Title: **Validation of Xenon Clearance as a Measure of CBF**

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Xenon 133 isotope clearance has been used to determine cerebral blood flow (CBF) during cardiopulmonary bypass (CPB) in laboratory and clinical studies, but the Xe^{133} method has not been validated under these conditions. We tested the hypothesis that Xe clearance and Kety-Schmidt methods yield identical results during cardiopulmonary bypass.

Methods: Seven dogs were anesthetized with fentanyl (5 µg/kg bolus and 0.1 µg/kg-min) and midazolam (50 µg/kg bolus and 1 µg/kg-min) and mechanically ventilated to normocarbia. A saggital sinus catheter was placed via a burr hole in the posterior occiput. A second catheter was placed in the right innominate artery via the right brachial artery. A median sternotomy was performed, the animal heparinized (300 u/kg), and CPB (right atrium to proximal aorta) initiated, with CPB flow held constant at 1.7 L/min-m^2. Mean arterial pressure was maintained at 60 mmHg via phenylephrine or sodium nitroprusside infusion. Animals were randomly assigned to a brain temperature (27°C, 32°C, or 37°C) and arterial pCO_2 (30, 40, 50 or 60 mmHg) while keeping the base excess less than -5 using an alpha stat technique. During steady state temperature and arterial pCO_2, a single bolus of 3 miCu of Xe^{133} was injected into the aortic cannula and Xe clearance measured over 15 min via a cadmium-telluride (CdTe) detector placed on the skull in the temporal region. After this data was recorded, a constant infusion of Xe^{133} (15 miCu total dose in 15 min) was begun. Blood was constantly recirculated from the saggital sinus and right innominate artery cannulae by an infusion pump at identical (range 300-600 ml/hr) rates. The recirculated blood from each cannula passed over a CdTe detector, and radiation counted over a 3 s period for 15 min. Xe clearance was analyzed by a CBF-infinity technique. A Kety-Schmidt determination was computed as the area between the arterial and saggital sinus curves. In all cases, the calculated Xe concentration curves had r values of >0.90 as compared to raw data points. The values obtained from Xe clearance and Kety-Schmidt values during similar physiologic conditions were plotted and compared to a line of identity.

Results: The correlation between Xe clearance and Kety-Schmidt techniques was high (r^2=0.97). Linear regression analysis yielded a slope of 0.97 with an intercept of 2.0 (n=7, see figure). This was not significantly different from the line of identity.

Discussion: Xe clearance and Kety-Schmidt determinations of global CBF measurements yielded identical results, thus confirming our hypothesis. Therefore Xe clearance methodology, using low dose Xe^{133} injected intra-arterially, is accurate in determining CBF during cardiopulmonary bypass.

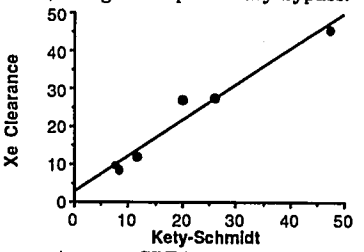

Figure: Axes are CBF in units of ml/min-100g

Title: High PO_2 Improves Flow and Function in Ischemic Myocardium

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Introduction: Although supplemental oxygen breathing is used to treat acute myocardial ischemia, evidence that this therapy is beneficial in absence of hypoxemia is lacking. To determine the effects of arterial hyperoxia on myocardial blood flow and function during acute low-flow ischemia, we used an acutely-instrumented swine model.

Methods: In 7 swine, anesthesia was induced with ketamine (10 mg/kg), then maintained with isoflurane, .7-.9%, and fentanyl (100 mcg/kg bolus and 20 mcg/kg/hr).Ventilation was controlled at FIO_2 = .21. Heart rate was held constant by atrial pacing. After heparinization, myocardial ischemia was induced by cannulating the left anterior descending (LAD) coronary artery, perfusing it with arterial blood and and reducing LAD pump flow to 48% of control values. Total LAD flow was thereafter held constant. In two subsequent, randomized measurement periods, the effects of arterial pO_2 on myocardial blood flow (microspheres) and systolic shortening (sonomicrometry) were measured by increasing FIO_2 to 1.0 (Period 1.0) or repeating measurements at FIO_2 = .21. (Period .21'). Results were analyzed by repeated-measures ANOVA, and the Newman-Keuls test, where appropriate.

Results: At high P_aO_2, LAD zone systolic shortening improved substantially. Endocardial blood flow increased by 25% and LAD zone I:O flow ratio improved. Mean arterial pressure and heart rate did not change significantly.

Table I: n=7 values = mean ± sd

FIO_2 Period:	.21, initial	.21'	1.0
PaO_2 (mmHg)	94.4 ± 6.6	90.4 ± 7.2	487.7 ± 83.1
SS (% control)	44.2 ± 7.8	43.2 ± 15.5	70.9 ± 17.0*
LAD Endo Flow (ml/g/min)	0.27 ± 0.06	0.26 ± 0.07	0.34 ± 0.10*
LAD I:O ratio	0.52 ± 0.17	0.47 ± 0.13	0.68 ± 0.22*
MAP (mmHg)	61.2± 10.2	55.5 ± 5.8	57.2 ± 9.2
Heart rate (bpm)	113.8 ± 9.6	116.0 ± 10.4	113.8 ± 9.1

* = different than values in periods .21 and .21', P <0.001.

Discussion: Although total ischemic zone coronary blood flow was held constant, coronary hyperoxia redistributed myocardial blood flow from the epicardium to the endocardium of the jeopardized zone. Oxygen-induced hemodynamic changes were minimal, suggesting that this flow redistribution was not caused by hemodynamic changes, but rather by metabolic autoregulation or direct vasoconstriction in the epimyocardium. The observed effects are not likely to be caused by increased collateral flow, as swine have minimal innate collateral flow. This is the first evidence to document that high pa_O2 improves both function and flow distribution in the ischemic myocardium.