Assessment and comparative analysis of renal function parameters in patients with liver cirrhosis and atrial fibrillation

Abstract. Background. Currently, there is insufficient scientific data on renal function in patients with comorbid course of liver cirrhosis (LC) and atrial fibrillation (AF), as well as the effect of anticoagulant treatment on kidney function in these patients. The aim of the study is assessment and comparison of renal function parameters in patients with liver cirrhosis and atrial fibrillation before and after warfarin and dabigatran treatment during three months. Materials and methods. A randomized clinical trial with a 2-stage design was conducted. At the I stage, 106 patients took part in the study: 70 of them with a comorbid course of LC and AF, 36 with LC alone. At the II stage, 56 people with LC and AF received warfarin and dabigatran for three months. A comparative assessment of creatinine, blood urea nitrogen (BUN), glomerular filtration rate (GFR) before and after treatment was carried out. Results and discussion. In patients with LC and AF, renal dysfunction is more severe due to deterioration of creatinine, BUN and GFR compared to those with LC alone (p < 0.05). Warfarin treatment of patients with LC and AF is characterized by a statistically significant worsening of creatinine, BUN and GFR (p < 0.05). On the other hand, in the group of patients with LC and AF treated with dabigatran, these parameters do not differ significantly from the baseline values (p > 0.05). Conclusions. Patients with the comorbid pathology of LC and AF have statistically worse renal function parameters compared to individuals with LC alone. After treatment of patients with LC and AF with anticoagulant drugs for three months, functional kidney parameters significantly worsened compared to those before treatment. Warfarin treatment of patients with LC and AF is characterized by a statistically significant worsening of creatinine, BUN and GFR compared to dabigatran-treated patients.

Keywords: liver cirrhosis; atrial fibrillation; kidney function; warfarin; dabigatran

Introduction
Renal dysfunction in patients with liver cirrhosis (LC), also known as hepatorenal syndrome, is a very common and well-studied complication of liver cirrhosis [1, 2]. Existing data states that approximately 1 out of 5 patients with LC have renal disorders with varying degrees of severity [3]. According to the current classification of The Acute Dialysis Quality Initiative (ADQI) group and the International Ascites Club (IAC) in 2011, renal dysfunction can manifest as acute kidney injury (AKI), a slowly progressive decline in kidney function with the development of chronic kidney disease (CKD) and the development AKI on the background of already existing kidney dysfunction, significantly worsening the prognosis of such patients [4–6]. Several most important pathophysiological mechanisms of kidney dysfunction can be impaired renal perfusion and vasoconstriction of renal vessels as a result of portal hypertension, reduced cardiac output and excessive activation of the renin-angiotensin-aldosterone system (RAAS), disruption of the internal structure of kidneys, urinary ducts obstruction and external risk factors (ascites, gastrointestinal bleeding, infection, drugs, visualization studies using contrast) [7–10]. Despite appropriate treatment, the presence of kidney dysfunction in patients with LC is a sign of poor prognosis and mortality can reach 60 % or even more [11].

Atrial fibrillation is the most common arrhythmia in the world, accompanied by such severe complications as ischemic stroke, heart failure, and myocardial infarction [12–14]. The
most common form of kidney dysfunction in patients with AF is CKD. Due to common risk factors and pathogenetic mechanisms, these two diseases often have a comorbid course, particularly approximately 50 % of patients with AF have some level of renal dysfunction [15]. It was also proven that AF is a significant risk factor for the progression of renal failure and the development of end-stage CKD [16, 17].

Recently, a lot of attention has been paid to the study of the comorbid course of LC and AF, given the worse prognosis, high rate of complications and mortality [18, 19]. Despite the well-studied effect of LC and AF separately on kidney function, there is almost no information on the effect of the combined course of these diseases on kidney function [16, 20, 21]. Also, the question of prescribing anticoagulant drugs in patients with these diseases and their effect on kidney function remains disputable. According to existing guidelines, long-term anticoagulant therapy is indicated for patients with AF according to the CHADS2-VASc2 score ≥ 2 for men and ≥ 3 for women, but this issue remains questionable for patients with AF and LC, as patients with chronic liver diseases were excluded from anticoagulant trials due to risk of bleeding [22, 23]. However, the modern theory of “rebalanced homeostasis” and the latest research on the hemostasis of liver cirrhosis indicate that patients may have a tendency to both thrombosis and bleeding, so treatment with anticoagulant drugs is scientifically based and can be safe and effective [24–26]. Currently, it is assumed that anticoagulant therapy may be an independent risk factor for the development of renal failure [27]. However, the mechanisms of development of this condition, the effect of individual oral anticoagulants and dose-dependent effects have not been sufficiently studied.

