Autoregulatory Reactions of the Skeletal Muscle Arterioles to a Decrease in Arterial Pressure

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Internal radius, wall thickness, and blood flow rate are measured in rat *m. cremaster* arterioles of different orders of branching under normal and stepwise decreased arterial pressure. Two types of reactions to a 20% decrease in arterial pressure are observed: active autoregulatory reaction (42% vessels) and passive reaction (58%). It is shown that relative changes in the diameter of arterioles in autoregulatory and passive reactions depend on the relative thickness of arteriolar wall and becomes more pronounced as this parameter increases.

Key Words: *microvessels; skeletal muscle; circulatory autoregulation; smooth muscle cells*

Published data show that redistribution of blood flow is strongly determined by different reactivity of terminal arterioles. These differences depend on various factors, in particular, on vessel morphology [2]. *In vivo* morphometrical studies showed that the arteriolar bed in *m. cremaster* represents a heterogeneous population of vessels with different internal diameters and relative wall thickness (w/r) [1,11]. This heterogeneity is observed both within one vessel generation and between vessels of different orders of branching. It was demonstrated that the w/r parameter depends on the vessel anatomy and tonic contractions of smooth muscle cells (SMC) in the vascular wall. The higher w/r, the higher vascular tone. It is known that mechanical properties of the vascular wall playing an essential role in autoregulation [9] depend on the degree of SMC contraction [7]. Therefore, it was hypothesized that there is a relationship between autoregulatory reactions of blood vessels and their mechanical properties and structure characterized by w/r parameter. The aim of the present study was to evaluate the response of some skeletal muscle arterioles to a decrease in arterial pressure (AP) as a function of their structure and order of branching.

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MATERIALS AND METHODS

Experiments were carried out on 14 random-bred male rats (90-130 g) under Nembutal anesthesia (5 mg/100 g, intramuscularly in 0.9% NaCl). Reactions of 26 arterioles were assessed. Biomicroscopy of *m. cremaster* was performed as described previously [4] using an Orthoplan microscope (Ernst Leitz) with a 0.46/L20 long-focus condenser. Plain picture was observed using 2.5× and 6.3× objectives, while isolated microvessels were studies using SW 50× and SW 100× salt-water immersion objectives. External (D) and internal (d) diameters of arterioles were measured using an RZD-DO semiautomatic linear meter (Ernst Leitz). The absolute wall thickness (w) was calculated from the formula: $(D-d)/2$, while relative thickness was determined as w/r, where r is the internal radius of the vessel. The linear blood flow rate (v) in microvessels was assessed from the rate of erythrocyte movement using the method of microprismatic lattice and an MPV-Compact-Vel device (Ernst Leitz) [3] and recorded synchronously with AP measured in the right femoral artery. The volume blood flow (Q) in separate microvessels was calculated as $Q=\pi r^2 v$. The decrease in AP was modeled by partial occlusion of the abdominal aorta using a specially designed occluder. The values of AP thus measured are proportional and reflect changes in

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Fig. 1. Fragment of microcirculatory bed of rat *m. cremaster*. Biomicroscopy. Objective 6.3/0.20. Ocular 2.0. *A*: arterioles; *V*: venulae. Arrows indicate the direction of blood flow, numbers correspond to branching order.

pressure in microvessels of several orders of branching [5].

At the beginning of each experiment, the microcirculatory bed was photographed and mapped. After the baseline values for all studied parameters had been recorded (5 min), AP was decreased by 10-15 mm Hg and maintained at this level for 1.5-2 min for redetermination of all studied parameters. Each experiment consisted of 5-6 such steps, after which occlusion was removed. In order to characterize the reaction of an arteriole to AP decrease, a *Gc* parameter (closed loop gain) was calculated from the slope of the curve $\Delta Q=f(\Delta P, \%)$ using the following formula: $Gc=(\Delta Q/Q/\Delta P/P-1)$ [13]. Negative values indicate autoregulation, while positive values imply passive reaction to the AP drop. Branching order was determined as described elsewhere [15].

