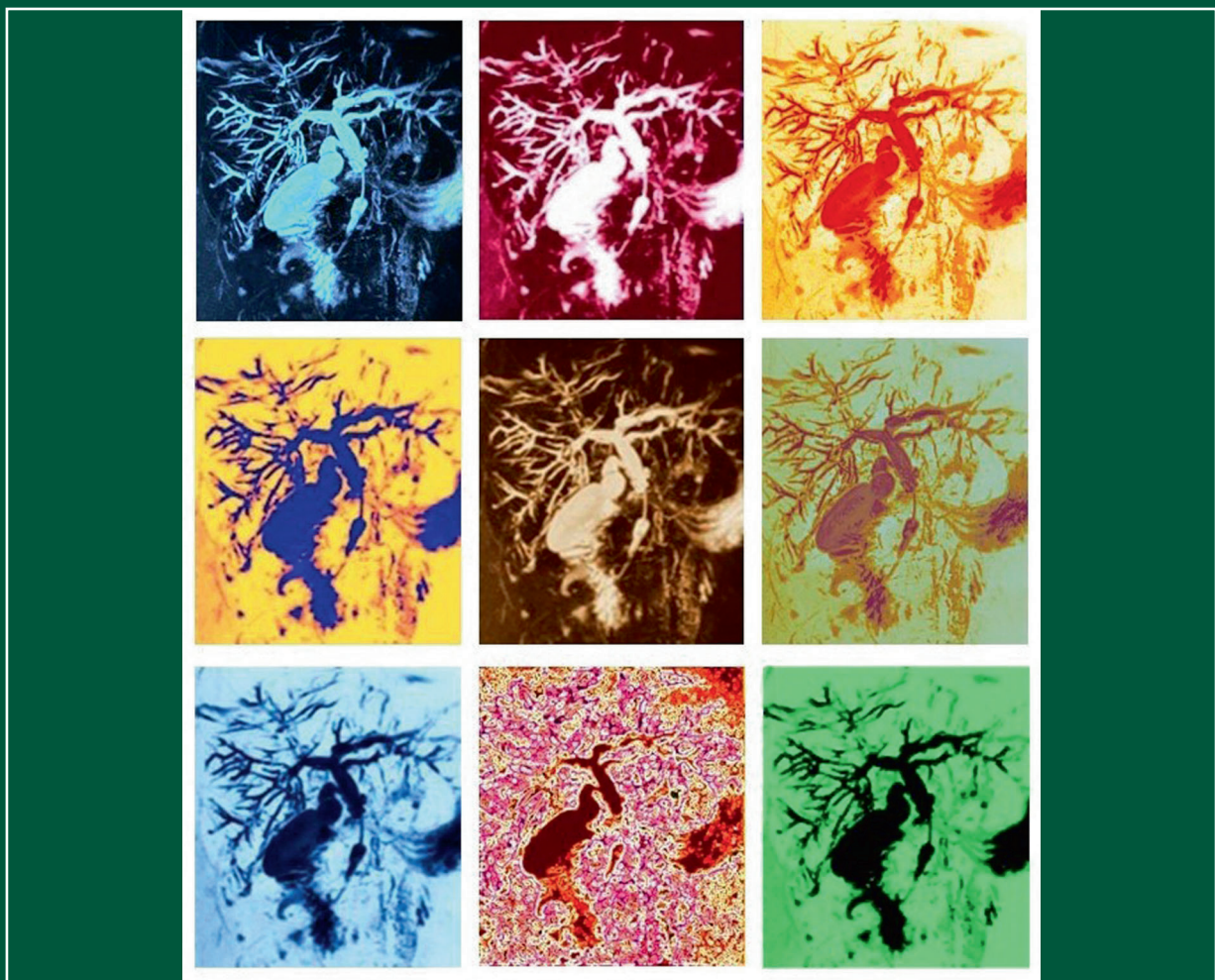


# European Journal of Clinical Investigation

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

# European Journal of Clinical Investigation

THE JOURNAL OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

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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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# European Journal of Clinical Investigation

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protein, blood cell count, neutrophils and as well as their related activation biomarkers: myeloperoxidase, matrix metalloproteinase (MMP)-8 and MMP-9. Over time median level of both OPN and resistin peak at cycle two and then dropped down until the last cycle. Survival analysis revealed a significant predictive ability toward OS for early OPN assay (HR at baseline 3.125 with a 95% CI of 1.41 to 6.94) and resistin (HR at second cycle 2.85 with a 95% CI of 1.22 to 6.67).

