ABNORMALITIES IN MYOCARDIAL
METABOLISM IN PATIENTS WITH UNSTABLE
ANGINA AS ASSESSED BY POSITRON
EMISSION TOMOGRAPHY

SUMMARY. Regional myocardial perfusion and glucose
metabolism were assessed in six normal volunteers and 29
patients with coronary heart disease and stable or unstable
angina using rubidium-82 (Rb-82) and F-18 fluoro 2-deoxy-
D-glucose (FDG) with positron emission tomography.

All normals and patients were studied following overnight
fasting, at rest, with no angina or electrocardiographic signs
of acute myocardial ischemia or necrosis. Rb-82 myocardial
cross-sectional images were obtained employing the con-
tinuous infusion technique, while dynamic FDG imaging
was employed after intravenous tracer bolus injection.
Regional Rb-82 and FDG myocardial concentrations were
then calculated by drawing regions of interest over the
interventricular septum, anterior and lateral wall of the
left ventricle.

The mean Rb-82 uptake for each left ventricular region
analyzed was found to be similar between both groups of
patients and normal volunteers. The mean myocardial
glucose utilization was found to be similar in normal volun-
teers and patients with stable angina (0.023 ± 0.032 vs. 0.012
± 0.008 μM/ml/min p<0.42). However, myocardial glucose
utilization was found to be significantly higher in patients
with unstable angina compared with both normals and
patients with stable angina (0.048 ± 0.047 μM/ml/min p<
0.001 for both comparisons). Thus, in patients with severe
coronary artery disease and unstable angina, myocardial
glucose utilization was enhanced in spite of the absence of
clinical, electrocardiographic, or detectable perfusion evi-
dence of acute ischemia.

KEY WORDS. myocardial metabolism, unstable angina,
glucose, deoxyglucose, coronary flow, positron emission
tomography

The impact of several episodes of transient reductions
in coronary blood flow on myocardial function and
metabolism is not clearly understood yet. Segmental
wall motion abnormalities are recognized to persist for
long periods of time after the ischemic episode is over
in both the clinical setting and experimental models of
reperfusion [1, 4].

Sustained regional low concentrations of ATP, im-
paired free fatty acid utilization, and increased ex-
ogenous glucose uptake were found after transient
ischemia in several animal models [5, 6]. Evidence of
abnormal myocardial metabolism, such as increased
glucose uptake and lactate production, was found in

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patients with coronary artery disease, employing in-
vasive techniques [7, 8]. Regional myocardial metabo-
lism can now be evaluated noninvasively with positron
emission tomography (PET). Recently, we reported
increased myocardial glucose utilization in the post-
ischemic myocardium of patients with exercise-in-
duced ischemia, as evaluated with this technique [9].
In the present study, we assessed noninvasively, re-
gional myocardial perfusion and metabolism in pa-
tients with coronary artery disease with stable or unst-
able angina, using rubidium-82 and F-18 fluoro2-
deoxy-D-glucose and PET.

Methods

Study Population

Six normal volunteers with an age ranging from 28 to
39 years and 29 patients with angiographically-proven
coronary artery disease were included in this study.
Normal volunteers had no history of symptoms, and
physical examination, electrocardiogram, and chest x-
rays were normal. Of the 29 patients with coronary ar-
tery disease seven had chronic stable angina. This
group of patients (six men and one woman) aged from
54 to 64 years, had a history of angina ranging from 2 to
15 years, and all had a positive exercise test with ST
depression > 0.1 mv. Multiple-vessel disease was pres-
ent in six and single-vessel disease in one. Global left
ventricular function was normal in six and mildly de-
pressed in one.

The remaining 22 patients had unstable angina
based on the following criteria:

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1. Clear history of angina with recent crescendo pattern and several episodes of angina at rest associated with transient ST depression
2. No evidence of acute myocardial infarction as assessed by electrocardiogram and serial enzyme determinations

This group of patients (14 men and 8 women) aged from 44 to 72 years and had a history of angina ranging from 1 to 12 years. Multiple-vessel disease was present in 17 patients and single-vessel disease in five. Global left ventricular function was normal in 13, mildly depressed in five, and severely depressed in four patients.

Study Protocol

Medical treatment of all patients with chronic stable angina was discontinued 48 to 72 hours before the study. Patients with unstable angina were admitted to the coronary care unit and maintained on aspirin and sublingual nitrates as required, but chronic administration of nitrates or calcium antagonists were discontinued 12 to 18 hours before the study. No patients were on beta blockers.

During that period, a 24-hour Holter monitoring was recorded immediately before the PET study. All normal volunteers and patients underwent the PET study following 12 to 15 hours fasting. None of the patients with unstable angina had symptoms or electrocardiographic signs of acute ischemia at the time of the PET study. Regional myocardial perfusion was assessed in all normals, all patients with chronic stable angina, and in 10 patients with unstable angina, and regional myocardial exogenous glucose utilization was studied in all subjects.

This study was approved by the Hammersmith Hospital Research Ethics Committee and the United Kingdom Administration of Radioactive Substances Advisory Committee. Written consent was obtained from all patients involved in this study.

Tracers and Procedures

PET was performed using a single slice scanner (ECAT II, CTI) with a spatial resolution of 17 mm (full width at half maximum) in the image plane and an axial resolution of 16 mm. The tomograph was cross-calibrated against a well counter used for measuring blood tracer concentrations. A mid-left ventricular slice was selected for each patient and then a 600-second transmission scan was recorded in order to correct all subsequent emission scans for tissue attenuation.

Myocardial Blood Flow

Regional myocardial perfusion was assessed by measuring myocardial uptake of the positron emitting potassium analogue rubidium-82 (Rb-82; half-life 76 seconds), according to the procedure previously described [9, 10]. Briefly, Rb-82 was eluted from a strontium-82/rubidium-82 generator in normal saline and then infused into a peripheral vein at a constant rate of 10 ml/min. Once dynamic equilibrium was achieved (3 to 4 minutes into the continuous infusion), a 120-second scan was recorded (equilibrium scan). Then, the tracer infusion was turned off, and after 30 seconds, when Rb-82 partially had cleared from the blood pool, a second scan (myocardial scan) was obtained for a period of 120 seconds.

Regional Rb-82 fractional uptake was calculated after the myocardial scan had been corrected for decay and normalized to the “arterial input” taken from the equilibrium scan. This measurement is proportional to the product of myocardial blood flow and the tracer extraction fraction. Although Rb extraction may vary with flow, in particular, it decreases with high flow, the method chosen in the present study was proven to be useful to detect transient ischemia in patients [9-11].

Myocardial Glucose Utilization

The glucose analogue F-18 2-fluoro, 2-deoxy-D-glucose (FDG) was used to assess regional myocardial glucose uptake. FDG competes with glucose for transport and phosphorylation by hexokinase in the cell. However, the phosphorylated compound FDG-6-P is not significantly further metabolized and is trapped within the cell in proportion to the rate of transport and phosphorylation of exogenous glucose [12]. Three minutes after injection of 5 to 10 mCi of the tracer, consecutive serial 5-minute scans were recorded over a period of 60 to 70 minutes. Venous blood samples were withdrawn while scanning, and the blood tracer concentration was measured in a well counter in order to obtain the input function.

At the end of FDG scanning, a blood pool scan was recorded after the in vivo labeling of red blood cells by inhalation of C-11 carbon monoxide (CO) [13].

An index of glucose utilization was obtained from the determination of the rate of increase of myocardial tracer concentrations over time. After subtracting