**Aim:** 1) to assess and compare renal function parameters in patients with comorbid liver cirrhosis and atrial fibrillation and patients with liver cirrhosis alone; 2) to assess and compare renal function parameters in patients with comorbid liver cirrhosis and atrial fibrillation before and after treatment with warfarin and dabigatran during three months.

**Materials and methods**

**Characteristics of study sample**

Recruitment and study research was carried out during 2021—2022. The research plan was approved by the Bioethics Commission of the Bogomolets National Medical University (protocol No. 156/21.01.2022). All patients signed informed consent given the experimental nature of the study.

Generally, 106 patients participated in the study, of which 70 patients had a comorbid course of liver cirrhosis and permanent AF and 36 patients had liver cirrhosis alone. The diagnosis of liver cirrhosis was established in accordance with the current international and local liver cirrhosis guidelines according to patient history, medical documentation data, patient complaints and physical examination, results of laboratory and instrumental research examination (abdominal ultrasound and liver transient elastography) in order to detect irreversible structural changes in the liver. The diagnosis of atrial fibrillation was established in accordance with current international and local recommendations for the diagnosis of atrial fibrillation based on the patient history, complaints, physical and comprehensive laboratory and instrumental examination. A permanent form of atrial fibrillation was established historically in the presence of a heart rhythm disturbance for more than 1 year when it was impractical or impossible to restore sinus rhythm.

Inclusion criteria: age of patients older than 18 years old, the presence of laboratory and instrumentally confirmed liver cirrhosis in patients with a permanent form of AF, the presence of individual consent of the patient to participate in the study.

Exclusion criteria from the study: the presence of hereditary or acquired coagulopathies of other genesis, systemic connective tissue diseases, oncological diseases, stage 4 and 5 chronic kidney disease (GFR < 30 ml/min/1.73 m²), HIV infection, gastrointestinal bleeding and intracranial hemorrhage in the anamnesis less than 2 weeks ago, neuropsychological disorders of the patient, which affect the result of observation and treatment.

Indications for treatment with anticoagulant drugs in patients were determined by the CHA2DS2-VASc score ≥ 2 points for men and ≥ 3 points for women. The risk of hemorrhagic complications was determined using the HAS-BLED score.

**Study design**

The study design consisted of 2 stages.

At the first stage, all 106 patients were divided into 2 research groups. The first group consisted of 70 patients with liver cirrhosis and a permanent form of atrial fibrillation, the second comparison group included 36 patients with liver cirrhosis alone. At the start of research current and past medical history was obtained and physical examination was performed. Laboratory tests were obtained, in particular, complete blood count, blood biochemistry (total bilirubin, total protein, albumin, ALT and AST, alkaline phosphatase, GGTP, creatinine, BUN), GFR, standard coagulation parameters. GFR was estimated according to Cockcroft-Gault formula, that is indicated specifically for patients on anticoagulation treatment. During laboratory and instrumental examinations, patients were advised to withhold from taking any anticoagulants and antiplatelets for 3 days. Patients of the study group I were further divided into 3 subgroups according to Child-Pugh score — classes A, B or C. All obtained parameters were compared with the control group and a comparative analysis of the group I and II parameters was carried out.

At the second stage 56 patients with liver cirrhosis and atrial fibrillation took part, who were further divided into two subgroups randomly. Group IA (n = 30) included 15 (50 %) patients with liver cirrhosis class A according to the Child-Pugh scale and 15 (50 %) patients of class B. Group IA was treated with dabigatran etexilate at a dosage of 110 mg twice daily. The IB group (n = 26) included 10 (38.5 %) patients with class A liver cirrhosis according to the Child-Pugh scale and 16 (61.5 %) class B patients. The IB group received warfarin at an initial dose of 5 mg, which dynamically varied depending on the INR within next 3 months. Patients were informed about prescription regimen and possible side effects. Based on the results of the examination, an assessment and comparative analysis of laboratory parameters (complete blood count, functional parameters of liver and kidneys, coagulation parameters) was carried out before and after the anticoagulation treatment, as well as between subgroups IA and IB.
## Table 1 — Patients' clinical information

