Original research

Nonalcoholic fatty liver disease and atrial fibrillation: the main markers of this association

O. B. Teslenko [ID] *[B,C,D,E], S. V. Fedorov [ID] [A,C,D,E,F], M. V. Bielinskyi [ID] [B,C,D,E], N. M. Serediuk [ID] [C,E,F]

Ivano-Frankivsk National Medical University, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article;
E – critical revision of the article; F – final approval of the article

The prevalence of nonalcoholic fatty liver disease (NAFLD) and atrial fibrillation (AF) has increased globally in recent years. According to recent studies, NAFLD and AF affect approximately 32 % and 0.51 % of the general population, respectively.

Aim. To examine the association between NAFLD and AF by using the FibroTest-4 (FIB-4) and the NAFLD Fibrosis score (NFS) and measuring periostin levels.

Materials and methods. In this study, we enrolled 96 patients diagnosed with NAFLD and divided them in two groups, the main group – 35 patients with NAFLD + AF and the control group – 61 patients with NAFLD alone. NFS and FIB-4 indices were calculated and serum periostin level was measured.

Results. The NAFLD + AF group had higher levels of periostin (10.80 ± 1.60 ng/ml vs. 9.80 ± 1.75 ng/ml, p < 0.001) and higher NFS (-1.05 ± 1.46 vs. -2.65 ± 1.63, p < 0.001) and FIB-4 scores (1.34 ± 0.86 vs 1.07 ± 0.60, p = 0.048). Periostin has been found to be associated with the risk of NAFLD + AF with an OR of 2.079 (95 % CI: 1.418–3.048, p < 0.001). Similar results were with NFS (OR = 3.233, 95 % CI: 1.970–5.303, p < 0.001) and FIB-4 (OR = 2.498, 95 % CI: 1.109–5.627, p = 0.027). The receiver operating characteristic (ROC) analysis was performed using three variables, NFS, FIB-4 and periostin, to determine their ability to distinguish between patients with NAFLD + AF and NAFLD alone. The results have shown that the NFS had the highest area under the curve (AUC) with a value of 0.868 (95 % CI: 0.792–0.943, p < 0.001), indicating excellent discriminatory ability. FIB-4 had an AUC of 0.651 (95 % CI: 0.537–0.765, p = 0.014), while periostin had an AUC of 0.759 (95 % CI: 0.660–0.858, p < 0.001).

Conclusions. These findings have suggested a strong association between NAFLD and AF and highlighted the importance of considering AF as a potential complication in patients with NAFLD. Both the use of the FIB-4 and NFS indices and measurement of periostin levels have been proved to be effective in detecting this association.

Неалкогольна жирова хвороба печінки та фібриляція передсердь: основні маркери цієї асоціації

О. В. Тесленко, С. В. Федоров, М. В. Бєлінський, Н. М. Середюк

Поширеність неалкогольної жирової хвороби печінки (НАЖХП) та фібриляції передсердь (ФП) за останні роки зросла в усьому світі. Згідно з результатами останніх досліджень, НАЖХП і ФП діагностують у майже 32 % і 0,51 % населення відповідно.

Мета роботи – дослідити зв'язок між НАЖХП і ФП за допомогою індексів FibroTest-4 (FIB-4) та Nonalcoholic Fatty Liver Score (NFS), а також шляхом вимірювання рівня періостину.

Матеріали та методи. У дослідження залучили 96 пацієнтів із діагнозом НАЖХП, яких поділили на дві групи: основну – 35 пацієнтів із НАЖХП + ФП, контрольну – 61 хворий на НАЖХП. Обрахували індекси NFS і FIB-4, а також виміряли рівень періостину в сироватці крові.

Результати. У групі НАЖХП + ФП виявили вищі рівні періостину (10,8 ± 1,6 нг/мл проти 9,80 ± 1,75 нг/мл, p < 0,001), вищі показники NFS (-1,05 ± 1,46 проти 2,65 ± 1,63, p < 0,001) та індексу FIB-4 (1,34 ± 0,86 проти 1,07 ± 0,60, p = 0,048). Встановили, що періостин асоціюється з ризиком НАЖХП + ФП з OR 2,079 (95 % ДІ: 1,418–3,048, p < 0,001). Аналогічні результати одержали для NFS (OR = 3,233, 95 % ДІ: 1,970–5,303, p < 0,001) і FIB-4 (OR = 2,498, 95 % ДІ: 1,109–5,627, p = 0,027). Аналіз робочої характеристики приймача (ROC) здійснили для трьох змінних, NFS, FIB-4 і періостину, щоб визначити їхню здатність розрізняти пацієнтів із НАЖХП + ФП і тільки з НАЖХП. Результати показали, що NFS мав найбільшу площу під кривою (AUC) зі значенням 0,868 (95 % ДІ: 0,792–0,943, p < 0,001), що вказує на відмінну дискримінаційну здатність. FIB-4 мав AUC 0,651 (95 % ДІ: 0,537–0,765, p = 0,014), а періостин мав AUC 0,759 (95 % ДІ: 0,660–0,858, p < 0,001).

