Transmural Differences in Myocardial Function and Metabolism During Direct Left Ventricular to Coronary Artery Sourcing

Sandra de Zeeuw, PhD, Cornelius Borst, MD, PhD, Cees W. J. Verlaan, and Paul F. Gründeman, MD, PhD

Experimental Cardiology Laboratory, Heart Lung Center, University Medical Center Utrecht, Utrecht, the Netherlands

Background. **We investigated the hypothesis that in the absence of collateral circulation, a left ventricle-coronary artery (LV-CA) bypass will maintain normal LV wall function and metabolism transmurally, both at rest and during stress, when the left anterior descending coronary artery (LAD) is acutely occluded proximally.**

Methods. **In 18 anesthetized pigs (74 ± 7 kg, mean ± standard deviation), a covered stent was placed transmurally in the lateral wall of the beating LV and connected to the proximal LAD via an arterial graft. Subepicardial and subendocardial segmental shortening as well as interstitial lactate and glucose concentrations were measured regionally by sonomicrometry and microdialysis, respectively.**

Results. **When the LAD was occluded proximally, direct left ventricular sourcing decreased the net LAD flow to 64 ± 25% of the native flow (n = 18, all animals). In the subepicardium, systolic shortening (SS) decreased to 87 ± 18% of baseline (p = 0.124), with the appearance of minor postsystolic shortening (PSS), and minor changes in interstitial lactate and glucose levels. In the subendocardium, in contrast, SS decreased to 54 ± 20% (p = 0.001). Marked PSS concurred with a sixfold increase in lactate (p = 0.008), and a 65 ± 31% decrease in glucose (p = 0.003), indicating subendocardial anaerobic metabolism. Stress induced by infusion of dobutamine increased lactate and decreased glucose concentration in the subepicardium to subendocardial levels, indicating transmural anaerobic metabolism.**

Conclusions. **In the anesthetized pig, direct sourcing by a LV-CA bypass distal to an acute coronary occlusion resulted in a 36% decrease in net forward coronary flow, subendocardial anaerobic metabolism, and loss of subendocardial contractile function at rest. These adverse effects extended into the subepicardium when the heart was stressed.**

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Left ventricle-coronary artery (LV-CA) shunting as an alternative revascularization procedure has recently been restudied [1–5]. These experimental studies demonstrate that a net forward coronary flow between 46% and 70% of baseline flow was obtained [1, 6] which, in theory, may be just sufficient to prevent otherwise intractable angina [2]. The decline in myocardial function measured in those studies correlated well with the decline in net forward flow, suggesting perfusion-contraction matching [1, 6].

Without a valve in the LV-CA bypass, massive coronary backflow to the LV cavity occurs during diastole caused by the precipitous drop in LV pressure at the onset of diastole [1]. Subendocardial perfusion, as a result, is down to 40% of native perfusion, whereas subepicardial perfusion remains at least 60% of native perfusion [6]. Unexpectedly, a comparable degree of coronary flow reduction induced by coronary artery constriction causes adequate subepicardial perfusion at the expense of subendocardial perfusion [7, 8]. The resulting subendocardial increase in lactate and decrease in glucose is the hallmark of anaerobiosis [9–11].

The impact of a coronary artery stenosis on transmural myocardial blood flow cannot be translated unambiguously to changes in coronary blood supply by a LV-CA bypass because, in the former condition, coronary flow is predominantly diastolic [12], whereas in the latter condition, flow is predominantly systolic [1, 6]. In previous studies with LV-CA shunting [1, 6], neither transmural myocardial metabolism nor contractile function was determined. Therefore, we investigated subepicardial and subendocardial LV wall function and metabolism in the pig, both at rest and in stress condition, when coronary blood supply was maintained by a LV-CA bypass after the coronary artery was acutely occluded proximally.

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Address reprint requests to Dr Gründeman, Experimental Cardiology Laboratory, Heart Lung Center, University Medical Center Utrecht, Heidelberglaan 100, Room G02.523 3584, CX Utrecht, the Netherlands; e-mail: p.f.grundeman@hli.azu.nl.

