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NITRIC OXIDE CONTRIBUTES TO RIGHT VENTRICULAR OXYGEN SUPPLY-DEMAND BALANCE IN CONSCIOUS DOGS EXPOSED TO HYPOXIA

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As arterial O_2 (PaO_2) is reduced during systemic hypoxia, right ventricular (RV) work and O_2 consumption (MVO_2) increase. Coronary blood flow increases, but the mechanism responsible for hypoxia-induced coronary vasodilation has not been delineated. To address this problem, right coronary (RC) blood flow and RV O_2 extraction were measured in nine conscious, instrumented dogs exposed to normobaric hypoxia. Catheters were implanted in the right ventricle for measuring pressure, in the ascending aorta for measuring arterial pressure and for sampling arterial blood, and in a RC vein. A flow transducer was placed around the RC artery. After recovery from surgery, the dogs were exposed to hypoxia in a chamber ventilated with N_2, and blood samples and hemodynamic data were collected as chamber O_2 was reduced progressively to 8-10 %. Following control measurements, the chamber was opened, and the dog was allowed to recover. N^{ω}-nitro-L-arginine (LNA) was then administered (35 mg/kg, via RV catheter) to inhibit nitric oxide (NO) production, and the hypoxia protocol was repeated. RC blood flow increased during hypoxia due to coronary vasodilation since RC conductance increased from 0.65 ± 0.05 to 1.32 ± 0.12 ml/min/100 g. LNA blunted the hypoxia-induced increase in RC conductance. RV O_2 extraction remained constant at 64 ± 4 % as PaO_2 was decreased, but after LNA, extraction increased to 70 ± 3 % during normoxia, and then to 78 ± 3% during hypoxia. RV MVO_2 increased during hypoxia, but after LNA, MVO_2 was lower at any respective PaO_2. To account for LNA-mediated decreases in RV MVO_2, O_2 demand/supply variables were plotted as functions of MVO_2. The slope of the conductance/MVO_2

relationship was depressed by LNA (P=0.03), whereas the slope of the extraction/MVO_2 relationship increased (P=0.003). In summary, increases in RV MVO_2 during hypoxia are met normally by increasing RC blood flow. When NO synthesis is blocked, the large RV O_2 extraction reserve is mobilized to maintain RV O_2 demand/supply balance. We conclude that NO contributes to RC vasodilation during systemic hypoxia, and, thus, NO is an important factor in maintaining right ventricular oxygen supply-demand balance under this condition. (This research was supported by U.S. National Institutes of Health grant HL-64785.)

NITRIC OXIDE CONTRIBUTES TO OXYGEN DEMAND – SUPPLY BALANCE IN HYPOPERFUSED RIGHT VENTRICLE

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The present study examined the role of nitric oxide (NO) in oxygen demand – supply balance in hypoperfused canine myocardium. The right coronary artery of anesthetized, open-chest dogs was perfused at pressures of 80, 60 and 40 mmHg, and right ventricular myocardial oxygen consumption, right coronary blood flow and other hemodynamic and cardiac function variables were measured. Right ventricular mechanical function was indexed as the product of heart rate X peak right ventricular systolic pressure X right ventricular dP/dt_{max}. NO synthesis blocker N^T–nitro-L-arginine methyl ester (L-NAME, 150 :g/min) was infused into the right coronary artery to block NO synthesis. Neither hypoperfusion nor L-NAME altered right ventricular function. Right ventricular myocardial oxygen consumption was significantly increased during L-NAME at right coronary perfusion pressure of 60 and 40 mmHg ($P < 0.05$ vs. untreated control condition). This increase in myocardial oxygen demand during coronary hypoperfusion was met by non-NO dependent vasodilation as reflected by a significant rise in right coronary blood flow during L-NAME ($P < 0.05$ vs. untreated control condition), but the relationship between oxygen consumption and flow became much steeper. Thus, NO improves right coronary conductance during hypoperfusion and also increases oxygen utilization efficiency. NO plays an important role in right ventricular oxygen demand – supply balance when oxygen delivery is restricted. (This research was supported by U.S. National Institutes of Health grant HL-64785.)