Co-existence of NASH with other liver diseases

In Romania, 60.8% of SG would diagnose NASH only after all other causes of liver disease had been excluded, while the rest would diagnose NASH irrespective of the co-existence of other CLD in the presence of metabolic risk factors. Only 23.5% of the SG allowed a diagnosis of NASH in males if they drank more than 40g/day of alcohol, and also only 24.2% of the SG that considered NASH only after excluding other

liver diseases allowed a consumption of more than 40g/day. In female patients, the diagnosis of NASH was assumed in 16.7% of females who drank over 30g/day, and a minority of SG (17.7%) that considered NASH only after excluding other liver diseases would allow an amount of alcohol consumption of more than 30g/day.

Perceived severity of NASH

NASH was categorized as a severe liver disease by 75.5% of SG, with 65.7% of them considering NASH a progressive disease leading to cirrhosis and HCC. However, only 51% of the SG considered that NASH-induced cirrhosis can be as severe as HCV-induced cirrhosis and only 18.5% of them admitted that they see more than 5 new cases of cirrhosis due to NASH per year. Despite this, 76.5% of the SG agreed that HCC can complicate the course of NASH.

Diagnosis Steatosis

Patients with ultrasound-detected steatosis and increased aminotransferase levels are “almost always” (score 4) explored for NASH by 51.5% of participants and “usually” (score 3) explored for NASH by 38% of them. In patients with ultrasound-identified steatosis but normal aminotransferases, 9.8% of SG would “almost never” (score 0) look for NASH. However, 27.5% of participants would “usually” (score 3) and 34.3% “almost always” search for NASH even in this category of patients.

Increased aminotransferase levels

In patients with persistent elevation of aminotransferases, only 39.2% of participants would “usually” or “almost always” take into consideration the diagnosis of NASH, while in patients with persistent increases of aminotransferases and steatosis on ultrasound, 88.2% of participants would do so. In patients with cryptogenic cirrhosis, only 44.2% of the surveyed subjects would “usually”/“almost always” consider the diagnosis of NASH, while 23.5% would “never”/“rarely” (i.e. scores 0 and 1) consider this diagnosis.

Overweight and/or diabetic patients

When aminotransferases are increased, a majority of SG (42.2%) “almost always” (score 4) undertake investigations for NASH in diabetic/overweight patients; in the presence of steatosis at ultrasound, the proportion almost doubles (81.4%).

Hyperferritinemia

In patients with hyperferritinemia, only 13.8% of participants would “frequently” or “almost always” consider the diagnosis of NASH, while more than half (61.8%) would “never” or “seldom” take into consideration the diagnosis of NASH.

Staging of NAFLD/NASH

Liver biopsy

It is worth noting that the median percentage of liver biopsy refusal by patients is 75% in Romania. However, when performing a liver biopsy, the main intention is to measure the degree of fibrosis (“always the case” for 38.2% of SG) or to diagnose steatohepatitis in a relatively similar percentage (“always the case” for 31.4% of SG). Similarly, the quantification of liver fat was considered the most important feature by 29.4% of participants; while the quantification of liver iron by liver biopsy was important for only 21.6% of SG.

When asked to choose a single indication for performing a liver biopsy in a patient with supposed NAFLD, the majority of SG (61.8%) answered that the main indication of liver biopsy is the presence of discordant results with two noninvasive methods of fibrosis evaluation. The presence of advanced fibrosis by a noninvasive method urged the SG to perform a liver biopsy in 13.7% of cases; 17.6% and 15.7%, respectively, of the participants would perform a liver biopsy in case of steatosis at ultrasound and persistent hepatocytolysis and, respectively, normal persistent transaminases despite clinical suspicion of NAFLD.

Non-invasive fibrosis markers

Non-invasive fibrosis markers were used by 100% of the surveyed physicians in their clinical practice (Fig. 1). Most interviewed practitioners (45.1%) used both serum markers and transient elastography, followed by transient elastography alone (35.3%).

Exploration and management of metabolic comorbidities

Initial diagnosis

In their clinical practice, a vast majority of SG collect information on BMI (100% responded “always” or “very frequently”), waist circumference (89.2%), blood pressure (80.4%), glucose (98%) and lipid metabolism (100%); on the other hand, a significant proportion of them “never” assessed surrogate markers of insulin resistance (68.6% do not measure fasting insulin and 66.7% HOMA levels).

Follow-up

All interviewed physicians would monitor aminotransferases at least twice a year (46.1%) or even 3 or 4 times a year (33.3%). Most SG monitor serum glucose (80.4%) and lipid parameters (96.1%) at follow-up. Serum insulin (9.8%), as well as ferritin levels (19.6%) are seldom followed up. However, 96.1% of the Romanian SG would perform a liver ultrasound during follow-up, while 52.9% would always perform a noninvasive procedure for monitoring NASH and only 1% would perform another liver biopsy during follow-up.