Висновки. Результати свідчать про сильний зв'язок між НАЖХП і ФП, підкреслюють важливість визначення ФП як потенційного ускладнення в пацієнтів із НАЖХП. Використання індексів FIB-4, NFS та вимірювання рівня періостину є ефективним для виявлення цього зв'язку.

Non-alcoholic fatty liver disease (NAFLD) is a condition in which there is an excessive fat accumulation in the liver of individuals who consume little or no alcohol. NAFLD is commonly associated with obesity, insulin resistance, and metabolic syndrome [1]. It can range from a benign condition, called fatty liver, to a more serious form, called non-alcoholic steatohepatitis (NASH) which can lead to liver inflammation, fibrosis, and eventually cirrhosis. If left untreated, NAFLD can increase the risk of liver failure, liver cancer, and death [2].

Atrial fibrillation (AF) is a type of heart rhythm disorder in which the heart beats in an irregular and often rapid manner.

This can lead to decreased blood flow to the body and cause the heart to beat less effectively. AF increases the risk for stroke and heart failure [3]. Other dangers associated with AF include a higher risk of myocardial infarction, cognitive decline, and an increased risk of death from any cause.

The prevalence of NAFLD and AF has increased globally in recent years. According to latest studies, NAFLD affects approximately 32 % of the general population worldwide and is becoming one of the most common causes of chronic liver disease [4]. The prevalence of AF is also rising and affecting 0.51 % of the worldwide population, an increase of 33 % compared to the 1997 figures, with a higher incidence in older individuals and those with underlying medical conditions [5].

The increasing prevalence of both NAFLD and AF is likely due to the higher incidence of obesity, metabolic syndrome, and other lifestyle-related risk factors. The exact mechanism behind the association between NAFLD and AF is not fully understood, but it is thought to be related to factors such as oxidative stress, inflammation, and metabolic abnormalities that are common in both conditions [6]. Additionally, NAFLD may also increase the risk of other cardiovascular diseases, which can contribute to the development of AF [7].

In recent years, periostin has become as a promising biomarker for the evaluation of liver fibrosis in patients with NAFLD. Periostin is a protein involved in the extracellular matrix (ECM) regulation and implicated in the development of NAFLD [8]. However, more research is needed to fully understand the exact role of periostin in the development and progression of NAFLD.

Aim

To examine the association between NAFLD and AF by using the FibroTest-4 (FIB-4) and the NAFLD Fibrosis score (NFS) and measuring periostin levels.

Materials and methods

In this study, we enrolled 96 patients diagnosed with NAFLD who visited the State Institution "Territorial Medical Association of the Ministry of Internal Affairs of Ukraine in the Ivano-Frankivsk region" to examine the association between NAFLD and AF. The study population was divided into two groups: the main group – 35 patients with both NAFLD and AF, and the control group – 61 patients with NAFLD alone. The data were collected from medical records including demographic information, clinical and anthropometric characteristics, laboratory and imaging findings. All the patients signed their informed consent to participate in the study in accordance with the principles of the Helsinki Declaration.

The diagnosis of NAFLD and AF were made based on the EASL-EASD-EASO Clinical Practice Guidelines for the Management of NAFLD [9] and the 2020 ESC Guidelines for the diagnosis and management of AF developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) [10], respectively.

Laboratory tests were performed in the clinical and diagnostic laboratory of State Institution "Territorial Medical Association of the Ministry of Internal Affairs of Ukraine in the Ivano-Frankivsk region". Full blood count was performed on an analyzer HTI MICROCC-20PLUS (High Technology, Inc. (HTI), Massachusetts, USA). Biochemical tests were performed on an analyzer HTI BioChem SA Semi-Auto Chemistry Analyzer BC-3002-C-UA (High Technology, Inc. (HTI), Massachusetts, USA).

All the patients underwent abdominal ultrasound examination to confirm NAFLD using a SonoScape S20 (SonoScape Medical Corporation, China) device.

