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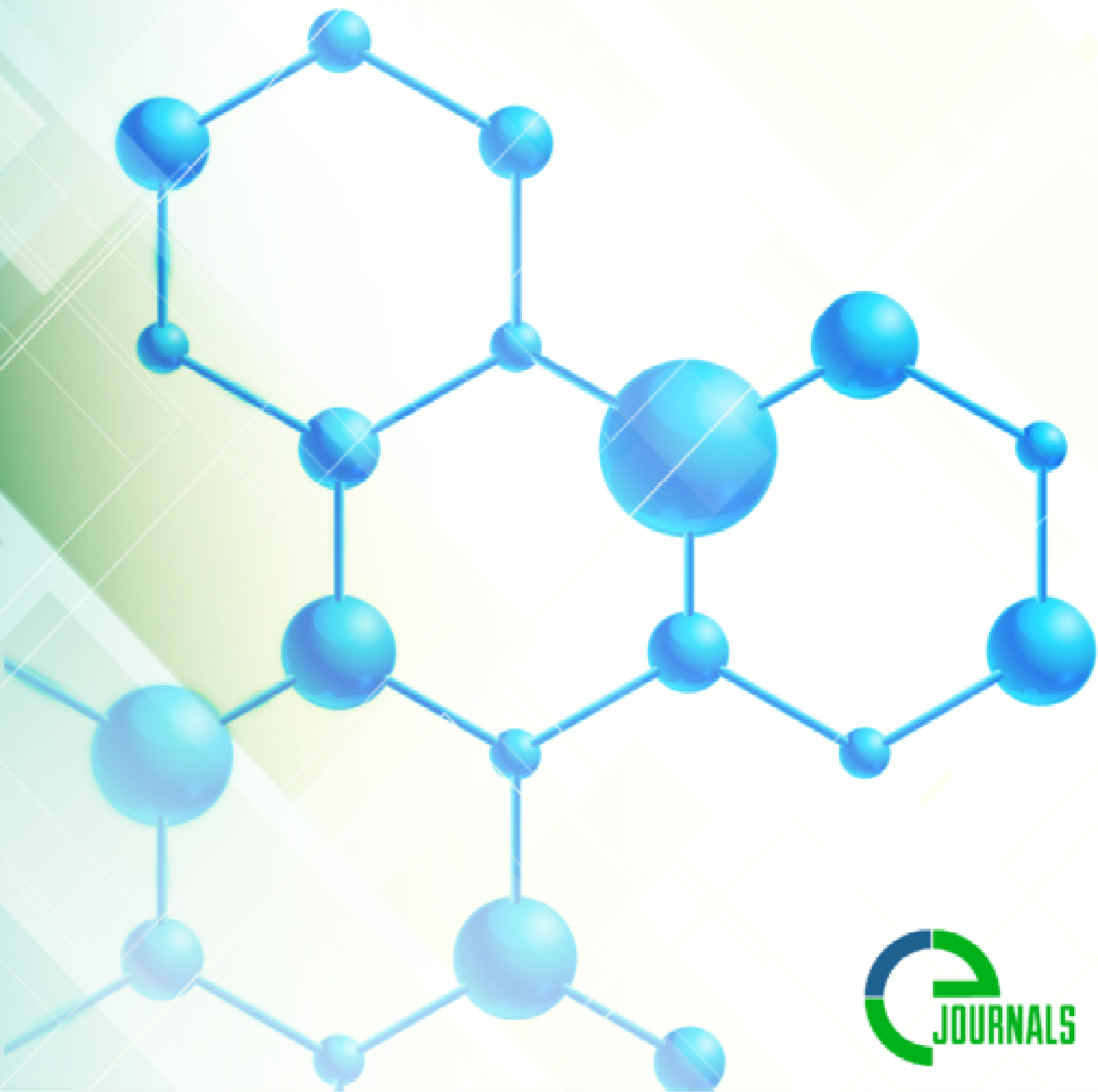

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CLINICAL CHARACTERISTICS OF PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING CORONARY REVASCULARIZATION WITH CONCOMITANT LIVER DAMAGE

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Relevance. Considering the severe clinical condition of patients with multifocal atherosclerosis, as well as the high percentage of complications that arise in the early hospital stage after surgical procedures, minimally invasive, low-trauma endovascular interventions have recently been used for the treatment of this category of patients (Henry M., Henry I., Polidor A., et al., 2007; Likharev A.Yu., Tarbaeva N.V., 2008).

Further research is being conducted to identify clinical and diagnostic markers of chronic myocardial ischemia progression in the course of invasive therapy. A comprehensive set of modern scales is accessible and effective for practical healthcare. The positive effects of antithrombotic therapy after PCI are undeniable but require additional investigation, particularly considering liver function status and the selection of safer treatment regimens.

