THE OXYGEN CONSUMPTION RATE OF ARTERIOLAR WALLS UNDER PHYSIOLOGICAL CONDITIONS

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Abstract: To examine the large drop of partial oxygen pressure (PO_2) in arterioles, the O_2 consumption rates of arteriolar walls were determined under physiological conditions. A phosphorescence quenching technique was used to quantify the intra- and perivascular PO_2 values in rat cremaster arterioles. Using the measured PO_2 values, and a theoretical model, the O_2 consumption rates of the arteriolar walls were then estimated. We found that the O_2 consumption rate of arterioles was 100 times greater than that seen in *in vitro* experiments, and the O_2 consumption rate under normal conditions was significantly higher than that during vasodilation. Furthermore, the O_2 consumption rate was the highest in the upstream arterioles. These findings suggest that the high O_2 consumption rates of arteriolar walls depend on the workload of the smooth muscle.

Keywords: oxygen consumption, oxygen transport, vascular wall, arterioles, skeletal muscle

Introduction

For nearly 100 years, the capillaries were believed to be the sole source of O_2 supply to the surrounding tissue [1]. However, since a significant downstream drop in arteriolar PO_2 was found, the existence of an O_2 supply to surrounding tissue through the arteriolar walls has been suggested [2]. On the other hand, analysis of the diffusion process based on arteriolar PO_2 drops has shown that the O_2 diffusivity in the vessel wall was much greater than the free diffusion constant; thus, such a large O_2 loss from arterioles seemed unlikely to be solely attributable to simple diffusion [3].

The arterioles possess an intrinsic regulatory mechanism that, when skeletal muscle is in a resting state, modulates vessel diameter and adjusts muscle perfusion to the minimum level required to maintain metabolism by contracting the smooth muscle in the vessel wall. Many studies have measured the O_2 consumption rate of endothelial cells and smooth muscle cells in suspension and of isolated vascular segments *in vitro* [4]. However, most of these studies were conducted in the absence of normal function; no reports have been made on the O_2 consumption rates of arteriolar walls with regard to their physiological state.

The objective of the present study was to quantify the O_2 consumption rate in the arteriolar wall and clarify its impact on the drop of PO_2 in the arterioles. To do so, we used phosphorescence quenching laser microscopy to determine the intra- and perivascular PO_2 values of rat cremaster arterioles of several different diameters, both under normal conditions and during vasodilation. Using the measured intra- and perivascular PO_2 values, we then calculated the O_2 consumption rate of the arteriolar wall.

Materials and methods

Animal preparation. Male Wistar rats (160-200 g) were anesthetized with urethane intra- muscularly. The cremaster muscle was spread out in a special bath chamber with an optical port for transillumination, and its surface was suffused with a 37˚C Krebs solution. After a 30-minute equilibration period, the suffusion was stopped and a cover slip was placed on the muscle to prevent dehydration and hyperoxia..

Experimental protocols. The intra- and perivascular PO_2 measurements were performed on arterioles of different sizes. Large arterioles with a diameter of 80-120 μm branching from the central cremasteric artery were designated as first order (1A). Branches in 1A arterioles were designated as second order (2A, 50–80 μm in diameter). Third order arterioles (3A) had a diameter of less than 60 μm and branched from 2A arterioles. The intravascular PO_2 measurements were carried out 30 minutes after the injection of a Pd-porphyrin solution into the cannulated jugular vein. The perivascular PO_2 measurements were then performed in the vicinity of the vascular walls of the same arterioles. After the PO_2 measurements of each order of arterioles had been made under normal conditions, papaverine (10^{-4}mol/L) was topically applied to the muscle surface to maintain vasodilation at a maximum. Under this condition, the PO_2 measurements were once again performed at the same sites measured under normal conditions.