To assess liver fibrosis, the following non-invasive indices were used: the FibroTest-4 (FIB-4) index and the NFS. The FIB-4 was calculated by the formula [11]:

FIB-4 = Age × AST/Platelet count (109/L) ÷ √(Alanine Aminotransferase (ALT) (U/L)),

where: age is the patient's age in years, AST is the patient's aspartate aminotransferase level in U/L, ALT is the patient's alanine aminotransferase level in U/L, platelet count is the patient's platelet count in 109/L. The FIB-4 score then was interpreted based on the following ranges: a score less than 1.45 was considered to indicate a low risk of liver fibrosis; a score between 1.45 and 3.25 was considered to indicate a moderate risk of liver fibrosis; a score greater than 3.25 was considered to indicate a high risk of liver fibrosis.

The formula for the NFS was [12]:

NFS = -1.675 + 0.037 × Age (years) + 0.094 × BMI (kg/m^2) + 1.13 × AST/ALT ratio + 0.99 × Platelet count (109/L) + (0.99 if diabetic, otherwise 0) + 0.66 × Serum protein (g/dL),

where: age (years) is the patient's age, BMI (kg/m^2) is the patient's Body Mass Index calculated as weight in kilograms divided by height in meters squared, AST/ALT ratio is the ratio of the patient's AST to ALT levels, platelet count (109/L) is the patient's platelet count in billions per liter, serum albumin (g/dL) is the patient's serum albumin level in grams per deciliter. The NFS is considered to be from 0 to 4 with higher scores indicating a greater likelihood of liver fibrosis. The NFS of less than 1.455 predicts the absence of advanced fibrosis, whereas a score greater than 0.675 predicts the presence of advanced fibrosis.

Periostin was measured by elisa method using a reader HTI ImmunoChem-2100 (High Technology, Inc. (HTI), Massachusetts, USA) and a Human Periostin/OSF2 ELISA Kit PicoKine® (Boster Biological Technology, Pleasanton CA, USA, Catalog No. EK0985).

The statistical analysis for this study was conducted using IBM SPSS Statistics, version 26.0 (License Code QA2WSWS3QTR5TG6Y7TG6RF59JUY7H). Categorical variables were expressed as frequencies and percentages and compared through the use of the χ^2 and the Fisher exact test where applicable. Continuous variables were represented by their mean ± standard deviation or median with 25 % to 75 % interquartile range (IQR 25–75 %). The Kolmogorov–Smirnov and Shapiro–Wilk tests were applied to determine normal distribution. Normally distributed continuous variables were compared between groups through the independent t-test, while non-normally distributed continuous variables were compared through the Mann–Whitney test. Receiver operating characteristic (ROC) curves were plotted, and the area under the curve (AUC) was calculated. Logistic regression analysis was used to evaluate the independent impact of the study variables on the study outcomes. Results were reported as two-tailed significance tests, with a p-value of less than 0.05 considered statistically significant.
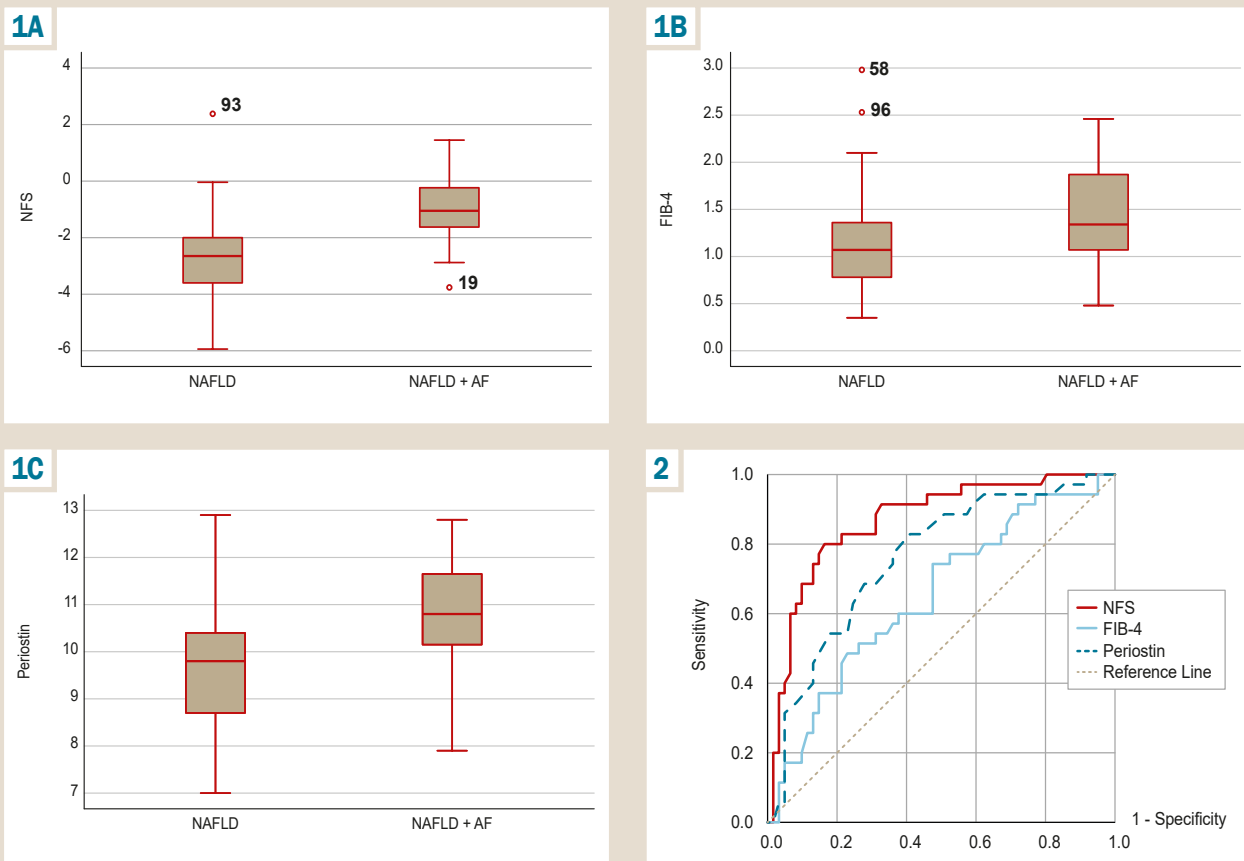
Fig. 1. The values of two non-invasive scoring systems, NFS and Fib-4, and periostin compared to those in patients with NAFLD based on the presence of AF.

