Characteristics of Intercalated Discs Responsible for Histological Changes of the Left Ventricle in the Experiment Involving Mechanical Loading on 30-Day-Old White Rats

Anzor Gogiberidze1,*, Ramaz Khetsuriani1, Marina Pailodze1, Manana Arabuli1, Sopiko Kandelaki1, Magda Tortladze2, Lizi Khitiri3, Irma Jikia4

1Tbilisi State Medical University, 33 Vazha-Pshavela Ave, Tbilisi, Georgia
2Caucasus International University, 73 Chargali St, Tbilisi, Georgia
3David Tvildiani Medical University, 2/6 Ljubljana St, Tbilisi, Georgia
4Tbilisi State University, 1 Ilia Chavchavadze Ave, Tbilisi, Georgia

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ABSTRACT
In our own experiment, we studied microscopic changes in the anterior wall of the left ventricle of young, middle-aged, and old rats on the 30th day after exercising. Plasmorrhagia, edema, stasis, bruising, dystrophic-necrotic changes, and eventually atrophic and sclerotic changes with the proliferation of connective tissue, an expansion of fibroblasts, and collagen synthesis emerge against the backdrop of tissue hyperemia typical of general venous hyperemia. In contrast to the young rats, the middle-aged rats have more severe lesions, while the old rats exhibit lesser alterations than the first two age groups. Compared to the control, an immunohistochemical examination of Desmin expression indicated peculiar morphodynamics. Morphometric analysis revealed that the number of intercalated discs is stable in young rats compared to control groups, rises in middle-aged rats (24.17%), and decreases in older rats (23.67%) compared to control. The intercalated discs in all three cell types mostly undergo disintegration, fragmentation, and shortening with a decrease in size. Compared to older rats, the experiment shows that sustained physical strain initially triggers the onset of adaptive, compensatory hypertrophy processes in striated and smooth muscle tissues. The compensating mechanism is disrupted when there are morphological alterations like acute heart failure and myocardial infarction, risk factors for acute hyperemia, venous and capillary congestion, edema, hemorrhage, and dystrophic and necrotic changes with the destruction and reduction in the size of intercalated discs. These conditions also cause functional weakening, decreased myocardial contractility, and hypoxic damage and are risk factors for acute heart failure and myocardial infarction.

* Corresponding author: Anzor Gogiberidze
E-mail: Anzor.gogiberidze1993@gmail.com
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Introduction

Chronic heart failure and ischemic disease [1-4] are common causes with substantial risks of morbidity and death, based on the World Health Organization (WHO). Ischemic heart disease was identified in 126.5 million persons globally in 2017. 10.6 million new cases were reported in that same year and in 2019, mortality from ischemic heart disease constituted 16% of all deaths worldwide.

In ischemic heart disorders, the blood flow to the myocardium is disrupted, the heat pump’s function is altered, and as a result, the blood circulation to the entire body is diminished. This is due to the total or partial blockage of coronary arteries. The authors examined the distribution of Desmin in the myocardium after acute ischemia [5]. Desmin expression has been demonstrated to be reduced in an experiment with myocardial ischemia in white rats by a reduction in the affected discs [5-10]. It is crucial to create the model of this pathology in an experiment on laboratory animals to clarify the mechanisms and morphogenesis of ischemic disease and assess cellular proteins [5]. Age-related features of mechanical loading in white rats at 30 days: Histology and morphodynamic changes of Desmin expression in discs filed in the anterior wall of the left ventricle.

Materials and Methods

Twenty-one white rats, ranging in age from young to old. Among them: In the control group, there are 9 cases (3 young, 3 middle-aged, and 3 old age rats). Twelve rats (six young, three middle-aged, and three old) were used in the experiment. Animal experiments complied with the bioethical guidelines outlined in The World Medical Association (WMA) of Helsinki (2013) [4, 5, 11].

Method

(1) Hematoxylin and eosin - to identify cardiomyocyte histological alterations in the anterior wall of the left ventricle.

(2) Masson's trichrome - to assess the fibrosis degree

(3) An immunohistochemical study- to examine the molecular basis of pathological processes, utilizing an antibody (Desmin).

Results and Discussion

On the 30th day of the experiment, the young population under a microscope revealed the following: hemodynamic disturbances, acute dilatation and stasis of the venous and capillary networks, focal vascular wall damage, partially empty blood vessels, and destructive changes in the cardiomyocytes with loss of striation. Cardiomyocytes without nuclei and fiber fragmentation fields are focally marked and wavy cardiomyocytes in some areas (Figure 1).
**Figure 1:** On Day 30 of the experiment, a young rat. The anterior wall of the left ventricle. Hematoxylin and eosin. Leika 1000 Led. MC170HD. x 0.65

**Figure 2:** On Day 30 of the experiment, a young rat. The anterior wall of the left ventricle. Masson’s Trichrome. Leika 1000 Led. MC170HD. X

**Figure 3:** Young white rat, immunohistochemistry, expression of desmin in the left ventricular anterior wall. Photo 6. The experiment’s 30th day. Leica 1000 Led. x 0.65 Leica MC170HD
In preparations stained with Masson’s trichrome, stasis of shaped elements was seen in contrast to acute ischemia, blood vessel dilatation, blood fullness and stasis, and lumens devoid of blood, there is also light to moderate, relatively well-defined fibrosis around the blood vessel walls and between the cardiomyocytes (Figure 2). Desmin is often expressed in the discs that make up the anterior wall of the left ventricle in young rats. The number of intercalated discs is higher in the experiment compared to the control. Nevertheless, most of them are shown as fragmented, shorter structures, while the reduced expression of Desmin is revealed compared to the control (Figure 3). According to the morphometric analysis, the number of discs utilized for young rats in the experiment (22.50%) remained unchanged as the number used in the control population (22.33%) (Figure 4).

