The numbers of deaths during the placebo run-in phase, which averaged 15 days, was 34 in 7092 patients (0.22% per week), compared with 4 deaths during the active run-in phase, which averaged 6 days in 7402 patients (0.06% per week). These data provide no evidence of early harm by the use of enalapril.

The issues raised by Dr Chaudhary and colleagues and by Dr Cruickshank (Dec 19/26, p 1547) warrant further studies of the effect of angiotensin-converting enzyme inhibitors in other high risk populations without low ejection fraction and heart failure. These studies should be ideally complemented by detailed mechanistic studies (eg, angiographic or ultrasound assessments of atherosclerosis) so that the generalisability of intriguing findings of reductions in MI and unstable angina can be assessed.

Department of Cardiology,
McMaster University,
Hamilton, Ontario, Canada;
Robertwood Johnson Medical School,
New Brunswick, New Jersey, USA;
and Division of Cardiology,
University of Michigan Medical Centre,
Ann Arbor, Michigan

**SALIM YUSUF**
**JOHN B. KOSTIS**
**BERTRAM PITT,**
on behalf of the
**SOLVD Investigators**

Phosphocreatine turnover and pH balance in forearm muscle of patients with syndrome X

Sir,—Syndrome X might encompass several pathophysiological entities.1 However, data on obvious restriction of flow is lacking and because perfusion disorders of skeletal muscle are unlikely, we speculate that an inherent metabolic defect could explain the low energy charge. Our first results derived from muscle biopsy specimens.2 To get in-vivo data, we investigated skeletal muscle oxidative performance by 31P nuclear magnetic resonance (NMR) spectroscopy of the forearm at rest and during exercise and recovery from exercise. In-vivo 31P-NMR spectroscopy allows following the changes in phosphorus metabolite levels and intracellular pH in human skeletal muscle non-invasively.3

We investigated 2 patients with syndrome X in a series of 7 in which myocardial and skeletal muscle biopsy samples showed low energy charge.2 The patients were chosen according to clinical presentation, 1 having heavy symptoms with angina and the other being clinically less severe. 8 informed, healthy/untrained, male volunteers aged 24-51 years acted as controls. NMR spectroscopy was done on a Bruker Biospec 24/30 with a 2.35 T magnet, giving an operating frequency of 40-55 MHz for 31P nuclei. The 31P-NMR spectra from the forearm muscles were acquired by accumulating 28-32 scans. The phosphocreatine (PCr), inorganic phosphate (Pi), the \( \gamma \)-ATP, and the \( \alpha \), \( \beta \)-ATP resonances were identified from their chemical shifts and calculated.4 Spectra from the patients were obtained at rest, during 12 min of exercise, and during 12 min of recovery. Exercise involved handgrip training equipment equilibrated to 100 N and each subject worked at 20% of his own maximum capacity. Myocardial biopsy specimens from the 2 patients displayed low energy charge values (0.56 and 0.59, respectively). Also, energy charge of skeletal muscle biopsy samples were abnormal (0.56 and 0.69, respectively).

Changes in PCr were followed continuously, spectrometrically, and expressed as PCr/(PCr + Pi). The initial resting values of the 2 patients and the controls for PCr and intracellular pH were similar. During exercise the rate of decrease of PCr and of pH was greater in patients than in controls (figure). PCr fell to 42% and 48% in the less severe patient, and to 58% (mean) of initial resting values in controls after 12 min of exercise. PCr resynthesis during post-exercise recovery was faster in controls. After exercise, pH was significantly lower in the patients (596 and 6.68, respectively) than in controls (p < 0.05. Obs = observed, exp = expected).