Therapeutic management

A proportion of 21.6% of SG would consider weight management as part of the therapy in >60% of cases, and 41.2% would recommend weight loss in <30% of cases, usually referring the patients to an endocrinologist or nutritionist for this purpose. On the other hand, 51% of SG would recommend both weight management and medical treatment in >60% of cases. Alcohol consumption by NAFLD patients is totally forbidden by 67% of SG in female patients and by 64.8% of SG in male patients. The mean daily alcohol consumption level allowed was 4.8±0.9g in female patients and 8.6±1.5g in male patients.

The most frequently (response “very often” or “sometimes”) prescribed drugs were: silymarin (88.2%), vitamin E (78.4%) and ursodeoxycholic acid (UDCA) (77.4%) (Fig. 1). However, 98% of the SG concluded that there is a stringent need of new therapeutic agents for NASH and 97.1% of them would recommend to their patients to participate in clinical trials investigating new molecules.

When asked to describe the most important outcome used in clinical practice for defining successful therapy, the following

were considered: regression of fibrosis evaluated by different tests (41.2%), normalization of liver function tests (34.3%), improvement of glucose and lipid abnormalities as well as weight loss (33.3%), improvement of steatohepatitis lesions (29.1%) and improvement of steatosis (15.7%).

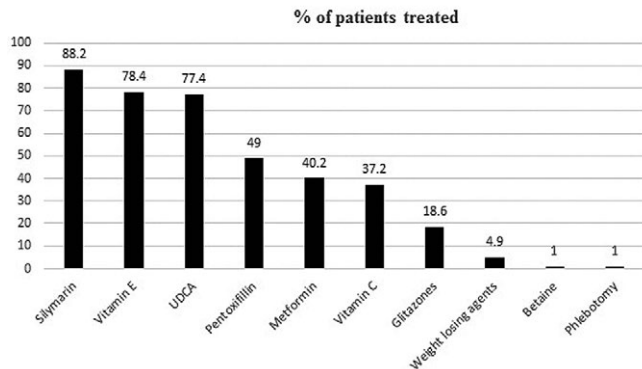


Fig. 1. Proportion of patients treated with different pharmacological agents.

Differential patterns of practice based on the level of specialization in hepatology

Survey participants highly specialized in hepatology (i.e. spending more than 60% of their clinical time caring for patients with liver diseases) accounted for 28.4% of the total number of physicians participating in the survey. Of the total number of medical doctors mainly interested in hepatology, 72.4% were female vs. only 57.5% female doctors among SG with mixed clinical practice (hepatology and gastroenterology) ($p=0.25$). We hypothesized that this high level of specialization in the field of hepatology might have impacted the patterns of practice and perception of the disease. Contrary to the expectations, there were no differences regarding diagnostic practices, excepting the higher performance of liver biopsy despite the normal level of aminotransferases in the group of hepatologists, as well as of both noninvasive tests for the diagnosis of NAFLD/NASH. Regarding the therapeutic measures, there were three agents more frequently used by the hepatologist: metformin, pentoxifillin and UDCA, without any differences regarding the other drugs shown in Fig.1. HOMA is followed significantly more often by the SG with a hepatology specialization, while ultrasound, noninvasive tests for fibrosis or liver biopsy is performed during the monitoring of NASH patients in the same proportion.

DISCUSSION

The aim of this survey was to assess the patterns of practice, disease awareness and recognition of NAFLD among Romanian hepatogastroenterologists and to compare them with data resulting from a similar survey conducted among French board certified gastroenterologists [8].

In Romania, the majority of the study participants were female, with gastroenterology experience of more than 5 years in the field, mainly from Bucharest and university centers, while in France the majority of the surveyed practitioners were males from non-university affiliated hospitals.

Romania has a higher percentage of female vs. male medical practitioners in general and the fact that the gap widens with hepatological overspecialization as opposed to the French case derives from how the two countries' medical systems function. In Romania, the majority of hepatogastroenterologists work within the state medical system in large university centres. Most county and regional hospitals (but not all) only have one or two gastroenterologists on their staff; the number of hepatogastroenterologists that work exclusively within the private healthcare sector is low and limited to large urban and university centres. The opposite is true in France, where the majority of hepatogastroenterologists work as private practitioners and are board-certified gastroenterologists but usually not university-affiliated.

The patient referral system is also different in the two settings. In Romania, patients have easily and rapid access to specialists in the university hospitals, being referred by family doctors or other specialties, therefore probably NAFLD is diagnosed in an earlier, usually mild form. In contrast, in the US, only 27% of primary care practitioners (PCP) referred NAFLD patients to a hepatologist for evaluation and those PCPs who reported seeing more than 5 NAFLD patients annually referred them even less frequently ($p=0.01$) [10].