Materials and Methods. In a prospective study conducted at the Republican Medical Scientific and Practical Center for Therapy and Medical Rehabilitation, patients with concomitant liver disease underwent minimally invasive interventional procedures. Patients were excluded from the study if they had liver cirrhosis or were candidates for liver transplantation. Indications for coronary angiography included stenosis of the left coronary artery greater than 50% and stenosis greater than 70% in the subepicardial coronary artery zones, as well as stenosis of large branches, assessed by an interventional cardiology specialist at the RMSPCT & MR.

All patients included in the study underwent laboratory tests, including complete blood count, urinalysis, and standard biochemical blood tests, which included total protein and fractions, total bilirubin, direct and indirect bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase, gamma-glutamyl transferase, and alkaline phosphatase. All patients were selected based on the presence of coronary artery disease and concomitant liver dysfunction. They were then divided into two groups. Patients in the first group, i.e., those with CAD and stable angina combined with liver dysfunction, underwent coronary angiography followed by stent placement. Patients in the second group, statistically comparable to the first group in terms of CAD, stable angina, liver dysfunction, sex, and age characteristics, received medical treatment for ischemic heart disease without interventional procedures.

Patients were stratified according to the severity of atherosclerosis progression, which in practice was reflected by the study of clinical data and angiographic findings. Radiation exposure was averaged for the contrast procedure, and access was through the femoral artery. Additionally, an analysis of both patient groups was conducted to assess the severity of liver dysfunction based on laboratory and instrumental indicators.

Acute kidney injury was defined as an increase in serum creatinine levels by at least 25% from baseline or by 50% within the first 24 hours. The risk of bleeding was assessed using the BARC (Bleeding Academic Research Consortium) scale. A bleeding risk was considered high at type 3B or above according to this scale. Patients were visually examined for hematomas (even minor ones) on the body. A history of blood transfusions or anemia was not considered significant bleeding.

As a primary endpoint, we assessed short-term outcomes, i.e., the risk of adverse cardiovascular events, including death, myocardial infarction, ACS, the need for repeated coronary revascularization, and acute cerebrovascular accidents in the perioperative (operative and early postoperative) period. Follow-up and treatment of patients were conducted for six months after PCI, after which patient data were compared based on secondary endpoints. Clinical and demographic characteristics were assessed both initially and during therapy. Statistical data analysis was performed. Data were compiled using MS Excel 2019. The Wilcoxon-Shapiro test was used for evaluation. Variables were presented as Me [25-75%] based on distribution. Additionally, Pearson's criterion with a two-tailed significance test was used to identify and assess the correlation between comparable quantitative indicators.

Study Results. In the first group, there were 59 men (61.5%) and 37 women (38.5%), while in the second group, there were 13 men (54.2%) and 11 (45.8%) women. The mean age of patients in the first group was 69 years ($p=0.029$). According to the data obtained, the risk of adverse outcomes was significantly higher in patients over 50 years old ($p<0.05$), with an odds ratio of 1.92 when comparing both groups. Analysis of hospital stay duration showed that the hospitalization period for the first group was 20 days, while for the second group, it was 19 days ($p=578$).

CRP is a non-specific acute-phase protein induced in the liver by interleukin-6 and serves as a biological marker of inflammation and tissue damage. Data analysis showed that patients with high CRP levels were more prone to more severe postoperative periods. The CRP level in the first group was 2.4 mg/dL, while in the second group, it was 7.6 mg/dL ($p<0.05$). The relative risk (RR) indicator was 1.3, indicating a direct relationshi p between CRP level and the likelihood of an adverse outcome.Correlation analysis revealed a strong association between CRP and oxygen saturation ($r=+0.74$). Thus, CRP can be used as a predictive marker for pathology risk.

According to recommendations from the International Society on Thrombosis and Haemostasis (ISTH), a high D-dimer level can be considered a marker of an unfavorable risk factor for thrombosis. In our study, D-dimer levels in the first group were 1.0 mcg/mL, while in the second group, they were 1.89 mcg/mL ($p=0.017$). A weak positive correlation was found between oxygen saturation and D-dimer levels ($r=+0.213$ and $+0.541$, respectively, in the first and second groups of patients).

ROC analysis was conducted to determine adverse outcome criteria. According to this analysis, predictors of poor prognosis included:

- Age >60 years (AUC=0.957, sensitivity 90.4%, specificity 94.2%).
- Ferritin >700 ng/mL (AUC=0.706, sensitivity 77.7%, specificity 75%).
- D-dimer >5 mcg/mL (AUC=0.602, sensitivity 100%, specificity 100%).
- CRP >6 mg/dL (AUC=0.656, sensitivity 95.7%, specificity 85.7%).

An ROC curve analysis of comorbid backgrounds revealed that the most unfavorable factor was a history of more than three diseases (AUC=0.647, sensitivity 95.8%, specificity 85.6%). The most adverse comorbid conditions were CKD, hypertension, and CHF. When assessing the risk of adverse outcomes, it is important to consider comorbid backgrounds. The Charlson Comorbidity Index was used for this purpose. In the first group, the index was 4 points, corresponding to a 10-year survival rate of 53.39%, while for the second group, the index was 13 points (10-year survival rate of 0.00%), confirming the poor prognosis for patients in the second group.