PO_2 measurements. A general observation of the microcirculation was performed using a modified Nikon microscope with a 20x objective lens (Fig. 1). The intra- and periarteriolar PO_2 values were measured using O_2-dependent phosphorescence

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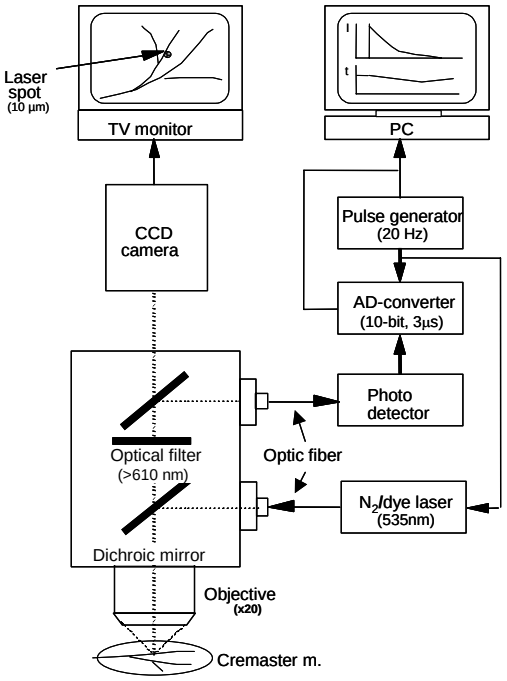


Figure 1: Arrangement of the intravital laser microscope using O_2-dependent phosphorescence quenching technique.

quenching technique [5] based on Stern-Volmer equation. Pd-meso-tetra (4-carboxyphenyl) porphyrin (Pd-porphyrin) bound to bovine serum albumin was used as the phosphorescent probe. The phosphorescent probe was excited by epi-illumination using an N_2/dye pulse laser with a 535 nm line at 20 Hz via the objective lens. The area of the epi-illuminated tissue was 10 μm in diameter. The phosphorescent emissions were captured by a photomultiplier through a long-pass filter at 610 nm. Signals from the photomultiplier were converted to 10-bit digital signals at intervals of 3 μs. The mean of ten decay curves was calculated and the decay of the phosphorescence was mathematically fitted to monoexponential curve. The typical example of digitized phosphorescence decay curve measured in the interstitial space of rat cremaster muscle is shown in Fig. 2.

Estimation of O_2 consumption. The basic model used in this study to estimate the O_2 consumption rate of the arteriolar wall was shown in Fig. 3. The Krogh Cylinder Model of the capillary-tissue system for O_2 delivery in skeletal muscles was modified to suit the arteriolar vascular wall [6]. The O_2 consumption rate per tissue volume per unit time in the arteriolar wall (QO_2) was expressed by the following modified Krogh-Erlang equation:

$$QO_2=(P_{in}-P_{peri})(4\alpha_t D_t)/[2R_o^2 \ln(R_o/R_i)-(R_o^2-R_i^2)],$$

where P_{peri} and P_{in} represent the PO_2 values of the outer surface on the arteriolar wall and within the arteriole, respectively. α_t and D_t represent O_2 solubility and O_2 diffusivity in the arteriolar wall, respectively. R_o and R_i represent the outer and inner radii of the arterioles, respectively. The O_2 consumption rate of the arteriolar wall was determined by utilizing the measured intra and perivascular PO_2 values of the arterioles.

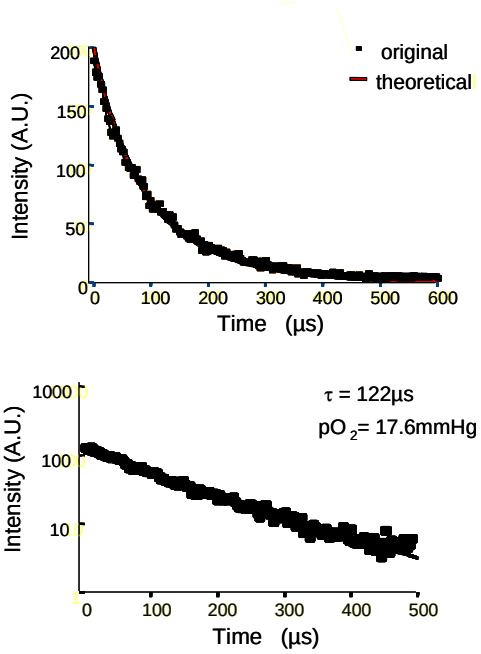
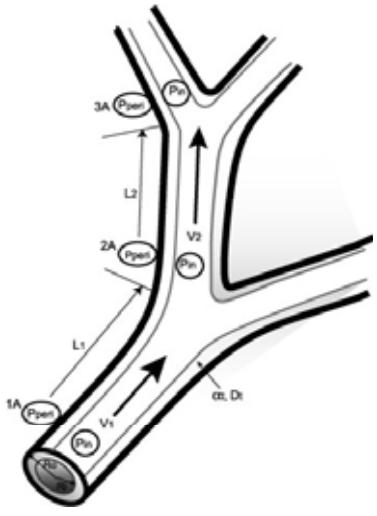