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Liver cirrhosis and AF (n = 70)</th>
<th>Liver cirrhosis (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>68.30 ± 1.08</td>
<td>58.30 ± 1.45</td>
</tr>
<tr>
<td><strong>Sex, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Male</td>
<td>46 (66)</td>
<td>22 (61)</td>
</tr>
<tr>
<td>— Female</td>
<td>24 (34)</td>
<td>14 (39)</td>
</tr>
<tr>
<td><strong>Etiology, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Alcohol</td>
<td>28 (40)</td>
<td>16 (44)</td>
</tr>
<tr>
<td>— HCV</td>
<td>4 (6)</td>
<td>5 (14)</td>
</tr>
<tr>
<td>— HBV</td>
<td>7 (10)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>— NAFLD</td>
<td>19 (27)</td>
<td>7 (20)</td>
</tr>
<tr>
<td>— Cardiac cirrhosis</td>
<td>3 (4)</td>
<td>N/A</td>
</tr>
<tr>
<td>— Combined</td>
<td>9 (13)</td>
<td>4 (11)</td>
</tr>
<tr>
<td><strong>Child-Pugh score, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— A</td>
<td>25 (36)</td>
<td>13 (36)</td>
</tr>
<tr>
<td>— B</td>
<td>31 (44)</td>
<td>16 (44)</td>
</tr>
<tr>
<td>— C</td>
<td>14 (20)</td>
<td>7 (20)</td>
</tr>
<tr>
<td><strong>Liver-related comorbidities, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Ascites</td>
<td>6 (9)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>— History of hepatic encephalopathy</td>
<td>2 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>— Jaundice</td>
<td>4 (6)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>— Esophageal or gastric varices</td>
<td>1 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Non-liver related comorbidities, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Hypertension</td>
<td>43 (61)</td>
<td>20 (56)</td>
</tr>
<tr>
<td>— Congestive heart failure</td>
<td>60 (86)</td>
<td>21 (58)</td>
</tr>
<tr>
<td>— Chronic kidney disease:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>— stage 1</td>
<td>2 (3)</td>
<td>N/A</td>
</tr>
<tr>
<td>— stage 2</td>
<td>2 (3)</td>
<td>N/A</td>
</tr>
<tr>
<td>— stage 3</td>
<td>3 (4)</td>
<td>N/A</td>
</tr>
<tr>
<td>— Coronary heart disease</td>
<td>31 (44)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>— Diabetes</td>
<td>9 (13)</td>
<td>N/A</td>
</tr>
<tr>
<td>— Obesity</td>
<td>7 (10)</td>
<td>2 (6)</td>
</tr>
<tr>
<td><strong>Laboratory tests:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Platelets, × 10⁹/l</td>
<td>200 [140; 230]</td>
<td>184 [150; 219]</td>
</tr>
<tr>
<td>— Total protein, g/l</td>
<td>66 [59; 72]</td>
<td>66.2 [62.1; 72.4]</td>
</tr>
<tr>
<td>— Albumin, g/l</td>
<td>34 [31; 36]</td>
<td>31.4 [28; 36.5]</td>
</tr>
<tr>
<td>— Total bilirubin, μmol/l</td>
<td>45.5 [33; 55]</td>
<td>39 [29; 55]</td>
</tr>
<tr>
<td>— ALT, U/l</td>
<td>63 [48; 112]</td>
<td>65 [52.5; 116]</td>
</tr>
<tr>
<td>— AST, U/l</td>
<td>64 [45; 144]</td>
<td>65.5 [51; 91.5]</td>
</tr>
<tr>
<td>— INR</td>
<td>1.4 [1.3; 1.52]</td>
<td>1.4 [1.3; 1.5]</td>
</tr>
<tr>
<td><strong>Antiaggregant use, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Clopidogrel</td>
<td>2 (3)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>— Aspirin</td>
<td>15 (21)</td>
<td>8 (22)</td>
</tr>
<tr>
<td><strong>Anticoagulants use, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Warfarin</td>
<td>17 (24)</td>
<td>N/A</td>
</tr>
<tr>
<td>— Dabigatran</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>— Rivaroxaban</td>
<td>4 (6)</td>
<td>N/A</td>
</tr>
<tr>
<td>— Apixaban</td>
<td>1 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>History of thrombotic events, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— Thromboembolic (MI, IS)</td>
<td>7 (10)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>— Splanchnic vein thrombosis</td>
<td>9 (13)</td>
<td>3 (8)</td>
</tr>
<tr>
<td><strong>History of hemorrhagic events, n (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— GI bleeding</td>
<td>6 (9)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>— Epistaxis</td>
<td>5 (7)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>— Gingival bleeding</td>
<td>2 (3)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

