A modified regionally ischemic porcine heart preparation with eligible residual blood flows

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Summary: The left anterior descending coronary artery was occluded in each of 28 thoracotomized pigs around an intracoronary catheter for periods between 30 and 240 min followed by 90 min of reperfusion. The catheter was connected via an external pump with another arterial catheter. The pump rate was set to deliver 1.5 ml (group I), 3 ml (group II), or 6 ml blood/min (group III) respectively during ischemia. The distribution of the residual blood flow during ischemia was determined in group II with non-radioactive microspheres. We delineated the risk region by a fluorescent dye and the infarcted tissue with a tetrazolium stain. The higher residual blood flow in groups II and III reduced the incidence of ventricular fibrillation during ischemia from 70% (group I) to 28%, suggesting that the amount of residual blood flow is one important determinant for this rhythm disturbance. The subendocardial-subepicardial blood flow ratio in the risk region of the anterior wall was 41%. Infarcts started to develop after 30 min of ischemia (groups I and II). In all groups necrosis progressed most rapidly within the first 90 min of ischemia indicating that besides the beneficial effect of a high residual blood flow only early reperfusion is able to salvage a substantial amount of jeopardized myocardium. Compared to conventional regionally ischemic canine and porcine heart preparations the described model offers the following advantages:

Accurate delineation of the risk region, eligible residual blood flow, reduction of ventricular fibrillation with higher residual blood flows, and the possibility to selectively test the metabolic influence of drugs on ischemic injury while avoiding systemic effects.

Key words: infarct size, pig, residual blood flow, ventricular fibrillation

Introduction

The most widely used animal model to study interventions to limit myocardial infarct size is the regionally ischemic canine heart which distinguishes itself by a relatively high subepicardial collateral blood flow. Although this preparation may imitate the clinical situation of a patient with chronic coronary artery disease it has the major disadvantage that its collateral blood flow varies largely from animal to animal rendering comparisons between a control and a treated group somewhat difficult (1). In the canine model transient occlusion of the left anterior descending coronary artery for 90 min results in infarct sizes ranging from 0 to 95% (2) if infarct sizes are expressed as infarcted tissue in percent of perfusion area. The best homogeneity of regional ischemia is found in those models which virtually lack collateral blood flow, e.g. the porcine heart (3, 4, 5). This model reflects the clinical condition of a patient with acute myocardial infarction who develops a ventricular aneurysm due to the lack of significant collaterals (6). Major drawbacks of this animal preparation are the rhythm instability and the inability to test pharmacological interventions during...
ischemia. To circumvent these disadvantages we developed a modified porcine heart model which disposes of different eligible residual blood flows. This preparation offers the chance to selectively test the metabolic effect of drugs on the ischemic injury at fixed residual blood flows. Furthermore this model may mimic the development of infarcts in patients with subtotal coronary artery stenoses.

**Methods**

*Premedication and anesthesia*

28 German farm pigs of either sex weighing between 43 and 54 kg were premedicated and anesthetized as described earlier (7) except for the neuromuscular blocking agent hexcarbachol bromide which sometimes induced malignant hyperthermia. In short, each was premedicated with intramuscular azaperon (7 mg/kg), metomidate hydrochloride (15 mg/kg), piritramide (15 mg), and atropine (0.5 mg intravenously). General anesthesia was maintained with the continuous infusion of metomidate hydrochloride (about 200 mg/h) and ventilation with nitrous oxide and oxygen by a Sulla 19 respirator (Dräger, W. Germany). Pancuronium bromide was used as neuromuscular blocking agent (about 8 mg/h intravenously).

*Experimental set-up*

A median thoracotomy was performed and the left anterior descending coronary artery (LAD) was prepared about 1 cm distal to the left atrial appendage. Before the first catheter was introduced a loading dose of 20,000 IU heparin followed by 5,000 IU/h was intravenously administered. A No. 6 F catheter was inserted through the left internal jugular vein via the coronary sinus into the ostium of the great cardiac vein under manual and visual control. Another No. 6 F catheter was introduced into the right atrium and connected with a Statham transducer for pressure recordings. Aortic pressure was measured with a fluid-filled catheter in the abdominal aorta with another Statham transducer. This catheter was inserted through a saphena artery. A No. 8 F Millar catheter-tipped manometer with lumen was placed into the left ventricle via the left carotid artery for measurements of left ventricular pressure and dp/dt. The lumen of this catheter was connected via the silicone tubing of a laboratory pump (LKB 2120 Varioperpex Bromma, Sweden) with a No. 4 F Lehman catheter (USCI). An external electromagnetic flow probe (CME cliniflow 601D Medical Electronics, Carolina) and a three way stop

![Fig. 1. Scheme of the extracorporeal bypass system. The direction of blood flow is indicated by the arrows.](image-url)