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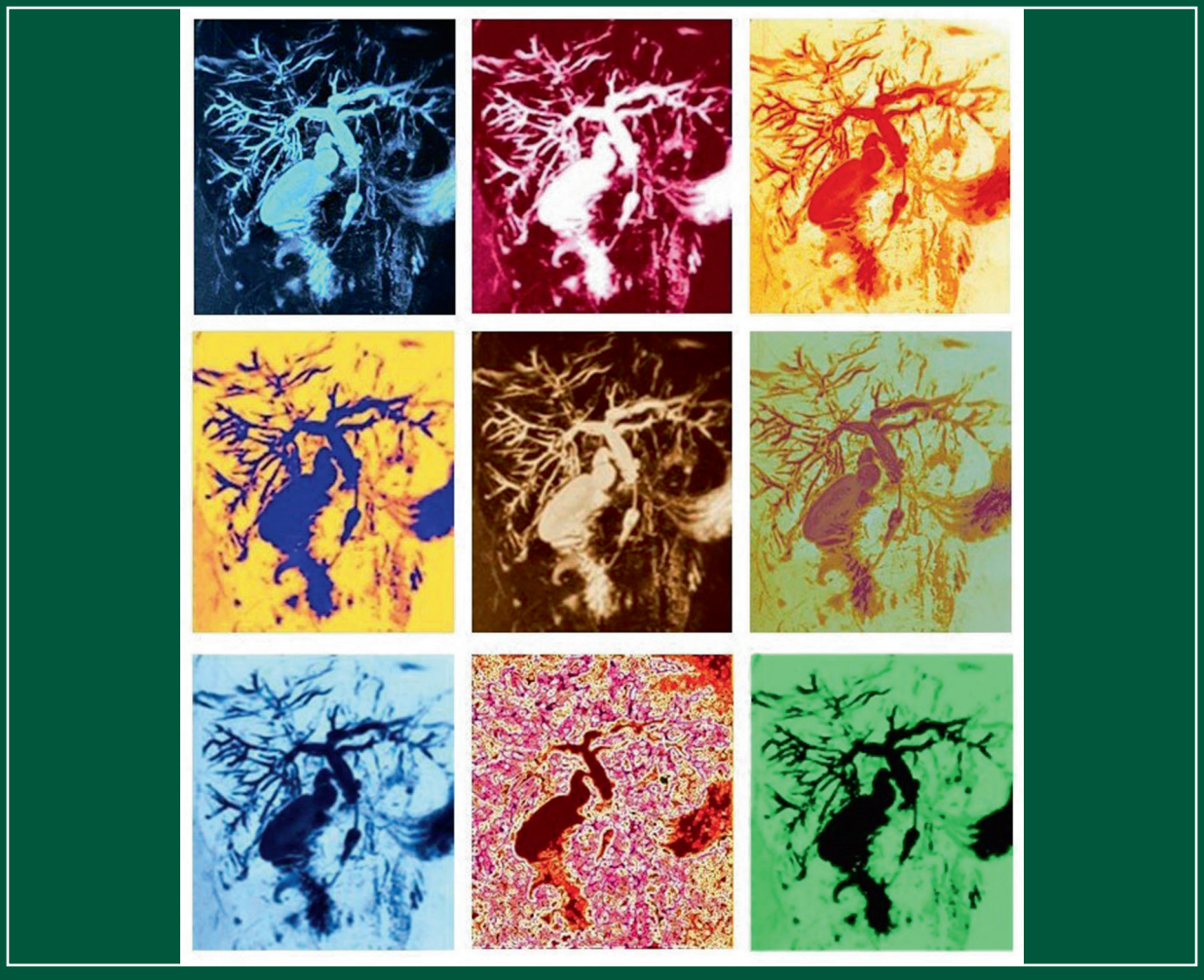
European Journal of Clinical Investigation

56TH ANNUAL SCIENTIFIC MEETING –
8–10 June 2022, Bari, Italy



Cholangiocarcinoma - 9 faces of the killer
It shows cholangiocarcinoma, an aggressive bile duct tumour with dismal prognosis,
It was captured during magnetic resonance cholangiopancreatography (MRCP)
Piotr Milkiewicz, Warsaw Poland

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ESCI EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