A: NFS; **B:** FIB-4 score; **C:** periostin (ng/ml) level.

Fig. 2. ROC curve of NFS, FIB-4 indices and periostin level for AF in NAFLD patients.

Results

The results have shown that patients in the NAFLD + AF group were significantly older (63 ± 12 years vs. 54 ± 13 years, p < 0.01) and mostly male (80.00 % vs. 54.09 %, p = 0.02) compared to the NAFLD group. Additionally, a higher proportion of patients in the NAFLD + AF group had diabetes mellitus (57.1 % vs. 21.3 %, p < 0.01) and higher BMI (26.82 ± 10.1 kg/m^2 vs. 24.64 ± 3.35 kg/m^2, p = 0.02); 37.1 % of the NAFLD+AF patients were obese compared to 9.8 % of those with NAFLD alone (p = 0.03). The NAFLD + AF group also had higher levels of periostin (10.83 ± 1.60 ng/ml vs. 9.81 ± 1.75 ng/ml, p < 0.01) and higher NFS (-1.05 ± 1.46 vs. -2.65 ± 1.63, p < 0.01) FIB-4 score (1.34 ± 0.86 vs 1.07 ± 0.60, p = 0.02). However, there was no significant difference in the levels of AST (27 ± 15 IU/L vs. 30 ± 13 IU/L, p = 0.06), ALT (34 ± 11 IU/L vs. 36 ± 21 IU/L, p = 0.74) between the two groups (*Table 1*, *Fig. 1*).

The results of the univariable binomial logistic regression have shown that NAFLD + AF was associated with a higher risk compared to NAFLD alone (*Table 2*).

Age, male sex, diabetes mellitus, BMI, and obesity were all found to significantly increase the risk of NAFLD + AF with a p-value less than 0.05. The odds ratio (OR) of NAFLD + AF increased by 1.09 (95 % CI: 1.04–1.15, p = 0.01) for every year increase in age, 3.39

(95 % CI: 1.29–8.95, p = 0.01) for male sex, 4.923 (95 % CI: 1.99–12.20, p = 0.01) for diabetes mellitus, 1.12 (95 % CI: 1.02–1.23, p = 0.02) for each increase in BMI, and 5.42 (95 % CI: 1.83–16.05, p = 0.01) for obesity.

Periostin has been found to be significantly associated with the risk of NAFLD + AF with an OR of 2.08 (95 % CI: 1.42–3.05, p < 0.01). Similar results were with NFS (OR = 3.23, 95 % CI: 1.97–5.30, p < 0.01) and FIB-4 (OR = 2.45, 95 % CI: 1.11–5.63, p = 0.03).

The results suggest that older individuals, males, those with diabetes, higher BMI, and obesity are at a higher risk for NAFLD + AF. Additionally, elevated periostin levels and NAFLD are also significant risk factors for NAFLD + AF.