**Figure 4:** The average amount of intercalated discs in young control [6, 12, 13] and experimental [11, 14, 15] rats

**Figure 5:** The 30th day of the experiment, middle-aged rat. The anterior wall of the left ventricle. Hematoxylin and eosin. Leika 1000 Led. MC170HD. x 0.65

**Figure 6:** The 30th day of the experiment, middle-aged rat. The anterior wall of the left ventricle. Masson's Trichrome. Leika 1000 Led. MC170HD. x 0.65
On the 30th day of the experiment, a hemodynamic disturbance was observed microscopically in the anterior wall of the left ventricle in middle-aged rats. Damaged cardiomyocytes with loss of striation and wavy structure, marked perfusion of the venous and capillary network, enlargement and stasis of their lumens, and empty blood vessels in certain locations (Figure 5), perivascular and interstitial fibrosis is revealed (Figure 6).

In middle-aged rats, the anterior wall of the left ventricle normally shows a marked expression of desmin in the intercalated discs. In the experiment, the number of implicated discs is slightly more than in the control, and the majority of them are shown as fragmented, reduced structures. As a result, the expression of Desmin is less apparent compared to the control (Figure 7).

Figure 7: Middle-aged rats, left ventricular anterior wall. Immunohistochemistry, Desmin expression. Photo. 12. 30 days of the experiment. Leika 1000 Led. MC170HD. x 0.65

Figure 8: Average amount of intercalated discs in middle-aged control (green box) and experimental (red box) rats

Figure 9: On the 30th day of the experiment. An elderly rat. left ventricle. Hematoxylin and eosin. Leika 1000 Led. MC170HD. x 0.65
Middle-aged rats with increased expression in their cardiomyocytes (probable), nonetheless, the old-aged rats' the left ventricle exhibits uneven hemodynamic disturbances, uneven blood filling of the capillary and venous network, mild dilatation and stasis, light and focal dissociation, and fiber fragmentation on the experiment's 30th day, featureless fatty dystrophy (Figure 9). Uneven and mild fibrosis appears around blood arteries and between cardiomyocytes in preparations stained with Masson's trichrome (Figure 10). Desmin exhibits moderate expression in the affected disks in the anterior wall of the left ventricle of aged rats under normal circumstances, and focused expression 30 days after the experiment (Figure 11), according to immunohistochemical examination. In the experiment, the number of discs present in the cardiomyocytes of aged rats decreased proportion of affected discs (24.17%) compared to controls (22.67%) was rather low (Figure 8). In old-aged rats, the left ventricle exhibit uneven and mild fibrosis around blood arteries and between cardiomyocytes in preparations stained with Masson's trichrome (Figure 10). Desmin exhibits moderate expression in the affected disks in the anterior wall of the left ventricle of aged rats under normal circumstances, and focused expression 30 days after the experiment (Figure 11), according to immunohistochemical examination. In the experiment, the number of discs present in the cardiomyocytes of aged rats decreased

**Figure 10:** On the 30th day of the experiment. An elderly rat's left ventricle. Masson's Trichrome. Leika 1000 Led. MC170HD. x 0.65

**Figure 11:** Rats of great age. The anterior wall of the left ventricle. norm. Immunohistochemistry. Desmin expression; Photo 18. The experiment's thirty-day mark. Leika 1000 Led. MC170HD. x 0.65

In the experiment, the number of discs present in the cardiomyocytes of aged rats decreased proportion of affected discs (24.17%) compared to controls (22.67%) was rather low (Figure 8). In old-aged rats, the left ventricle exhibit uneven and mild fibrosis around blood arteries and between cardiomyocytes in preparations stained with Masson's trichrome (Figure 10). Desmin exhibits moderate expression in the affected disks in the anterior wall of the left ventricle of aged rats under normal circumstances, and focused expression 30 days after the experiment (Figure 11), according to immunohistochemical examination.
### Conclusion

1) The anterior and lateral walls of the left ventricle of the heart of young, middle, and old rats revealed: A. Hyperemia and congestion of the veins and capillaries, stasis, localized damage to the vascular walls, destructive alterations to the cardiomyocytes, focal fragmentation, wavy cardiomyocytes, and unevenly expressed mild fibrosis in the adventitia, between the cardiomyocytes, and surrounding blood vessels are all present in young rats.

2) In comparison to their young age, middle-aged rats exhibit pronounced hyperaemia, congestion of veins and capillaries, stasis, focal vascular wall damage, destructive changes in cardiomyocytes, fragmentation, undulation, micronecrosis, and pronounced fibrosis around the vascular walls and between cardiomyocytes.

3) Young rats in the experiment had the same number of intercalated discs as controls, middle-aged rats had a modest increase in the number of intercalated discs, and adult rats had fewer included discs than controls. Accordingly, we may presume that the destruction and reduction in the size of the discs involved in cardiomyocytes, along with a minimal expression of Desmin, constitute the damage to these discs rather than quantitative alterations.

4) This suggests that middle-aged rats, as opposed to young and old age groups, have the capacity for compensatory hypertrophy. Inertness is a defining characteristic of youth, and the decrease of engaged discs in adult rats shows a drop in compensatory function with advancing age.

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### Disclosure Statement

No potential conflict of interest was declared by the authors.

### Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the article and agreed to be responsible for all aspects of this work.

### Orcid

Anzor Gogiberidze
https://orcid.org/0000-0001-8722-192X

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