RESULTS

A fragment of microcirculatory bed of *m. cremaster* (low magnification) is shown in Fig. 1. The main afferent arteriole of the first order of branching (*1A*) gives rise to several arterioles (*2A*). Generally, 4-5 orders of branching were seen within the arteriolar part of the microcirculatory bed.

There are two main patterns of changes in *Gc* in response to AP decrease, which corresponds to autoregulatory and passive reactions (Fig. 2, *a*). In 42% vessels, after a moderate decrease in AP *Gc* was negative. Further decrease in AP was accompanied by progressive rise of *Gc*, which became positive at AP constituting 40-50% of the initial level. In 58% of cases, *Q* decreased more rapidly than AP, and *Gc* was positive throughout the entire AP range. Thus, active autoregulation was observed in less than half of the total number of the studied vessels. It should be noted that in 64% of cases different vascular reactions were simultaneously observed in the same preparation, suggesting that the development of autoregulatory response did not depend on external factors such as anesthesia and surgical trauma. No visible differences were noted between vessels with autoregulatory and passive reactions. The ability of vessels to actively preserve blood flow level is presumably associated with their functional state rather than with their anatomy. Different responses to changes in perfusion pressure within the same vascular bed were observed by others [10]; however, the question what factors determine the ability of blood vessels to actively maintain blood flow remains unanswered.

In our experiments, dilatation in response to a decrease in AP was noted in 27% and constriction in 73% of cases (Fig. 2, *b*). In order to compare the reactivity of studied arterioles, we determined the relative changes in their internal diameter (Δd, %) in response to a standard decrease in AP (by 20% of the initial level) using individual curves $\Delta d=f(\Delta P, \%)$ for each vessel. The points on the plot (Fig. 3) correspond to vessels with different initial w/r values, in which a 20% decrease of AP induced a change in the internal diameter by Δd.

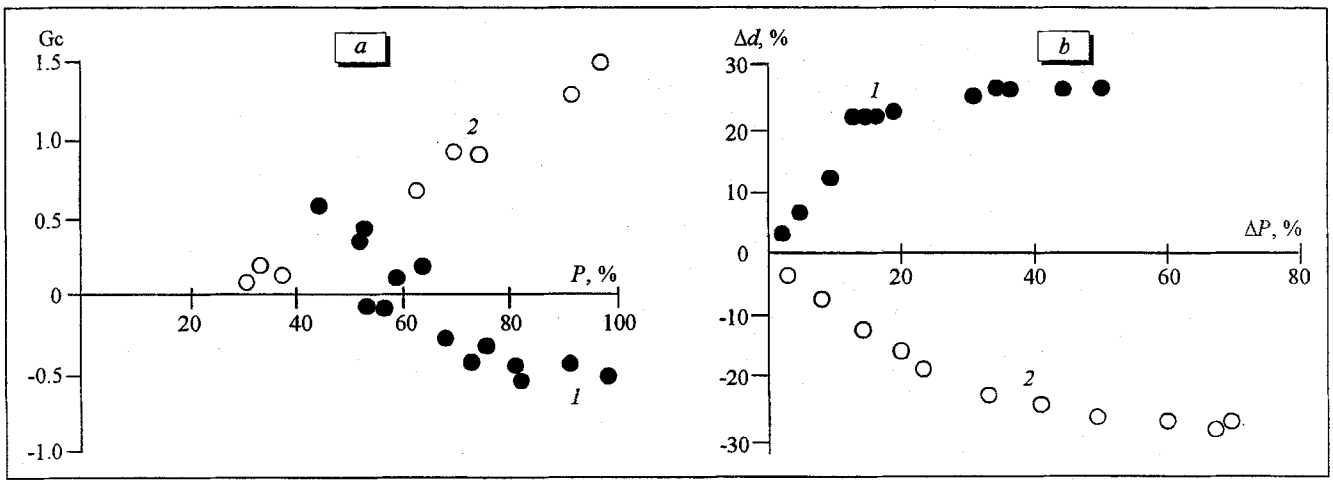

Fig. 2. Changes in *Gc* and diameter of actively and passively reacting arterioles to a decrease in arterial pressure (AP). *a*) *Gc* as a function of AP for autoregulated (*1*) and nonautoregulated (*2*) vessels; *b*) relative changes in internal diameter of arterioles (Δd, %) as a function of AP drop (ΔP, %) for actively (*1*) and passively (*2*) reacting vessels.