The ROC analysis was performed on three variables, NFS, FIB-4 and periostin, to determine their ability to distinguish between patients with NAFLD + AF and NAFLD alone. The results have shown that NFS had the highest AUC with a value of 0.87 (95 % CI: 0.79–0.94, p < 0.01), indicating excellent discriminatory ability. FIB-4 had an AUC of 0.65 (95 % CI: 0.54–0.77, p = 0.02), while periostin had an AUC of 0.76 (95 % CI: 0.66–0.86, p < 0.01) (*Table 3*, *Fig. 2*).

These results suggest that NFS is the most effective variable in differentiating between the two patient groups followed by periostin and then FIB-4. However, it should be noted that there was at least one tie between the positive

and negative actual state groups in the data, which could potentially bias the results.

Overall, the results suggest that the NFS risk and periostin level have good discriminative ability, while the FIB-4 score has moderate discriminative ability, in predicting a positive state variable (presence of AF in patients with NAFLD) among patients enrolled in the study.

Discussion

The current healthcare is marked by the rapid increase in NAFLD and AF, two conditions which are not only affect increasing numbers of individuals globally, but also pose significant challenges to the healthcare system.

The findings about statistically significant differences in NFS, FIB-4 and periostin levels in patients with both NAFLD and AF compared to those with NAFLD alone are consistent with the growing body of evidence linking the two conditions. The presence of AF in patients with NAFLD has been shown to have a significant impact on the degree of liver fibrosis.

While the exact mechanisms linking NAFLD and AF remain unclear, several common risk factors, such as obesity, diabetes mellitus, and male sex, have been implicated in the development of both conditions.

Other studies have investigated the underlying mechanisms linking NAFLD and AF, and suggested that the presence of inflammation, oxidative stress, and metabolic dysfunction in patients with NAFLD may increase the risk of AF. A meta-analysis of 6 cohort studies including over 600.000 individuals conducted by X. Cai et al. has shown that NAFLD was associated with an increased risk of AF compared to non-NAFLD, even after adjusting for multiple cardiometabolic risk factors. The RR was 1.19 (95 % CI 1.04–1.31) with a significant increase in the absolute risk of 1.3 per 1000 person-years [13].

The use of NFS, FIB-4 in the evaluation of patients with NAFLD and AF may provide valuable information for the identification of patients at higher risk for liver fibrosis and adverse outcomes. A study by Kang et al. has found that AF patients were older, had higher BMI, and larger waist circumference than those without AF. AF was independently linked to advanced liver fibrosis in NAFLD patients, as assessed by both NFS and Fib-4 cut-off values (COVs). The final adjusted odds ratios were 2.85 (p = 0.004) for NFS low-COV group and 12.29 (p < 0.001) for NFS high-COV group, and 2.49 (p < 0.001) for FIB-4 low-COV group and 3.84 (p = 0.016) for Fib-4 high-COV group [14].

A meta-analysis by Mozes et al. has found that NFS was a reliable and non-invasive tool for the assessment of liver fibrosis in these patients. The accuracy of FIB-4, NFS and LSM-VCTE for detecting advanced fibrosis was 0.76, 0.73 and 0.85, respectively. Using a combination of FIB-4 and LSM-VCTE, 66 % of patients with advanced fibrosis were correctly identified with a specificity of 86 %, but 33 % still needed a biopsy for confirmation [15].

NFS and FIB-4 indicators have also been shown to have prognostic value in patients with NAFLD and AF after ablation. A study by Wang et al. has found that one year after ablation, 38.8 % of patients had a recurrence of AF. Higher scores on FIB-4 and NFS tests were linked to a greater likelihood of persistent AF and its longer duration. AF recurrence

Table 1. Baseline characteristics of enrolled participants

Parameters, units of measurement	NAFLD + AF (n = 35)	NAFLD (n = 61)	p-value
Age, years	63 ± 12	54 ± 13	<0.01
Male	28 (80.00 %)	33 (54.09 %)	0.02
Diabetes mellitus	20 (57.14 %)	13 (21.31 %)	<0.01
Body mass index, kg/m^2	26.82 ± 10.1	24.64 ± 3.35	0.02
Obesity	13 (37.14 %)	6 (9.83 %)	0.03
Aspartate aminotransferase, IU/L	27 ± 15	30 ± 13	0.06
Alanine aminotransferase, IU/L	34 ± 11	36 ± 21	0.74
Serum protein, g/L	44 ± 7	49 ± 9	<0.01
Platelet count, K/µL	223 ± 53	279 ± 58	<0.01
Periostin, ng/mL	10.83 ± 1.60	9.81 ± 1.75	<0.01
NFS	-1.05 ± 1.46	-2.65 ± 1.63	<0.01
FIB-4	1.34 ± 0.86	1.07 ± 0.60	0.02

Table 2. Single-factor evaluation of contributing factors for AF in NAFLD patients