Official journal of the European Society for Clinical Investigation

European Journal of Clinical Investigation

THE JOURNAL OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

Aims & Scope

The European Journal of Clinical Investigation (EJCI), in publication since 1970, is a peer-reviewed general-interest biomedical journal with a broad readership. It is the official journal of the European Society for Clinical Investigation (ESCI) and it is published monthly by Wiley. It considers any original contribution from the most sophisticated basic molecular sciences to applied clinical and translational research and evidence-based medicine across a broad range of subspecialties. The EJCI publishes reports of high-quality research that pertain to the genetic, molecular, cellular, or physiological basis of human biology and disease, as well as research that addresses prevalence, diagnosis, course, treatment, and prevention of disease. We are primarily interested in studies directly pertinent to humans, but submission of robust in vitro and animal work is also encouraged. Interdisciplinary work and research using innovative methods and combinations of laboratory, clinical, and epidemiological methodologies and techniques is of great interest to the journal. Several categories of manuscripts (for detailed description see below) are considered: editorials, original articles (also including randomized clinical trials, systematic reviews and meta-analyses), reviews (narrative reviews), opinion articles (including debates, perspectives and commentaries); and letters to the Editor.

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THE JOURNAL OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

European Society for Clinical Investigation

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Objectives

The objectives of the Society are the advancement of medical practice through science; the cultivation of clinical research by the methods of the natural sciences; the correlation of science with the art of medical practice; the fostering of high standards of ethical practice and investigation; and the diffusion of a spirit of fraternity and international co-operation among and through its members.

Membership

Any person who has been actively involved in medical research in Europe, for example by involvement in original investigations in clinical or allied sciences of medicine, can apply for membership of ESCI. Members will receive the *EJCI* monthly. Any company, corporation, organisation, or trust can apply for corporate membership in the Society.

Meetings

The Society holds one Annual Scientific Meeting each year, usually in April/May. Meetings are held in different cities in Europe. Other Society's activities include the sponsorship of Workshops and Postgraduate Courses and the encouragement of the exchange of Scientists between Laboratories.

Contact information ESCI

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effect of myocardial infarction on the contractility of the isolated rat heart at different stages of MI.

Materials and Methods: The experiments were performed ex vivo on isolated hearts of intact and rats with a model of MI after 1 day, 54 days and 120 days after the simulation. MI was performed according to the classical technique - ligation of the anterior branch of the left coronary artery. The contractile activity was studied on the Langendorff System. The data were statistically processed using Student's t-test.

Results: A comparative analysis of the effect of MI on the initial values of contraction force in the studied groups revealed that in rats the contraction force decreased one day after MI and tended to increase 54 and 120 days after the simulation of MI.

Conclusions: Thus, it was shown that at different stages of the postinfarction period, multidirectional changes of the isolated rat heart myocardium contractions force are observed. The study was supported by Russian Science Foundation (grant No. 21-15-00121, https://rscf.ru/project/21-15-00121/)

56ASM-0102 | Effect of HCN channel blocker in the regulation of chronotropic effects in rats with limited motor activity

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Background: In the modern world, limitation of motor activity is an acute problem, because there are many reasons leading to this way of life. Hypokinesia causes atrophy of the musculoskeletal system, complicates the digestive, respiratory and cardiovascular systems. The involvement of HCN channels in the mechanism of heart rhythm acceleration has been shown. It is interesting to see the effect of blockade of If-currents and their role in the regulation of chronotropy of the heart against the background of increased heart rate (HR) in response to hypokinesia.

Materials and Methods: The experiments were conducted on two groups of rats: 1- control group, rats 7 weeks old; 2 - experimental group, rats with restriction of motor activity for 30 days. This effect was achieved by placing 3-week-old rats in penal cages under conditions of increasing hypokinesia. The effect of If blocker ZD7288 (10^{-9}M and 10^{-6}M) on chronotropic effects was studied using Langendorff PowerLab8/35 (ADInstruments, Australia).

Results: After the introduction into the perfused solution ZD7288 (10^{-9}M), a decrease in heart rate by 15% was observed in control rats ($p < 0.01$) and by 11% ($p < 0.05$) in the experimental group. The blocker If in concentrations 10^{-6}M decreased heart rate in the control group by 28% ($p < 0.01$) and by 17% in experimental group.

Conclusions: If-current blocker ZD7288 at all concentrations caused a decrease in heart rate in control rats and rats, with limitation of motor activity. However, more pronounced changes in heart rate were observed in the control group of rats and after application of the maximum concentration. It is possible that in rats with limited motor activity, against the background of an increase in heart rate, the density of HCN channels decreases compensatory, which leads to decrease their role in the regulation of heart rate. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030)

56ASM-0103 | Isolated rat heart after restriction of motor activity and recovery

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Background: Restriction of motor activity becomes a medical and social problem. Restriction of muscle activity leads to violations of all organ systems of the human body. Namely, in the cardiovascular system, prolonged restriction of motor activity leads to coronary vessels, the heart muscle weakening, decreasing of the heart energy potential and minute volume. The aim of our study was to study possible age-related changes in the parameters of the isolated rat heart after hypokinesia and subsequent recovery.

