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Impact of different topical negative pressure levels on myocardial microvascular blood flow ☆

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Abstract

Background: We have previously shown that a myocardial topical negative pressure (TNP) of −50 mmHg significantly increases microvascular blood flow in the underlying myocardium in normal, ischemic, and reperfused porcine myocardium. The present study was designed to elucidate the effect of different TNP levels between −50 and −150 mmHg on microvascular flow in normal and ischemic myocardium.

Materials and methods: Seven pigs underwent median sternotomy. The microvascular blood flow in the myocardium was recorded, before and after the application of TNP, using laser Doppler velocimetry. Analyses were performed before left anterior descending artery (LAD) occlusion (normal myocardium) and after 20 min of LAD occlusion (ischemic myocardium).

Results: A TNP of −50 mmHg significantly increased microvascular blood flow in both normal (from 320.0±56.1 PU before TNP application to 435.7±65.5 PU after TNP application, P=.028) and ischemic myocardium (from 110.0±36.7 PU before TNP application to 194.3±56.2 PU after TNP application, P=.012). TNP between −75 and −150 mmHg showed no significant increase in microvascular blood flow in normal or ischemic myocardium.

Conclusions: Of pressures between −50 and −150 mmHg, a TNP of −50 mmHg seems to be the most effective negative pressure concerning significant increase in microvascular blood flow in both normal and ischemic myocardium.

Keywords: TNP; Microvascular blood flow; Ischemia; Revascularization

1. Introduction

Topical negative pressure (TNP) has been shown to facilitate the healing of chronic and problematic wounds [1,2] including diabetic wounds [3] and poststernotomy mediastinitis [4–7]. The physiological and molecular biological mechanisms by which TNP promotes wound healing are, to a large extent, unknown. However, one of the mechanisms by which TNP promotes wound healing is by stimulating wound edge blood flow, which has been shown in both peripheral [8] and skeletal muscle in sternotomy wounds [9]. TNP produces a mechanical stress and a

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pressure gradient across the tissue, which may cause a surge of blood to the area. Mechanical forces and increased blood flow are known to stimulate granulation tissue formation, that is, endothelial proliferation, capillary budding, and angiogenesis, or secondary new vessel formation [10–12].

The majority of patients who require intervention for coronary artery disease are adequately treated by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). However, a major reason for failure of these treatments is their dependency on luminal size and coronary outflow. Methods of stimulating myocardial neovascularization that are not dependent on vessel caliber therefore provide an important alternative treatment. Numerous studies have evaluated the efficacy of gene therapy in the treatment of ischemic heart disease for the restoration of myocardial function by stimulation of angiogenesis and collateral vessel formation [13–17].

TNP is known to stimulate blood flow in tissues [1], such as the skeletal muscle [9,18]. We have earlier shown that a TNP of −50 mmHg significantly increases microvascular blood flow in the underlying tissue, in both normal and ischemic myocardium [19]. No study has been performed to examine the effects of different negative pressure levels on microvascular blood flow in the myocardium. The aim of the study was to elucidate the optimal negative pressure level for the heart muscle that would induce maximal increase in myocardial microvascular blood flow. In this study, blood flow was measured using laser Doppler velocimetry in a porcine model. The effect of different TNPs, between −50 and −150 mmHg, on microvascular blood flow was investigated in the myocardium before and during occlusion of the left anterior descending artery (LAD) to imitate ischemic coronary disease.

2. Materials and methods

2.1. Experimental animals

A porcine model was used for the present study. Seven domestic Landrace pigs of both genders, with a mean body weight of 70 kg, were fasted overnight with free access to water. The Ethics Committee for Animal Research, Lund University, Sweden, approved the study. The investigation complied with the *Guide for the Care and Use of Laboratory Animals* as recommended by the U.S. National Institutes of Health and published by the National Academies Press (1996).

2.2. Anesthesia

All the animals were premedicated intramuscularly with ketamine (30 mg/kg) before they were brought into the laboratory. Before commencing surgery, sodium thiopental (5 mg/kg), atropine (0.02 mg/kg), and pancuronium (0.5 mg/kg) were given intravenously. Tracheotomy was performed with a Portex endotracheal tube (7.5 mm internal diameter, Medcompare, USA). A Servo ventilator (Siemens Elema 300A, Stockholm, Sweden) was used for mechanical ventilation throughout the experiment. The ventilator settings used were the following: minute volume=100 ml/kg, FiO_2=0.5, breathing frequency=16 breaths/min, and positive end expiratory pressure=5 cm H_2O.

Anesthesia and muscular paralysis were maintained by continuous intravenous infusion of Diprivan (propofol, AstraZeneca, Sweden) 8–10 mg/kg/h, Leptanal 0.15 mg/kg/h (fentanyl, Lilly, France), and Pavulon 0.6 mg/kg/h (pancuronium, Organon Teknika, Boxtel, the Netherlands).

2.3. Data acquisition

Mean arterial pressure, central venous pressure, body temperature, and ventilatory parameters were recorded throughout the experiments.

2.4. Surgical procedure

Surgery was performed through median sternotomy. After heparinization (400 IU/kg), a cardiopulmonary bypass (CPB) was installed with an arterial cannula (22 French, DLP Elongated One-Piece Arterial Cannula, Medtronic Inc., Minneapolis, MN, USA) in the distal ascending aorta and a venous cannula (32 French, MC2 Two-Stage Venous Cannula, Medtronic Inc.) inserted through the right atrium. Before cannulation of the heart, the cannulae were inserted through the thoracic wall to prevent air leakage during TNP application. CPB was conducted in normothermia. Ventricular fibrillation was subsequently induced in the heart. No aortic cross clamping was performed, and no cardioplegia was employed. The mean arterial pressure was maintained between 60 and 80 mmHg. A left ventricular vent (DLP Vent, Medtronic Inc.) was used to protect the left chamber from overloading. Pulmonary ventilation was applied at 4 l/min during the experiments.

CPB was used to facilitate the measurement of microvascular blood flow using laser Doppler velocimetry. Fibrillation of the heart minimizes the movement artifacts, while the physiological conditions are, to a large extent, conserved. Moreover, CPB prevents the risk of circulatory failure during LAD occlusion, thereby facilitating experimental analysis in the ischemic myocardium.

Microvascular blood flow was measured by laser Doppler velocimetry (Peri Flux System 5000, Perimed, Stockholm, Sweden), using a technique that quantifies the sum of the motion of the red blood cells in a specific volume, extensively applied in plastic surgery procedures [20]. In this method, a fiber-optic probe carries a beam of light. Light impinging on cells in motion undergoes a change in wavelength (Doppler shift), while light impinging on static objects remains unchanged. The magnitude and frequency distribution of the changes are directly related to the number and velocity of red blood cells. The information