Parameters, units of measurement	Odds ratio (95 % CI)	p-value
Age, years	1.09 (1.04–1.15)	0.001
Male	3.39 (1.29–8.95)	0.01
Diabetes mellitus	4.92 (1.99–12.20)	0.01
Body mass index, kg/m^2	1.12 (1.018–1.23)	0.02
Obesity	5.41 (1.83–16.05)	0.01
Aspartate aminotransferase, IU/L	0.96 (0.92–1.00)	0.06
Alanine aminotransferase, IU/L	0.99 (0.96–1.03)	0.69
Serum protein, g/L	0.88 (0.82–0.95)	0.01
Platelet count, K/µL	0.97 (0.95–0.98)	<0.01
Periostin, ng/mL	2.08 (1.42–3.05)	<0.01
NFS	3.233 (1.97–5.30)	<0.01
FIB-4	2.45 (1.11–5.63)	0.03

Table 3. ROC analysis of NFS, FIB-4 indices and periostin level for AF in NAFLD patients

Variable	AUC (95 % CI)	p-value
NFS	0. 87 (0.79–0.94)	<0.01
FIB-4	0. 65 (0.54–0.77)	0.02
Periostin	0.76 (0.66–0.86)	<0.01

risk was higher for patients in intermediate and high-risk categories based on NFS and FIB-4 results through the Kaplan–Meier analysis. In a multivariate Cox regression analysis, intermediate and high-risk scores on NFS and FIB-4 were independently associated with AF recurrence (high risk: NFS HR: 3.11, 95 % CI: 1.68–5.76, p < 0.001; FIB-4 HR: 3.91, 95 % CI: 2.19–6.98, p < 0.001; intermediate risk: NFS HR: 1.85, 95 % CI: 1.10–3.10, p = 0.020; FIB-4 HR: 2.08, 95 % CI: 1.27–3.41, p = 0.003) [16].

Several previous studies have investigated the relationship between NAFLD and AF and found that patients with NAFLD and AF tended to have higher levels of periostin.

High periostin levels are also strongly associated with severity of NAFLD and AF. A study by Zhu et al. has demonstrated that elevated NFS and periostin levels were independently associated with an increased risk of liver-related and cardiovascular events in patients with NAFLD. The frequency of NAFLD was increased with higher periostin levels (29.8 % to 67.2 %, p < 0.001) and periostin was found

to be associated with higher odds of NAFLD. The 2nd and 3rd tertiles of periostin showed significant links with NAFLD (2.602, 95 % CI 1.030–6.575, p = 0.043 and 2.819, 95 % CI 1.629–4.878, p < 0.001, respectively). Periostin was found to be effective in predicting NAFLD (area under ROC = 0.693, 95 % CI 0.614–0.771, p < 0.001) [17].

A study by Fang et al. has found that 26.2 % of 103 patients with AF who underwent catheter ablation experienced a recurrence after 3 months. Patients with AF recurrence had larger left atrial volume and serum periostin levels. Left atrial volume (HR 3.81, 95 % CI 1.54–9.44, p = 0.004) and serum periostin A (HR 1.07, 95 % CI 1.02–1.13, p = 0.008) were identified as independent predictors of AF recurrence [18].

But that is not a common opinion. Another study by Smirne et al. has found, that among all 155 patients, there was no significant difference in periostin levels between males and females, whether considered as a whole or separated into hepatitis C virus (HCV) and NAFLD subgroups. The median periostin levels were 11.9 ng/mL (IQR 8.2–16.8) in males and 11.1 ng/mL (IQR 8.5–14.8) in females (p = 0.196). In the HCV subgroup, the median periostin levels were 12.9 ng/mL (IQR 10.7–17.4) in males and 11.3 ng/mL (IQR 9.2–16.0) in females (p = 0.275). In the NAFLD subgroup, the median periostin levels were 11.8 ng/mL (IQR 7.8–16.1) in males and 10.5 ng/mL (IQR 7.1–13.3) in females (p = 0.418) [19].

The observed differences in NFS, FIB-4 and periostin levels in patients with NAFLD and AF compared to those with NAFLD alone highlight the importance of considering the presence of AF in patients with NAFLD, as it may impact the assessment of liver fibrosis and the selection of appropriate therapeutic strategies. Further studies are needed to fully examine the clinical implications of these findings and gain a better understanding of the underlying mechanisms linking NAFLD and AF.

Conclusions

1. These findings have suggested a strong association between NAFLD and AF and highlighted the importance of considering AF as a potential complication in patients with NAFLD.

2. Both the use of the FIB-4 and NFS indices and measurement of periostin levels have been proved to be effective in detecting this association.