Materials and Methods: Restriction of motor activity was carried out by placing animals in pencil cases in conditions of increasing hypokinesia for 30 days. The recovery stage after hypokinesia for 14 days was carried out in order to study the mechanisms of adaptation of the animal to changes in the motor regime. The following parameters of the isolated heart were recorded - the pressure developed in the left ventricle (LVL), heart rate (HR) and coronary flow (CP) on the Langendorff PowerLab 8/35 unit (ADInstruments, Australia). Statistical processing was carried out in Excel, the reliability was determined using the Student's t-test.

Results: After hypokinesia, unidirectional changes in the parameters of the isolated heart were observed in 7-week-old and adult rats: a decrease in the parameters of the LVL, CP and an increase in heart rate. However,

during readaptation after hypokinesia, adult rats reacted with a tendency to restore LVL, CP and a complete restoration of heart rate values. The recovery period in rat pups led to a decrease in the parameters of LVL (29%) and CP (23%) below the control values and a decrease in heart rate parameters by 27% of heart rate ($p < 0.05$).

Conclusions: Thus, unlike adult animals, a recovery period of two weeks is insufficient for young developing rats. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).

56ASM-0104 | Nitric oxide effect on rat myocardial contractility during mobility restriction

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Background: Nitric oxide (NO) is a signaling molecule involved in the regulation of myocardial contractility. The action of many drugs used in cardiology is based on the release of NO, but the vascular and cardiac effects are not fully understood. Research on the role of NO in the body during motor activity limitation is of interest. There is evidence that prolonged limitation of mobility causes significant changes in the contractile function of the heart.

Materials and Methods: Experiments were carried out on random-bred albino rats. Restrictions of motor activity were achieved by placing rats in a small box: the first two days, the time of inactivity was 1 hour, and then increased by 2 hours every 2 days. By day 25, the time spent by animals in the cage-cases reached 23 hours. We determined the response of ventricular myocardial contractile function to the action of SNP (SNP at a dose of 10-6M) and against the background of L-NAME at a dose of 10 mg/kg. The contractile activity of myocardium was examined in vitro in a PowerLab setup equipped with a MLT 050/D Force Transducer (ADInstruments). We calculated the response of contraction force in response to pharmacological agents as a percentage of the initial force (100%). Experiments were performed in accordance with the regulatory guidelines for the treatment of laboratory animals.

Results: Under the action of SNP there was an increase in ventricular myocardial striatal contraction force by 23% ($p < 0.05$). Against the background of the action of L-NAME ventricular myocardial stripe contractile force with the addition of SNP increased by 55% compared with the baseline ($p < 0.05$).

Conclusions: The positive effect of SNP is increased 2.5-fold in rats growing under mobility restriction against the background of non-selective NO synthase blockade. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).

56ASM-0105 | In vivo ultrasonographic evaluation of skeletal muscle and cardiac function and structure in animal models of neuromuscular disorders: a new approach to improve preclinical translational research

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Background: Neuromuscular disorders induce structural and functional muscle changes relevant for diagnosis and disease progression. The absence, in many cases, of specific therapies makes it necessary to improve predictability of pre-clinical studies also regarding methodology. Ultrasonography is a useful method for assessing quantitative changes in human muscle such as muscle size and presence of fat or fibrous tissue infiltrations through echodensity measures. Today, it is possible to apply ultrasound in preclinical settings obtaining more predictive data to translate in patients. We recently set up an ultrasonographic technique for ultrasound acquisition suitable for rodent skeletal muscle and validated this new approach to assess disease progression and pharmacological efficacy.

Materials and Methods: Ultrasonography experiments were carried out using the Vevo2100 set up equipped with a probe working at 40 HMz (cardiac acquisitions) and a probe working at 21 MHz (diaphragm and hindlimb acquisitions).

Results: By ultrasound, we showed that the treatment with growth hormone secretagogues prevent the FDL muscle loss occurring in a rat model of cisplatin induced cachexia. Subsequently, we showed that the long-term treatment with taurine of mdx mice, a model of Duchenne Muscular Dystrophy, exerted a protective action improving the left ventricular function as demonstrated by the restoration of ejection fraction, shortening fraction, and stroke volume values.

In mdx mice, the morphological and functional properties of diaphragm muscle were investigated showing a significant decrease in diaphragm contractile amplitude and a significant increase in mean pixel echodensity as an index of fibrosis.