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Abbreviations and Acronyms

EDL	= end diastolic segment length
Endo	= subendocardium
Epi	= subepicardium
ESL	= end systolic segment length
HR	= heart rate (beats per min)
ITA	= internal thoracic artery
LAD	= left anterior descending coronary artery
L min	= minimum segment length
LV-CA bypass	= left ventricle-coronary artery bypass
LV dP/dt max	= maximal rate of rise in left ventricular pressure (mm Hg/s)
LV dP/dt min	= maximal rate of fall in left ventricular pressure (mm Hg/s)
LVEDP	= left ventricular end diastolic pressure (mm Hg)
MAP	= mean arterial pressure (mm Hg)
PSS%	= postsystolic shortening (%)
RPP	= rate pressure product (mm Hg · beats per min)
SS%	= systolic shortening (%)

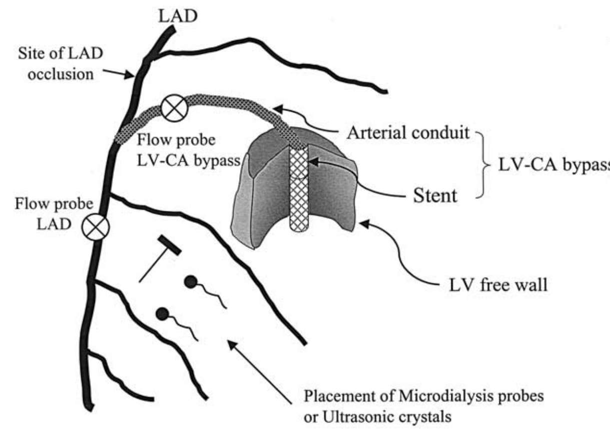

*Fig 1. Schematic presentation of the surgical procedure. First, a right internal thoracic artery (ITA) bypass to the distal left anterior descending (*LAD*) coronary artery was created to allow distal perfusion during the creation of the left ventricle-coronary artery (*LV-CA*) bypass. In this way the myocardial area of interest would be perfused at all times. The proximal LAD bypass had its origin in the LV lumen and consisted of a free left ITA graft (arterial conduit) with a polytetrafluoroethylene-covered stent at one end inserted through the LV wall. In this way direct left ventricular sourcing of the LAD was established. Blood flow was measured by placement of transonic flow probes (⊗) on the mid-LAD ($Q_{mid\text{-}LAD}$), and on the* LV-CA *bypass ($Q_{LV\text{-}CA\ bypass}$). To measure myocardial contractile performance, two pairs of ultrasonic echocrystals were embedded in the subendocardium and subepicardium. For measurement of myocardial metabolism, interstitial lactate and glucose concentrations were determined using microdialysis probes (⊤). During the protocol, the distal ITA-LAD bypass was closed and three different blood supply conditions were compared.*

Material and Methods

Animals

All experiments were performed in accordance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (revised 1996) and with prior approval by the Animal Experimentation Committee of the Faculty of Medicine, Utrecht University, The Netherlands. One day before the experiment, all animals received 560 mg of acetylsalicylic acid orally.

Anesthesia

After an overnight fast, Landrace pigs of either sex (74 ± 7 kg, n=18) were sedated with ketamine (10 mg/kg, intramuscular) and anesthetized with thiopental (4 mg/kg, intravenous [IV]) before they were intubated and connected to a respirator for intermittent positive pressure ventilation with a mixture of oxygen and air (1:1 vol/vol). A venous catheter was placed in the jugular vein for continuous administration of saline and anesthetic drugs. Anesthesia was maintained using 0.5% to 1.0% halothane and by continuous infusion of midazolam (0.3 mg/kg/h, IV), while analgesia was obtained by continuous infusion of sufentanylcitrate (1 μg/kg/h, IV) and muscle relaxation by infusion of pancuronium bromide (0.1 mg/kg/h, IV). To reduce the mechanical irritability of the heart during surgery, a bolus of propranolol was given (0.05 mg/kg, IV) prior to surgery.

Surgery

The surgical procedure has been described previously [13]. Briefly, the left anterior descending coronary artery (LAD) was suction stabilized as before [13] using one suction pod exclusively along the side of the right ventricle to prevent any influence of – 400 mm Hg suction on left ventricular performance. First, an auxiliary right internal thoracic artery (ITA) graft was anastomosed to the distal LAD. During proximal segmental LAD occlusion needed for the construction of the left ITA graft-proximal LAD anastomosis, the graft perfused the myocardium retrogradely thus preventing myocardial injury to the future area under study. For creation of a LV-CA bypass, a 4 to 5 cm segment of the left ITA was sutured end-to-end to a specially designed polytetrafluoroethylene covered stent (Percardia Inc, Merrimack, NH). After implantation of the stent [1], the left ITA conduit (free graft) was anastomosed to the proximal part of the LAD between the first and second diagonal branch (Fig 1). A snare was placed around the LAD proximal from the LV-CA bypass-LAD anastomosis for occlusion of the proximal LAD during direct blood supply from the LV. After the stent implantation, the temporary distal ITA graft was clamped during the further course of the experiment.

Instrumentation and Measurements

Transit time flow probes (Transonic Systems, Inc, Ithaca, NY) were placed around the mid-LAD and the LV-CA

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