Figure 2: The typical example of digitized phosphorescence decay curve measured in the interstitial space of rat cremaster muscle.



The parameters used for estimating O_2 consumption rates

		1A	2A	3A
Inner radius of arteriole	(R_i: μm)	50	40	30
Outer radius of arteriole	(R_o: μm)	60	48	36
O_2 diffusivity in the arteriolar wall	(D_t: cm^2/s)	1.5×10^{-5}		
O_2 solubility in the arteriolar wall	(α_t: ml/g/Torr)	3.0×10^{-5}		

Figure 3: Schematic interpretation of the arteriolar model used to estimate oxygen consumption rate of vascular walls.

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Results

Systemic arterial PO_2, PCO_2, and pH were measured using a blood analysis system in samples from the carotid arteries after performing PO_2 measurements. The arterial PO_2 averaged 97.8 ± 10.5 mmHg, while the arterial PCO_2 and pH averaged 46.1 ± 8.2 mmHg and 7.31 ± 0.05, respectively. The diameters of the 1A, 2A, and 3A arterioles, before and after the application of papaverine, were 102 ± 16 vs. 119 ± 14 μm, 81 ± 12 vs. 95 ± 13 μm, and 45 ± 14 vs. 52 ± 14 μm, respectively.

The intra- and perivascular PO_2 values of the 1A, 2A, and 3A arterioles under normal conditions and during the papaverine-induced vasodilation are shown in Fig. 4. The intravascular PO_2 values of the 1A arterioles in both conditions were lower than the systemic arterial PO_2 level. The intravascular PO_2 values of the arterioles under normal conditions decreased significantly along the vessel from 1A to 3A, and the perivascular PO_2 values of the different arteriole orders were also significantly lower than the intravascular PO_2 values. During vasodilation, all the PO_2 values of the intra- and periarterioles were significantly higher than the PO_2 values under normal conditions, possibly because of the increased regional blood flow, but the longitudinal and radial rates of decrease were lower than those under normal conditions. Figure 5 shows the estimated O_2 consumption rates in 1A, 2A, and 3A arteriolar walls under normal conditions and during vasodilation using the intra- and perivascular PO_2 data shown in Fig. 4. The O_2 consumption rate of the arteriolar walls under normal conditions was significantly higher than that during vasodilation, excluding the 3A arterioles. Under normal conditions, the O_2 consumption rate of the 1A arteriolar wall, located furthest upstream, was the highest, and the O_2 consumption rate sequentially decreased downstream in 2A and 3A arterioles. The workload of the arteriolar smooth muscle of 1A vessels is thought to be greater than that of the smooth muscles of 2A and 3A arterioles, since the intravascular pressure is highest in 1A arterioles. During papaverine-induced vasodilation, the O_2 consumption rates of the arteriolar walls in the 1A, 2A, and 3A vessels all decreased to approximately the same level. The estimated O_2 consumption rates of the arteriolar walls ranged from 1-2 × 10^{-2} under normal conditions to 7-8 × 10^{-3} ml/s/g during vasodilation. These levels are 100-1000 times higher than seen in *in vitro* experiments.