Notes: values are presented as median [25%; 75%], number (%) or mean ± standard deviation; AF — atrial fibrillation; HCV — hepatitis C virus; HBV — hepatitis B virus; NAFLD — non-alcoholic fatty liver disease; INR — international normalized ratio; MI — myocardial infarction; IS — ischemic stroke.
Statistical analysis

Statistical analysis was performed using the statistical package IBM SPSS Statistics Base version 22.0, EZR version 3.4.1 (R Foundation Statistical Computing). The Kolmogorov-Smirnov criterion was used to determine the distribution of variables. Quantitative variables were presented as mean with standard deviation of the mean (± SD) if the data were normally distributed or as median (Me), as 25 and 75 percentiles [25%; 75%] if data distribution was abnormal. The Student’s t-test was used to determine significant differences when comparing quantitative parameters, and the chi-square or Fisher’s test was used for categorical variables. A significance level of \( p < 0.05 \) was considered statistically significant.

Patients’ clinical information

Table 1 presents the main clinical and anamnestic data of the patients. It is important to note that concomitant cardiovascular and endocrine diseases and complications were significantly more common in patients with liver cirrhosis and AF. Also, patients of this group were characterized by a greater number and variety of comorbid conditions, which were not present in patients with liver cirrhosis alone. Laboratory parameters did not statistically differ in patients of both groups.

Results

According to study results, renal function parameters were impaired in patients of both groups (Tables 2, 3).

Renal function assessment revealed that the total average levels of creatinine and BUN in group I patients were statistically higher, and GFR was statistically lower than in the control group (\( p < 0.001 \)), and gradually worsened as the severity of liver cirrhosis progressed (\( p < 0.05 \)). In patients of the II group, renal dysfunction was less pronounced, in particular, the average levels of creatinine and BUN were slightly higher than controls without a significant statistical difference between classes of liver cirrhosis (\( p > 0.05 \)). GFR in patients of the II group was slightly reduced, compared to the control, and statistically differed only in patients of classes B and C (\( p < 0.05 \)). Thus, the level of creatinine in patients of group I was higher by 8.6 %, the level of BUN by 24.5 %, and GFR lower by 14.3 % than the similar parameters in patients of group II (\( p < 0.05 \)).

At the second stage of the study, the impact of treatment with anticoagulant drugs warfarin and dabigatran etexilate on the kidney function of patients with liver cirrhosis and atrial fibrillation was evaluated compared to the initial parameters and between patients of both groups after 3 months of treatment.

Analysis of the results of renal function assessment after the treatment revealed statistically significant changes in the levels of BUN, creatinine and GFR (\( p < 0.05 \)), which indicates a negative effect of the treatment on kidney’s function, worsening of existing or previously absent renal failure (Table 4).

After more detailed analysis of the IA and IB subgroups that received different treatment, it was found a statistically

### Table 2 — Parameters of renal function in patients with liver cirrhosis and atrial fibrillation, \( X \pm SD \) or Me [25%; 75%]

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control, ( n = 20 )</th>
<th>Group I (LC and AF), ( n = 70 )</th>
<th>Class A, ( n = 25 )</th>
<th>Class B, ( n = 31 )</th>
<th>Class C, ( n = 14 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN, mmol/l</td>
<td>5.48 ± 3.36</td>
<td>7.38 ± 2.35*</td>
<td>6.50 ± 2.67</td>
<td>7.40 ± 3.05*</td>
<td>8.25 ± 3.34**</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>74.38 ± 6.67</td>
<td>106.31 ± 10.36*</td>
<td>88.14 ± 6.31</td>
<td>108.00 ± 8.03**</td>
<td>122.78 ± 16.73**</td>
</tr>
<tr>
<td>GFR, ml/min/1.73 m²</td>
<td>105.42 ± 6.60</td>
<td>65.94 ± 7.73*</td>
<td>76.54 ± 7.23*</td>
<td>68.31 ± 8.45*</td>
<td>52.96 ± 7.52**</td>
</tr>
</tbody>
</table>

**Notes:** * — level of statistical difference from healthy control; ** — level of statistical difference from class A according to the Child-Pugh scale; *** — level of statistical difference from class B according to the Child-Pugh scale; GFR — glomerular filtration rate; BUN — blood urea nitrogen.