**Conclusions:** Our data indicate for the early assessment of both OPN and resistin a potential role in the outcome of NSCLC treated with nivolumab. Although unpowered and lacking a clear pathophysiological explanation, these preliminary findings call the attention toward the innate immune activation in NSCLC, potentially linked with metabolic profile.

#### 56ASM-0011 | Influence of clonidine hydrochloride on the effect of If blockade on isolated rat heart

T. Zefirov; A. Kuptsova; I. Khabibrakhmanov; R. Bugrov; M. Sungatullina; N. Ziyatdinova.

*Kazan Federal University, Department of Human Health Protection, Kazan, Russia C.I.S.*

**Background:** Sympathetic control of heart rate plays an important role in the pathophysiology of arrhythmias, hypertension, coronary heart disease, and chronic heart failure. Alpha<sub>2</sub>-adrenergic receptors (α<sub>2</sub>-AR) and hyperpolarization-activated currents (If) are involved in the regulation of heart function. The aim of this study was to investigate the effect of clonidine hydrochloride after of preliminary blockade of If-currents on isolated by Langendorff rat heart.

**Materials and Methods:** Experiments were carried out ex vivo on isolated hearts of 3-week-old rats (n=14). This age is characterized by significant properties of the heart function associated with the formation of adrenergic innervation. During the experiment, an electrogram of the heart was recorded using atraumatic electrodes. Changes in heart rate (HR) and coronary flow (CF) were recorded after application of the If blocker ZD7288 (10<sup>-9</sup>mol/L and 10<sup>-5</sup>mol/L) and the α<sub>2</sub>-AR agonist clonidine hydrochloride (10<sup>-6</sup>mol/L). The data were statistically processed using Student's t-test.

**Results:** Stimulation of α<sub>2</sub>-AR by clonidine hydrochloride after If blockade by ZD7288 (10<sup>-9</sup>mol/L) in isolated heart of 3-week-old rats increased the HR decline by 20% (*p* < 0.01) and increased CF by 15% (*p* < 0.01). ZD7288

in concentration 10<sup>-5</sup> mol/L decrease the effect of bradycardia after the application of clonidine hydrochloride by 12% (*p* < 0.01).

**Conclusions:** Thus, in experiments to studying the role of α<sub>2</sub>-AR and If in regulation 3-week-old rats isolated heart was shown that preliminary If blockade enhanced the bradycardic effect and increased blood supply in the isolated heart. The study was supported by Russian Science Foundation (grant No. 21-15-00121, <https://rscf.ru/project/21-15-00121/>)

**Study group:** A. Kuptsova, I. Khabibrakhmanov, R. Bugrov, M. Sungatullina, N. Ziyatdinova

#### 56ASM-0012 | Isolated rat heart function after new cardioplegic solution perfusion

T. Zefirov; R. Kobzarev; I. Khabibrakhmanov; A. Kuptsova; N. Ziyatdinova.

*Kazan Federal University, Department of Human Health Protection, Kazan, Russia C.I.S.*

**Background:** Cardioplegic heart failure is the most popular method of providing open-heart surgery. Negative changes of ischemia and reperfusion are reduced by quality cardioplegic protection. There is no consensus what types of cardioplegic solutions (CPS) is better. Unfortunately, studies of various cardioplegic solutions are carried out on different experimental models, which makes difficult comparison them with each other. The aim of our study was to evaluate the efficacy of created in Kazan Federal University new extracellular crystalloid CPS in the experiments on isolated rat heart model.

**Materials and Methods:** Isolated hearts were perfused on a Langendorff apparatus (ADInstruments) with an oxygenated Krebs-Henseleit solution (KH) (37°C, pH = 7.3-7.4) at a constant pressure of 80-82 mmHg. After stabilization of the heart activity, the initial values were recorded. The work was performed according to the following protocol: new solution was administered for 3 minutes, then ischemia was prolonged for 20 minutes, then the heart perfusion was resumed with KH solution. The heart rate was recorded during 40 minutes of reperfusion. The assessment of the contractility of the myocardium was carried out according to the indicator of left ventricular developed pressure (LVDP). The signals were recorded on the PowerLab 8/35 setup using the "LabChart Pro" program. Statistical processing of the obtained results was carried out using the Student's t-test.

**Results:** Asystole was achieved within 1 minute of CPS administration. Recovery of spontaneous cardiac activity after myocardial ischemia induced by the new CPS occurred within the first minute of reperfusion in 100%



cases. Decrease in myocardial contractility compared to the initial values was not observed during the entire reperfusion period (LVDP<sub>initial</sub> = 52±5.2 mmHg and LVDP<sub>reperfusion</sub> = 58±5.8 mmHg), what allows us to conclude about the effectiveness of myocardial protection by the new CPS.