Table 1. Risk ratio of adverse outcomes depending on comorbid background

Comorbid Conditions	Prevalence in 1st Group, %	RR	Prevalence in 2nd Group, %	RR	p
Hypertension	54.3	1.4	77	1.7	0.084
COPD	8.5	0.6	35.4	0.2	0.052
Chronic Heart Failure	41.6	0.7	56	1.1	0.085
Chronic Liver Diseases	11.6	0.3	40	1.72	0.041
Chronic Kidney Disease	11.5	0.4	41	1.7	0.041
Type 2 Diabetes Mellitus	26.4	0.7	31.4	1.1	0.042
Post-Infarction Cardiosclerosis	8.8	0.9	29.5	1.2	0.037

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Table 2 Baseline Angiographic Indicators of the Studied Patients

Indicator	Group 1 (n=40)	Group 2 (n=40)
Number of Affected Coronary Arteries		
Single-vessel disease	12	24
Two-vessel disease	28	16
Anterior descending CA (%)	76	72
Circumflex CA (%)	26	23
Right CA (%)	29	35
Type of Lesion by ABC Classification (%)		
Stenosis type A-B1 (%)	60*	49
Stenosis type B2 (%)	34	41
Stenosis type C (%)	6	10
MDS (mm)	0.69±0.38	0.73±0.33
DDS (mm)	2.75±0.25	2.83±0.27
Stenosis Diameter (%)	76±14	78±16
Stenosis Diameter (mm)	11.8±7.1	12.5±6.9

The baseline angiographic indicators were largely similar in both groups (Table 2), except for a higher proportion of uncomplicated lesions (types A-B1) in the CAD group compared to the CAD+DM group (p=0.016) and a trend towards a relatively smaller minimum vessel diameter (MDS) in the CAD+DM group.

Table 3 Angiographic Follow-up After 6 Months

Indicator	CAD+DM Group	CAD Group
Number of patients examined in follow-up	40	40
Number of segments	51	49
Affected segment	35	16
Unaffected segment	7	2
Frequency of affected segments in the sample of patients undergoing repeat angiography	30.2%*	20.8%

Repeat angiography was performed in all surviving patients in both groups who experienced recurrent angina or developed non-fatal MI. Quantitative coronary analysis revealed that the minimal lumen decreased in both groups, but by 6 months, it was significantly smaller in the CAD+DM group (1.21±0.47 mm) than in the CAD group (1.78±0.53 mm, p=0.001). Late lumen loss in both groups at 6 months was 1.32±0.40 mm for the CAD+DM group and 1.01±0.38 mm for the CAD group. The final lumen of the target segment was significantly larger in the CAD group—1.25±0.73 mm compared to 0.52±0.58 mm in the CAD+DM group (p=0.001).

Indicators such as the need for repeat revascularization and acute myocardial infarction were similar in both groups (50% vs. 40%, p=0.383). In the PCI group, the combined frequency of adverse events such as stroke, AKI, and episodes of severe bleeding during the 1-year follow-up was 40% higher compared to the first group. Massive bleeding (BARC scale - 3B and higher) during DAPT occurred in 23% of PCI patients, while the number of AKI cases was 26% higher in the PCI group compared to the standard treatment group. The total number of bleeding cases of BARC grade 2 and higher approached 46%. In 4 PCI patients with pre-existing renal dysfunction (GFR < 60), AKI developed, requiring renal replacement therapy. The group of patients receiving conservative treatment had significantly fewer adverse effects of therapy, particularly stroke, AKI, and severe bleeding (18% vs. 41%, p=0.032) and a lower number of AKI cases (6% vs. 26%, p=0.02). The total number of major and minor bleeding events was similar between the PCI and conservative treatment groups (45% vs. 39%, p=0.658). The frequency of severe bleeding was lower in the conservative treatment group compared to the PCI group (11% vs. 23%, p=0.25). In total, 11 patients in the PCI group had severe liver dysfunction, of whom only 7 underwent full preoperative percutaneous revascularization; 4 patients were eventually transferred to the gastroenterology department. In the conservative treatment group, 9 patients had serious indicators of liver dysfunction, of whom 6 were referred for further treatment in the gastroenterology department. One case of myocardial infarction without ST-segment elevation occurred in the PCI group.

Conclusions

Thus, timely detection of CAD patients using coronary angiography followed by revascularization significantly reduces the risk in CAD patients. Existing protocols for managing CAD patients allow identifying those with liver dysfunction. Even in this severe patient category, it was possible to achieve target LDL cholesterol levels and blood pressure and to timely determine the indications for revascularization. At the same time, emphasis should be placed on evaluating functional liver parameters, risk stratification among patients with different functional classes of CAD and various comorbidities, as well as different variants of coronary artery involvement. Protocols for managing CAD patients with liver involvement are required, especially for the category requiring PCI.

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