### Table 3 — Parameters of renal function in patients with liver cirrhosis, \( X \pm SD \) or Me [25%; 75%]

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control, ( n = 20 )</th>
<th>Group II (LC), ( n = 36 )</th>
<th>Class A, ( n = 13 )</th>
<th>Class B, ( n = 16 )</th>
<th>Class C, ( n = 7 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN, mmol/l</td>
<td>5.48 ± 3.36</td>
<td>5.93 ± 3.62</td>
<td>5.30 ± 3.22</td>
<td>5.80 ± 3.34</td>
<td>6.7 ± 3.3</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>74.38 ± 6.67</td>
<td>97.90 ± 17.12*</td>
<td>82.13 ± 6.79</td>
<td>95.42 ± 26.13*</td>
<td>116.1 ± 18.45*</td>
</tr>
<tr>
<td>GFR, ml/min/1.73 m²</td>
<td>105.42 ± 6.60</td>
<td>76.87 ± 4.22*</td>
<td>94.35 ± 4.16</td>
<td>71.16 ± 3.28*</td>
<td>65.09 ± 5.23*</td>
</tr>
</tbody>
</table>

**Note.** * — level of statistical difference from healthy control.

### Table 4 — Parameters of renal function in patients with liver cirrhosis and atrial fibrillation before and after treatment with anticoagulants for 3 months, \( X \pm SD \) or Me [25%; 75%]

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment (( n = 56 ))</th>
<th>After treatment (( n = 56 ))</th>
<th>Statistical significance, ( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN, mmol/l</td>
<td>7.46 ± 0.90</td>
<td>8.00 ± 1.36</td>
<td>0.027</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>103.5 ± 15.0</td>
<td>110.30 ± 12.71</td>
<td>0.048</td>
</tr>
<tr>
<td>GFR, ml/min/1.73 m²</td>
<td>66.08 ± 9.83</td>
<td>60.00 ± 7.04</td>
<td>0.005</td>
</tr>
</tbody>
</table>
significant deterioration of renal function parameters in warfarin group, while in the dabigatran group parameters did not differ from the initial values (Table 5).

**Discussion**

As a result of the first stage of the study, it was found that patients with comorbid course of liver cirrhosis and AF have statistically worse renal function parameters than in healthy individuals and there is also a gradual worsening of renal function in such patients as the severity of liver cirrhosis progresses. It is especially important that renal function of group I patients with LC and AF was significantly worse compared to patients of group II with liver cirrhosis alone. Such results can be explained by more frequent and pronounced kidney damage in patients of the I group due to comorbid chronic kidney disease, which was present at the beginning of the study in a certain proportion of patients, as well as cardiovascular and endocrine pathology, in particular, due to chronic heart failure, arterial hypertension, diabetes, etc. In addition, AF is potential independent risk factor for the development of CKD.

At the second stage of the study, the analysis of renal function parameters after anticoagulant treatment revealed a statistically significant deterioration of BUN, creatinine, and GFR generally in all patients with LC and AF, that indicates a negative effect of the treatment on the kidneys function, worsening of existing or previously absent renal failure. In a more detailed analysis of the IA and IB subgroups that received different treatment, it was found statistically significant worsening renal function parameters in warfarin group, while the same parameters in the dabigatran group did not differ from the initial values. Therefore, short-term treatment with warfarin is accompanied by a more pronounced increase in BUN, creatinine levels and decrease in GFR compared to dabigatran. The scientific data of several retrospective studies and meta-analysis, the purpose of which was to establish the effect of anticoagulants on the development of renal complications (acute kidney injury and chronic kidney disease), are comparable with the results obtained in our study [28, 29]. Currently, it is believed that new oral anticoagulant (NOAC) treatment is associated with a lower risk of renal complications compared to warfarin [30].

Deterioration of renal function in patients in warfarin group is most likely caused by warfarin-associated nephropathy. The main pathogenetic mechanism of this condition is damage to the filtration barrier of the nephron and hemorrhage in Bowman’s space and renal tubules. Microscopically, hemoglobin molecules and erythrocyte cylinders can be seen that damage the tubules, causing ischemia and obstruction. Pathophysiologically, this process is very similar to acute kidney damage in rhabdomyolysis. At the molecular level, damage to the filtration barrier can be explained by a decrease in thrombin generation and its effect on PAR — proteinase-activated receptors (anti-coagulant effect of warfarin). Thrombin is thought to stimulate proteinase-activated receptors (PARs) that support endothelial integrity and vascular nutrition, including nephron arterioles. Decreased activation of these receptors leads to disruption of barrier integrity and hemorrhage. This effect is also present on NOAC treatment, but is stronger in vitamin K antagonists (VKA). After reducing the dose or canceling the drug, the functional state of the kidneys improves, but with long-term treatment or presence of some concomitant risk factors (advanced age, existing severe chronic kidney disease, diabetes and hypertension), the damage may remain irreversible.