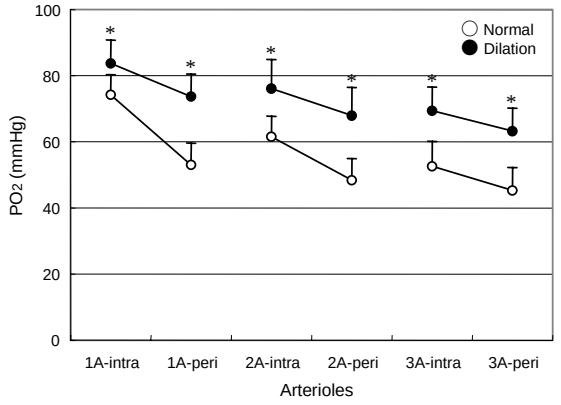

Figure 4: The intra- and perivascular PO_2 of 1A, 2A and 3A arterioles under normal conditions and during papaverine-induced vasodilation

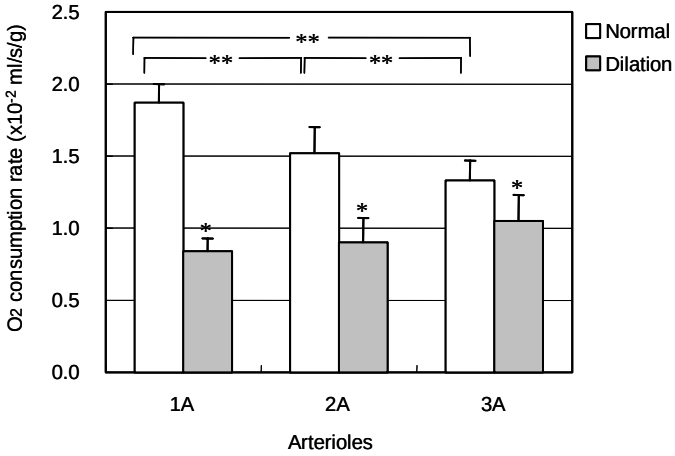

Figure 5: The oxygen consumption rates in the arteriolar walls under normal conditions and during vasodilation.

Discussion

The O_2 consumption rates of vascular walls of different order arterioles were quantitatively demonstrated at different levels of vascular tone in rat cremaster muscle. The principal finding of this study is that reducing vascular tone of arteriolar walls decreases the O_2 consumption rate of vascular walls. Our results also strongly support the previous findings that the arteriolar walls, under normal condition, consume a significant amount of O_2 as compared with the surrounding tissue. Furthermore, the present study demonstrated that the O_2 consumption rate is highest in the arteriolar wall of 1A vessels, located upstream, and sequentially decreases in a downstream direction in 2A and 3A vessels under normal condition. During vasodilation induced by papaverine, on the other hand, the O_2 consumption rates of the vascular walls all decrease to similar levels, suggesting that the high O_2 consumption rate of 1A arteriolar walls under normal conditions is likely dependent on the workload of vascular smooth muscle, rather than the endothelium.

Many studies have analyzed O_2 transport to tissues during exercise and under normal conditions using a theoretical model, but none these reports have taken O_2 consumption in the vessel wall itself into account. The O_2 consumption rates of skeletal muscle observed in such studies were 2-4 × 10^{-5} ml/s/g at resting state, while the O_2 consumption rate of the arteriolar walls obtained in the present study was 1–2 × 10^{-2} ml/s/g under normal condition. Assuming that the volume ratio of the arteriolar walls to the skeletal muscle tissue was 0.7%, the O_2 consumption rate of the arteriolar walls was approximately 500 times higher than that of the skeletal muscle tissue, resulting in the

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arteriolar walls consuming an amount of O_2 equivalent to, or greater than, that of the skeletal muscle tissue.

Conclusions

About 100 times more O_2 is consumed by functional arteriolar walls, compared with the vascular segments or vascular cell suspensions measured *in vitro* experiments, and the O_2 consumption rates of the arteriolar walls are significantly higher under normal condition than during vasodilation. The highest O_2 consumption rate of the 1A arteriolar walls under normal condition suggests the vascular O_2 consumption is dependent on the workload of vascular walls. These results strongly support the hypothesis that the arteriolar wall consumes a significant amount of O_2 as compared with the surrounding tissue. Furthermore, the reduction of vascular tone of arteriolar walls may facilitate an efficient supply of O_2 to the surrounding tissue.

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