When considering Δd as a function of ΔP for nonautoregulated vessels, changes in the vessel diameter depend on w/r. Minimal constriction was observed in the most thin-walled vessels, it increased with the rise of w/r and attained the maximum in the most thick-walled vessels. The dependence between the degree of constriction and the initial w/r for nonautoregulated vessels is described by the following equation:

$$\Delta d=-30+28.56/(1+10^{(-2.21+4.47\ w/r)})$$

($r=0.81$, $p<0.001$).

Our findings suggest that vessel dilation in response to applied pressure depends on w/r and is maximally pronounced in relatively thick-walled vessels. It has been previously showed that the w/r ratio reflects the degree of tonic contraction of vascular SMC [1]. Moreover, mechanical properties of vascular wall depend on SMC activity. Within normal values of AP, vessels with activated SMC are characterized by higher dilatation capacity than atonic vessels [6]; therefore, standard shifts in AP induce greater dilatation in vessels with contracted SMC than in those with relaxed SMC.

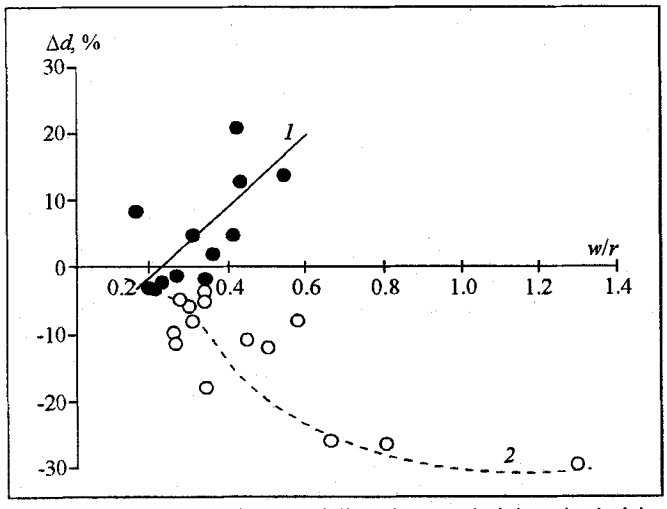

Fig. 3. Relationship between relative changes in internal arteriolar diameter (Δd, %) and initial thickness of the arteriolar wall w/r in response to a 20% decrease in arterial pressure. Autoregulated (*1*) and nonautoregulated (*2*) vessels.

The relationship between Δd and w/r in response to a 20% decrease in AP was also established for autoregulated vessels. Dilation of autoregulated vessels increases along with the increase in w/r and attains a maximum in the most thick-walled vessels. This relationships is described by linear regression equation $\Delta d=-13.1+51.6\ w/r$ ($r=0.62$, $p<0.05$). These findings can be explained from the viewpoint of the miogenic autoregulation theory [8]. Indeed, if changes in the length of SMC or circulatory tension of the vascular wall ($T=P\times r$) are directly responsible for the autoregulatory reaction [14], the most pronounced reaction should be expected in vessels where these parameters are maximally changed. Our findings agree with previous reports. For instance, Morff and Granger [12] showed that relative changes in the internal diameter in autoregulation are most pronounced in arterioles of high branching orders characterized by higher w/r values.

Thus, our findings suggest that the magnitude of both autoregulatory and passive reactions to a decrease in AP depends on w/r of individual arterioles and increases along with the increase of this parameter. On the other hand, the ability to preserve blood flow under conditions of decreased AP does not depend on this parameter.

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