**Conclusions:** In our experiment on a model of an isolated rat heart, which is widely used for the study of various CPR, we showed that the new solution is able to quickly and effectively cause myocardial plegia, and also does not interfere with the rapid and full recovery of its function after the start of reperfusion. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030)

### 56ASM-0099 | The effect of $\alpha_2$ -adrenoreceptors on the isolated rats heart contractility with a model of myocardial infarction in the acute stage

L. Khisamieva; A. Kuptsova; R. Bugrov; N. Ziyatdinova; T. Zefirov  
Kazan Federal University, Department of Human Health Protection, Kazan, Russia C.I.S.

**Background:** Stimulation of  $\alpha_2$ -adrenergic receptors ( $\alpha_2$ -AR) has a direct cardioprotective effect. The researchers revealed an increase in the expression of  $\alpha_2$ -AR subtypes in rats with spontaneous hypertension, as well as the dysfunction of  $\alpha_2$ -AR and the inefficiency of signaling pathways associated with  $\alpha_2$ -AR. The aim of this study was to investigate the effect of  $\alpha_2$ -AR stimulation of the isolated heart contractility with a myocardial infarction (MI) model 24 hours after the influence.

**Materials and Methods:** Ex vivo experiments were performed on isolated hearts of intact rats ( $n = 7$ ) and rats with a model of MI ( $n = 10$ ) 24 hours after the operation. IM is reproduced by ligation of the anterior branch of the left coronary artery. Agonist  $\alpha_2$ -AR clonidine hydrochloride was used in concentration of  $10^{-9}$  Mol. The data were statistically processed using Student's t-test.

**Results:** A comparative analysis of  $\alpha_2$ -AR stimulation revealed that in intact rats, the agonist reduced contractility by 21% ( $p < 0.05$ ), and with the MI model, 24 hours after modeling, it increased by 38% ( $p < 0.01$ ).

**Conclusions:** Thus, in our experiments  $\alpha_2$ -AR stimulation revealed multidirectional effects on inotropy reaction of intact rats isolated heart and rats with the MI model. The study was supported by Russian Science Foundation (grant No. 21-15-00121, <https://rscf.ru/project/21-15-00121/>)

### 56ASM-0100 | If-currents are involved in heart contractility regulation of rats with acute myocardial infarction model

L. Khisamieva; R. Bugrov; A. Kuptsova; N. Ziyatdinova; T. Zefirov  
Kazan Federal University, Department of Human Health Protection, Kazan, Russia C.I.S.

**Background:** Many factors have been identified in the development of coronary heart disease, such as hypertension, diabetes, smoking and an increase in heart rate. "Funny currents" (If-currents) play a key role in the electrogenesis of cardiomyocytes. The density of If currents increase in atrial and ventricular myocytes in patients with heart failure. The aim of this study was to investigate the effect of the blockade If-currents on the contractility of isolated heart with a model of myocardial infarction (MI) 24 hours after experimental influence.

**Materials and Methods:** Ex vivo experiments were performed on Langendorff-isolated hearts of intact ( $n = 7$ ), sham-operated ( $n = 6$ ) rats and with a model of MI ( $n = 10$ ) 24 hours after experimental influence. IM is reproduced by ligation of the anterior branch of the left coronary artery. To block If currents, ZD7288 was used at a concentration of  $10^{-9}$  Mol. The data were statistically processed using Student's t-test.

**Results:** Blockade of If-current revealed that in intact rats group ZD7288 increased contractility by 47% ( $p < 0.05$ ), in sham-operated animals – by 23% ( $p < 0.01$ ), in the MI model 24 hours after the simulation increased by 20% ( $p < 0.01$ ).

**Conclusions:** Thus, our study showed that in the group of rats with a model of acute myocardial infarction, the effect of If on the contractility of the isolated heart decreases. The study was supported by Russian Science Foundation (grant No. 21-15-00121, <https://rscf.ru/project/21-15-00121/>)

### 56ASM-0101 | Analysis of rats myocardial contraction force at different stages of experimental infarction

L. Khisamieva; R. Bugrov; A. Kuptsova; N. Ziyatdinova; T. Zefirov  
Kazan Federal University, Department of Human Health Protection, Kazan, Russia C.I.S.

**Background:** The study of experimental models of myocardial infarction (MI) is necessary for the development of innovative methods of treatment of this disease. The aim of this study is to conduct a comparative analysis of the