3. Furthermore, these may work for clinical practice, including the need for greater vigilance and monitoring for AF in NAFLD patients.

Prospects for further research. Future plans include closer examination of left atrial and left ventricular changes in patients with NAFLD and AF and the development of new treatment strategies to alleviate the inflammatory damage.

Information about the authors:
Teslenko O. B., MD, PhD-student of the Department of Therapy, Family and Emergency Medicine of Postgraduate Education, Ivano-Frankivsk National Medical University, Ukraine.
ORCID ID: 0000-0003-0424-2560
Fedorov S. V., MD, PhD, DSc, Professor, Head of the Department of Therapy, Family and Emergency Medicine of Postgraduate Education, Ivano-Frankivsk National Medical University, Ukraine.
ORCID ID: 0000-0002-2202-4279
Bielinskyi M. V., MD, PhD-student of the Department of Internal Medicine No. 2 and Nursing, Ivano-Frankivsk National Medical University, Ukraine.
ORCID ID: 0000-0001-5013-3838
Serediuk N. M., MD, PhD, DSc, Professor, Head of the Department of Internal Medicine No. 2 and Nursing, Ivano-Frankivsk National Medical University, Ukraine.
ORCID ID: 0000-0002-3616-2445

Відомості про авторів:
Тесленко О. Б., аспірант каф терапії, сімейної та екстреної медицини післядипломної освіти, Івано-Франківський національний медичний університет, Україна.
Федоров С. В., д-р мед. наук, професор, зав. каф. терапії, сімейної та екстреної медицини післядипломної освіти, Івано-Франківський національний медичний університет, Україна.
Бєлінський М. В., аспірант каф. внутрішньої медицини № 2 та медсестринства, Івано-Франківський національний медичний університет, Україна.
Середюк Н. М., д-р мед. наук, професор, зав. каф. внутрішньої медицини № 2 та медсестринства, Івано-Франківський національний медичний університет, Україна.

References

[1] Pouwels, S., Sakran, N., Graham, Y., Leal, A., Pintar, T., Yang, W., Kassir, R., Singhal, R., Mahawar, K., & Ramnarain, D. (2022). Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC endocrine disorders*, *22*(1), 63. https://doi.org/10.1186/s12902-022-00980-1

[2] Ahmad, M. I., Khan, M. U., Kodali, S., Shetty, A., Bell, S. M., & Victor, D. (2022). Hepatocellular Carcinoma Due to Nonalcoholic Fatty Liver Disease: Current Concepts and Future Challenges. *Journal of Hepatocellular Carcinoma*, *9*, 477-496. https://doi.org/10.2147/JHC.S344559

[3] Brundel, B. J. J. M., Ai, X., Hills, M. T., Kuipers, M. F., Lip, G. Y. H., & Groot, N. M. S. de. (2016). Atrial fibrillation. *Nature Reviews. Disease Primers*, *2*(1), 16017. https://doi.org/10.1038/NRDP.2016.17

[4] Riazi, K., Azhari, H., Charette, J. H., Underwood, F. E., King, J. A., Afshar, E. E., Swain, M. G., Congly, S. E., Kaplan, G. G., & Shaheen, A. A. (2022). The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. *The Lancet. Gastroenterology & Hepatology*, *7*(9), 851-861. https://doi.org/10.1016/S2468-1253(22)00165-0

[5] Lippi, G., Sanchis-Gomar, F., & Cervellin, G. (2021). Global epidemiology of atrial fibrillation: An increasing epidemic and public health challenge. *International Journal of Stroke*, *16*(2), 217-221. https://doi.org/10.1177/1747493019897870

[6] Ismaiel, A., & Dumitrașcu, D. L. (2019). Cardiovascular Risk in Fatty Liver Disease: The Liver-Heart Axis-Literature Review. *Frontiers in Medicine*, *6*, 202. https://doi.org/10.3389/FMED.2019.00202

[7] Gong, G., Liu, X., & Cheng, F. (2021). Relationship between non-alcoholic fatty liver disease and cardiac arrhythmia: a systematic review and meta-analysis. *The Journal of International Medical Research*, *49*(9), 3000605211047074. https://doi.org/10.1177/03000605211047074

[8] Jia, Y., Zhong, F., Jiang, S., Guo, Q., Jin, H., Wang, F., Li, M., Wang, L., Chen, A., Zhang, F., Shao, J., & Zheng, S. (2019). Periostin in chronic liver diseases: Current research and future perspectives. *Life Sciences*, *226*, 91-97. https://doi.org/10.1016/J.LFS.2019.04.021