Although the academic definition of NAFLD implies the exclusion of concurrent liver diseases, a majority of SG from France consider that NAFLD can coexist with other chronic liver diseases if risk/metabolic factors are present and the clinical and lab features and histological lesions are compatible. In Romania, however, over 60% of the surveyed specialists considered the diagnosis of NASH after excluding/only in cases of the absence of other concomitant diseases and categorize it as severe, although only a minority of them see more than 5 new cases of NASH-related liver cirrhosis annually. This is extremely different from how many new cases of HCV related liver cirrhosis are diagnosed by the Romanian SG annually and from the new cases of NASH-related liver cirrhosis evidenced by French practitioners (more than double), in accordance to the different prevalence rates of HCV infection and new antivirals available in the two countries [11, 12].

Screening for NAFLD/NASH is recommended in patients with metabolic risk factors and/or well characterized insulin resistance despite the fact that the majority of patients with NAFLD at large have normal ALT [13]. In Romania, there is an increased awareness of NAFLD diagnosis in patients at risk (patients with steatosis at ultrasound, obese or with diabetes despite normal transaminases) as compared to almost 40% of the French SG [8] that do not actively search for NAFLD in patients with normal ALT. In the USA, 54% of PCPs do not screen at all for NAFLD in patients with obesity and/or diabetes, while only 19% screen the majority of these patients [10]. On the other hand, in patients with increased transaminases, only 39.2% of the Romanian participants would screen from the beginning for NAFLD/NASH in contrast to 76% of the French specialists in relation to the significantly higher prevalence of HBV/HCV/HDV infection in Romania [11, 14, 15].

Liver biopsy should be accepted in order to diagnose and better classify the whole spectrum of liver injury in patients with suspected NASH. However, the majority of Romanian SG perform a liver biopsy only when two noninvasive methods

Table I. Different patterns of practice according to the level of specialization in hepatology

	Mainly hepatological practice	Mixed practice	P value
Diagnostic practices			
I suspect NAFLD when metabolic risk factors are present, even if other CLD co-exists (%)	24.1	45.2	0.08
When suspecting NAFLD my initial work-up includes:			
Body mass index (% frequently)	82.8	69.9	0.27
Waist circumference (% frequently or almost always)	89.7	89	0.79
HOMA (% frequently or almost always)	44.8	28.8	0.18
Serum triglycerides (% frequently)	86.2	86.3	0.75
HDL cholesterol (% frequently or almost always)	89.7	90.4	0.80
The distinction NASH vs steatosis is relevant	89.7	97.3	0.27
When I prescribe a liver biopsy in patients with NAFLD, it is mainly with the intent to:			
Distinguish NASH from steatosis: diagnostic purpose (% always)	34.5	30.1	0.89
Stage fibrosis: prognostic purpose (% always)	31	41.1	0.64
Single situation best reflecting my indication for liver biopsy (%)			0.79
Any patient with increased aminotransferases and non-alcoholic steatosis on ultrasound	13.8	19.2	
Only if there is clinical suspicion of fibrosis			
Only if non-invasive fibrosis procedures are compatible with advanced fibrosis	10.3	15.1	
Only if results of non-invasive fibrosis procedures are discordant	69	58.9	
Others	6.9	6.8	
In what proportion of the following patients do you perform a liver biopsy? (mean±SD, %)			
Non-alcoholic steatosis and increased aminotransferases	19.1 ± 5.3	10.6 ± 1.7	< 0.001
Non-alcoholic steatosis and normal aminotransferases	5.8 ± 2.2	1.1 ± 0.3	< 0.001
What proportion of your patients refuse a liver biopsy? (mean±SD, %)	60±5.3	64.6±3.9	0.30
Which non-invasive fibrosis procedure do you routinely use with priority? (%)			
Serum biomarkers alone	6.9	24.7	0.04
Elastometry alone	31	37	
Combination of serum biomarkers and elastometry	62.1	38.4	
Therapeutic management			
In what proportion of your patients do you prescribe a pharmacological therapy? (% mean±SD)			
Metformin (% frequently)	13.8	9.6	0.03
Pentoxifillin (% frequently)	34.5	19.2	0.04
UDCA (% frequently)	62.1	28.8	0.01
What is the daily alcohol consumption you authorize for your NASH patients? (% mean±SD, men/women)			
Men	6.7±2.4	9.4±1.9	0.38
Women	3.2±1.2	5.6±1.2	0.02
Follow-up			
How often do you use the following procedures for the follow-up of NASH patients:			
Ultrasound, all patients (%)	96.6	95.9	0.80
HOMA, all patients/some only (%)	86.2	60.3	0.03
Non-invasive fibrosis procedures, all patients (%)	62.1	49.3	0.44
Liver biopsy, all patients/some only (%)	27.6	32.9	0.25