For this study, dabigatran was chosen from all other DOACs, because this drug is the most promising for the treatment of patients with liver cirrhosis and atrial fibrillation, based on its pharmacokinetic and pharmacodynamic properties. In particular, dabigatran is almost not metabolized in the liver, approximately 80% of the drug is excreted through the kidneys, also among all DOACs, dabigatran has the lowest level of binding to plasma proteins and, in addition, almost does not use the cytochrome P450 system of the liver for metabolism and is therefore theoretically less harmful for patients with reduced liver function. The dabigatran dosage of 110 mg twice daily was chosen because, according to the literature, a reduced dabigatran dose is effective and safer for patients with additional risk factors. Patients with LC and AF are a special category of patients that may have an increased risk of bleeding, and the average age of patients was 68 years, which is the second important risk factor for bleeding.

A limitation of this study is the exclusion of patients with CKD stages 4 and 5. Severe stages of CKD are associated with a high risk of bleeding, as well as the presence of coagulopathy, which could significantly affect the results of the study. Also, at the II stage, patients with cirrhosis of the liver class C according to the Child-Pugh scale were excluded from the study. Patients of this class were not included in the study, because according to the existing recommendations for anticoagulation treatment, DOACS are not recommended for use in this subgroup. Currently, few clinical studies have been conducted to evaluate the effectiveness and safety of DOACs in this category of patients, and their use can have an unpredictable effect on the risk of bleeding and patient survival.

**Conclusions**

1. In patients with comorbid liver cirrhosis and atrial fibrillation, renal function parameters are statistically worse compared to patients with liver cirrhosis alone, with a gradual deterioration of kidney function as the severity of liver cirrhosis progresses.
2. After anticoagulant treatment of patients with liver cirrhosis and atrial fibrillation for 3 months, renal function parameters significantly worsened compared to initial values.
3. Warfarin treatment of patients with liver cirrhosis and atrial fibrillation is characterized by a statistically significant deterioration of creatinine, BUN and GFR, on the other hand, in dabigatran group these parameters do not differ statistically from the initial values.

References


Оцінка й порівняльний аналіз функції нирок у пацієнтів із цирозом печінки та фібриляцією передсердь

Резюме. Актуальність. Зараз існує мало наукових даних стосовно функціонального стану нирок у пацієнтів із поєднаним перебігом цирозу печінки (ЦП) й фібриляції передсердь (ФП), а також впливу антикоагулянтів на функціональний стан нирок у цих осіб. Мета: оцінити та порівняти показники функції нирок у пацієнтів із цирозом печінки та фібриляцією передсердь до та після призначення антикоагулянтних препаратів варфарину та дабігатрану.

Матеріали та методи. Було проведено рандомізоване клінічне дослідження, що за дизайном складалося з 2 етапів. На І етапі в дослідженні взяли участь 106 пацієнтів: 70 із поєднаним перебігом ЦП та ФП, 36 тільки з ЦП. На II етапі 56 хворих із ЦП та ФП отримували варфарин протягом 3 місяців. Була проведена порівняльна оцінка рівнів креатиніну, сечовини, швидкості клубочкової фільтрації (ШКФ) до та після лікування. Результати та обговорення. У пацієнтів із ЦП та ФП порушення функції нирок є більш виразеними за рахунок погіршення показників креатиніну, сечовини та ШКФ порівняно з особами тільки з ЦП (р < 0,05). Лікування хворих із ЦП та ФП за допомогою варфарину характеризується статистично значущим погіршенням показників креатиніну, сечовини та ШКФ (р < 0,05). Натомість у групі пацієнтів із ЦП та ФП, які отримували дабігатран, показники більш вірогідно не відрізняються від початкових значень (р > 0,05). Висновки. В осіб із поєднаною патологією (ЦП та ФП) спостерігаються статистично гірші показники функціонального стану нирок порівняно з хворими тільки з ЦП. Після лікування антикоагулянтними препаратами протягом 3 місяців показники функціонального стану нирок у пацієнтів із ЦП та ФП вірогідно порівняно з початком терапії. Лікування варфарином характеризується статистично значущим погіршенням рівнів креатиніну, сечовини та ШКФ у пацієнтів із ЦП та ФП порівняно з тими, хто отримував дабігатран.

Ключові слова: цироз печінки; фібриляція передсердь; функція нирок; варфарин; дабігатран