[9] Marchesini, G., Day, C. P., Dufour, J. F., Canbay, A., Nobili, V., Ratziu, V., Tilg, H., Roden, M., Gastaldelli, A., Yki-Järvinen, H., Schick, F., Vettor, R., Frühbeck, G., & Mathus-Vliegen, L. (2016). EASL-EASD-EASO Clinical Practice Guidelines for the Management of Non-Alcoholic Fatty Liver Disease. *Obesity Facts*, *9*(2), 65. https://doi.org/10.1159/000443344

[10] Hindricks, G., Potpara, T., Dagres, N., Arbelo, E., Bax, J. J., Blomström-Lundqvist, C., Boriani, G., Castella, M., Dan, G. -A., Dilaveris, P. E., Fauchier, L., Filippatos, G., Kalman, J. M., la Meir, M., Lane, D. A., Lebeau, J. -P., Lettino, M., Lip, G. Y. H., Pinto, F. J., … Zakirov, N. U. (2021). 2020 ESC Guidelines for the diagnosis and mana-

gement of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal*, *42*(5), 373-498. https://doi.org/10.1093/eurheartj/ehaa612

[11] Sterling, R. K., Lissen, E., Clumeck, N., Sola, R., Correa, M. C., Montaner, J., Sulkowski, M. S., Torriani, F. J., Dieterich, D. T., Thomas, D. L., Messinger, D., & Nelson, M. (2006). Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology (Baltimore, Md.)*, *43*(6), 1317-1325. https://doi.org/10.1002/HEP.21178

[12] Angulo, P., Hui, J. M., Marchesini, G., Bugianesi, E., George, J., Farrell, G. C., Enders, F., Saksena, S., Burt, A. D., Bida, J. P., Lindor, K., Sanderson, S. O., Lenzi, M., Adams, L. A., Kench, J., Therneau, T. M., & Day, C. P. (2007). The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology (Baltimore, Md.)*, *45*(4), 846-854. https://doi.org/10.1002/HEP.21496

[13] Cai, X., Zheng, S., Liu, Y., Zhang, Y., Lu, J., & Huang, Y. (2020). Nonalcoholic fatty liver disease is associated with increased risk of atrial fibrillation. *Liver International* , *40*(7), 1594-1600. https://doi.org/10.1111/LIV.14461

[14] Kang, M. K., Park, J. G., & Kim, M. C. (2020). Association between Atrial Fibrillation and Advanced Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease. *Yonsei Medical Journal*, *61*(10), 860. https://doi.org/10.3349/YMJ.2020.61.10.860

[15] Mózes, F. E., Lee, J. A., Selvaraj, E. A., Jayaswal, A. N. A., Trauner, M., Boursier, J., Fournier, C., Staufer, K., Stauber, R. E., Bugianesi, E., Younes, R., Gaia, S., Lupșor-Platon, M., Petta, S., Shima, T., Okanoue, T., Mahadeva, S., Chan, W. K., Eddowes, P. J., … Doward, L. (2022). Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis. *Gut*, *71*(5), 1006-1019. https://doi.org/10.1136/GUTJNL-2021-324243

[16] Wang, Z., Wang, Y., Luo, F., Zhai, Y., Li, J., Chen, Y., Li, Q., Zhu, L., Jiao, S., Liu, P., Zhou, Y., Chen, Y., Dong, J., & Sun, Y. (2022). Impact of advanced liver fibrosis on atrial fibrillation recurrence after ablation in non-alcoholic fatty liver disease patients. *Frontiers in Cardiovascular Medicine*, *9*, 960259. https://doi.org/10.3389/fcvm.2022.960259

[17] Zhu, J. Z., Zhu, H. T., Dai, Y. N., Li, C. X., Fang, Z. Y., Zhao, D. J., Wan, X. Y., Wang, Y. M., Wang, F., Yu, C. H., & Li, Y. M. (2016). Serum periostin is a potential biomarker for non-alcoholic fatty liver disease: a case-control study. *Endocrine*, *51*(1), 91-100. https://doi.org/10.1007/S12020-015-0735-2

[18] Fang, L., Jin, H., Li, M., Cheng, S., & Liu, N. (2022). Serum periostin as a predictor of early recurrence of atrial fibrillation after catheter ablation. *Heart and Vessels*, *37*(12), 2059-2066. https://doi.org/10.1007/S00380-022-02115-X/METRICS

[19] Smirne, C., Mulas, V., Barbaglia, M. N., Mallela, V. R., Minisini, R., Barizzone, N., Burlone, M. E., Pirisi, M., & Grossini, E. (2020). Periostin Circulating Levels and Genetic Variants in Patients with Non-Alcoholic Fatty Liver Disease. *Diagnostics*, *10*(12), 1003. https://doi.org/10.3390/diagnostics10121003