CLD: chronic liver disease; UDCA: ursodeoxycholic acid

are discordant. This is due to the large disponibility of serum markers and transient elastography in Romania and to the reluctance of patients to undergo nowadays an invasive procedure that might have significant incidents and adverse events [16]. A significantly lower percentage of participants

(17.6%) would perform a liver biopsy in Romania in case of steatosis at ultrasound and persistent hepatocytolysis compared to American (57%) [9] or French (62%) gastroenterologists [8]. Also, in Romania a significantly higher proportion of patients would refuse to accept a liver biopsy in cases of NAFLD

(approximately 60%) in comparison to only 22% in French patients [8]. In both France and Romania, the SG would use both serum markers and transient elastography for staging NAFLD in similar proportions (41% vs 45.1%). This leads to increased diagnostic accuracy of the non-invasive methods for the assessment of liver fibrosis stage [17]. Maybe the clinical practice worldwide would change with the more widespread availability of the Fibroscan with a controlled attenuation parameter (CAP) for assessing both liver fat and fibrosis and for the follow-up of NAFLD patients [18]. Also liver biopsy seems to be performed less often than required for making treatment decisions by both gastroenterologists and hepatologists [9].

All guidelines agree that lifestyle changes including weight loss, dietary changes and physical exercise should always be implemented as the first-line option in all NAFLD patients [13, 19, 20] and this is the practice also in the real life setting.

In the clinical practice in Romania, silymarin is extensively used by gastroenterologists although it is not recommended in any guidelines. This is a widespread practice reflecting the lack of specific therapy in NAFLD/NASH and it is prescribed in order to answer the patient's concern regarding the fact that nothing is being done for his/her disease. However, there are recent experiments showing that silybinin, the main component of silymarin, exerts hepatoprotective and cardioprotective effects, as well as ameliorates insulin resistance [21]. Vitamin E has been shown to improve both ALT levels and histology with and without weight loss and is included in the guidelines recommendations for the management of NAFLD [13, 19]. Romanian SG indicate vitamin E in 78.4% of the patients compared to only 31% of French gastroenterologists [8], but relatively similar to the American hepatologists (76.3%) [9]. The use of UDCA to treat patients with NAFLD is frequent in Romanian physicians, but also in the French ones (77.4% vs 53%), although UDCA did not show any clear benefits in a single randomized, placebo controlled study [22]. The use of insulin sensitizers has been widely explored in the field of NAFLD. However, Romanian gastroenterologists do not usually recommend metformin or glitazones in comparison to French gastroenterologists who use them more frequently. In a network meta-analysis realized by Singh et al. [23], pentoxifylline, thiazolidinediones and vitamin E were superior to placebo and comparable to one another for improving fibrosis, ballooning degeneration, steatosis and lobular inflammation, supporting their clinical use.

The majority of SG follow NAFLD patients both in France and Romania. Follow-up includes regular monitoring of glycemic and lipid parameters, liver ultrasound and also a non-invasive test for fibrosis progression. However, NAFLD patients should undergo regular follow-up not only for liver-related complications but also for metabolic and cardiovascular diseases [24].

A potential drawback of this study is the very low response rate (18.6%) of the invited physicians compared to 28% of the American study [7] and to 43% in the French study [6]. This could potentially bias the results as non-responders might hold divergent views on some aspects of the disease and its management or have lower levels of overall interest in it. Also, many of these NAFLD patients were seen in private practices,

at least in Romania, and also the view may differ from patients who were seen in University gastroenterology centers.

CONCLUSION

This study identified practice patterns regarding the diagnosis, management and follow-up of NAFLD/NASH among Romanian gastroenterologists/hepatologists that are rather different on some aspects to the current guidelines. Because liver biopsy is seldom recommended, NASH may be underdiagnosed even in tertiary gastroenterology centers. By publishing this survey, we tried to increase the awareness of NAFLD and NASH in Romania and to identify the differences of real life practice from current guidelines. Projects to train primary care physicians, cardiologists, endocrinologists, nutritional practitioners to screen for liver disease patients with metabolic syndrome, to diagnose and stage NAFLD should become a priority for hepatologists in order to decrease, in time, liver and non-liver related morbidity and mortality.

Conflicts of interest: No conflicts to declare.

Authors' contribution: V.R.: study concept; V.R., L.G.: study design; S.I., C.E., M.L.: literature research; C.E., M.L.: data acquisition; S.I.: data analysis/interpretation, statistical analysis; S.I., L.G.: manuscript preparation; S.I., V.R., L.G.: manuscript definition of intellectual content, manuscript editing and revision.

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