

Acute haemodynamic effects of the β_1 -adrenoceptor partial agonist xamoterol at rest and during supine exercise in patients with left ventricular dysfunction due to ischaemic heart disease: a double-blind randomized trial

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The effects of xamoterol 0.2 mg kg⁻¹ i.v. and placebo on left ventricular function at rest and on exercise were compared in patients with left ventricular dysfunction due to ischaemic heart disease. Improvements were seen in systolic and diastolic function at rest, and at up to 50% of maximal exercise, without evidence of worsening myocardial ischaemia.

Introduction

Xamoterol, a cardioselective β_1 -adrenoceptor partial agonist, was developed for use in patients with mild to moderate heart failure. Previous studies have demonstrated improvement contractility and relaxation of the heart at rest, during acute^[1,2] and long-term^[3] treatment. Recently published large double-blind studies have demonstrated that xamoterol improves exercise tolerance^[4,5]. On exercise in patients with overt heart failure, xamoterol maintains the expected increase in cardiac output at a lower filling pressure and heart rate^[2]. The mechanism for these improvements in haemodynamics on exercise has not, however, been elucidated. This study assessed the effects of xamoterol on isovolumic indices of contractility and relaxation in patients with global or segmental left ventricular dysfunction due to ischaemic heart disease.

Methods

PATIENTS

Twenty-four patients were studied, all male, of mean age 58.3 yr (range 39–70 yr). The criteria for inclusion were: stable angina pectoris [New York Heart Association (NYHA) Classes II–III], left ventricular dysfunction due to previous myocardial infarction (not more recently than 3 months previously), sinus rhythm and no overt clinical evidence of heart failure. Eighteen patients were in NYHA

Class II and six in Class III. Mean left ventricular ejection fraction (on ventriculography) was 48% (range 18–67%). Nineteen patients had ejection fractions of less than 50%. Beta-blocking drugs were stopped at least 72 h prior to the study and other cardioactive drugs, including calcium antagonists, diuretics and vasodilators, were withdrawn 48 h before the study.

PROTOCOL

The design of the study was a double-blind, randomized, between-group comparison of a single intravenous infusion of xamoterol at 0.2 mg kg⁻¹ or placebo. Patients attending for routine angiography performed a continuous supine symptom-limited bicycle exercise test at a work rate of 10 W min⁻¹. The patients then rested for 15 min or until the haemodynamic variables returned to baseline. They were then infused with xamoterol or placebo and the exercise test repeated. The maximal exercise capacity was individualized for each patient and the second exercise duration was identical to the first exercise test. Data were examined by analysis of variance for repeated measures.

Haemodynamic measurements (cardiac output and pulmonary artery pressure) were assessed by a thermodilution catheter floated into the pulmonary artery. Left ventricular measurements were taken from an 8 French pigtail catheter (Millar) in the left ventricle.

Results

Left ventricular contractility [$V_{\max}(s)$, (+) LV dP/dt] increased significantly following xamoterol infusion at rest and at up to 50% maximum exercise compared with placebo ($P < 0.05$) (Fig. 1). Xamoterol also increased left ventricular relaxation as measured by (-) dP/dt_{\max} and the time constant of isovolumic

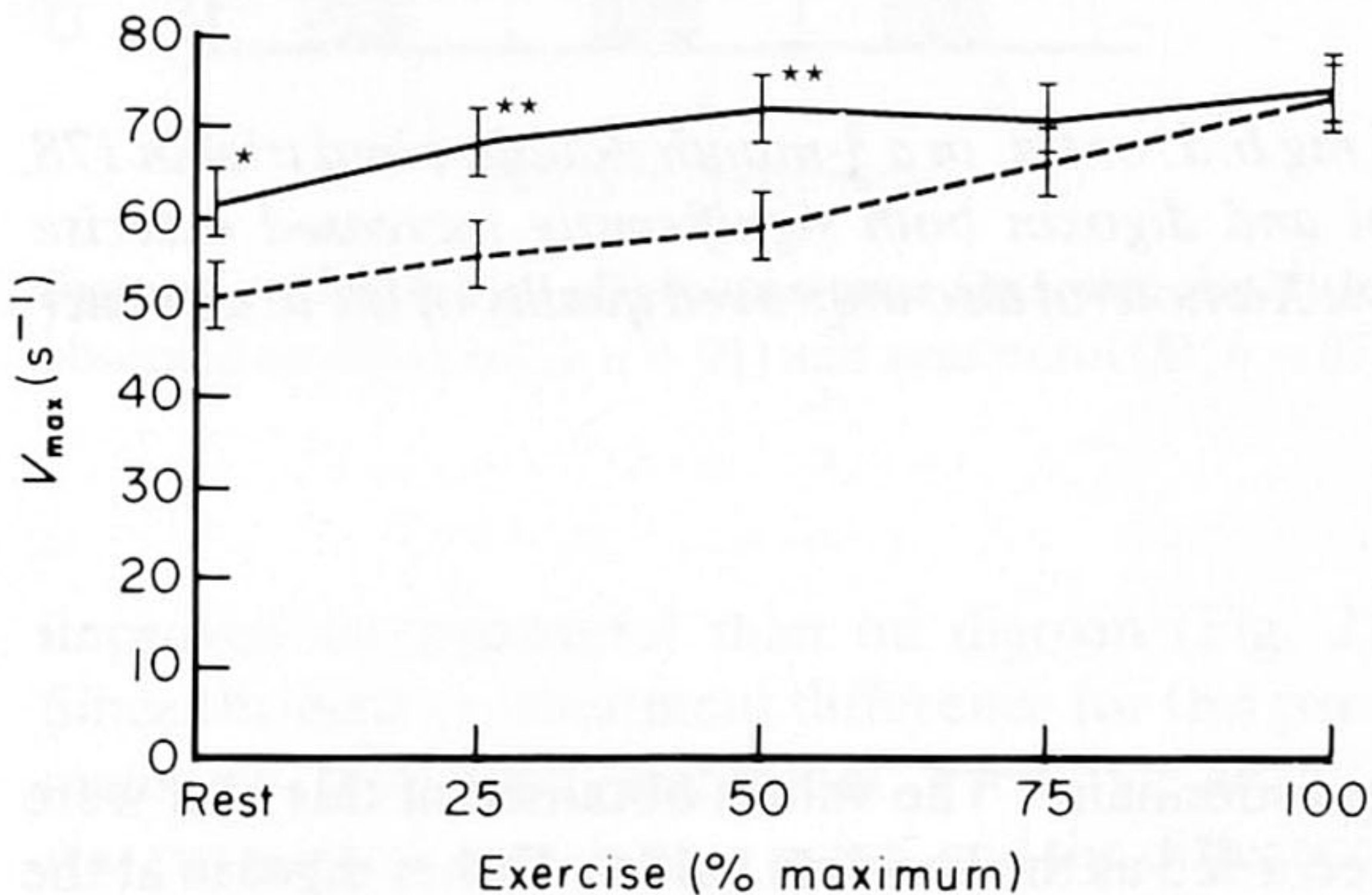


Figure 1 Effect of xamoterol (-; $n = 12$) on left ventricular contractility during exercise and that of placebo (---; $n = 12$) (* $P < 0.05$ and ** $P < 0.001$).

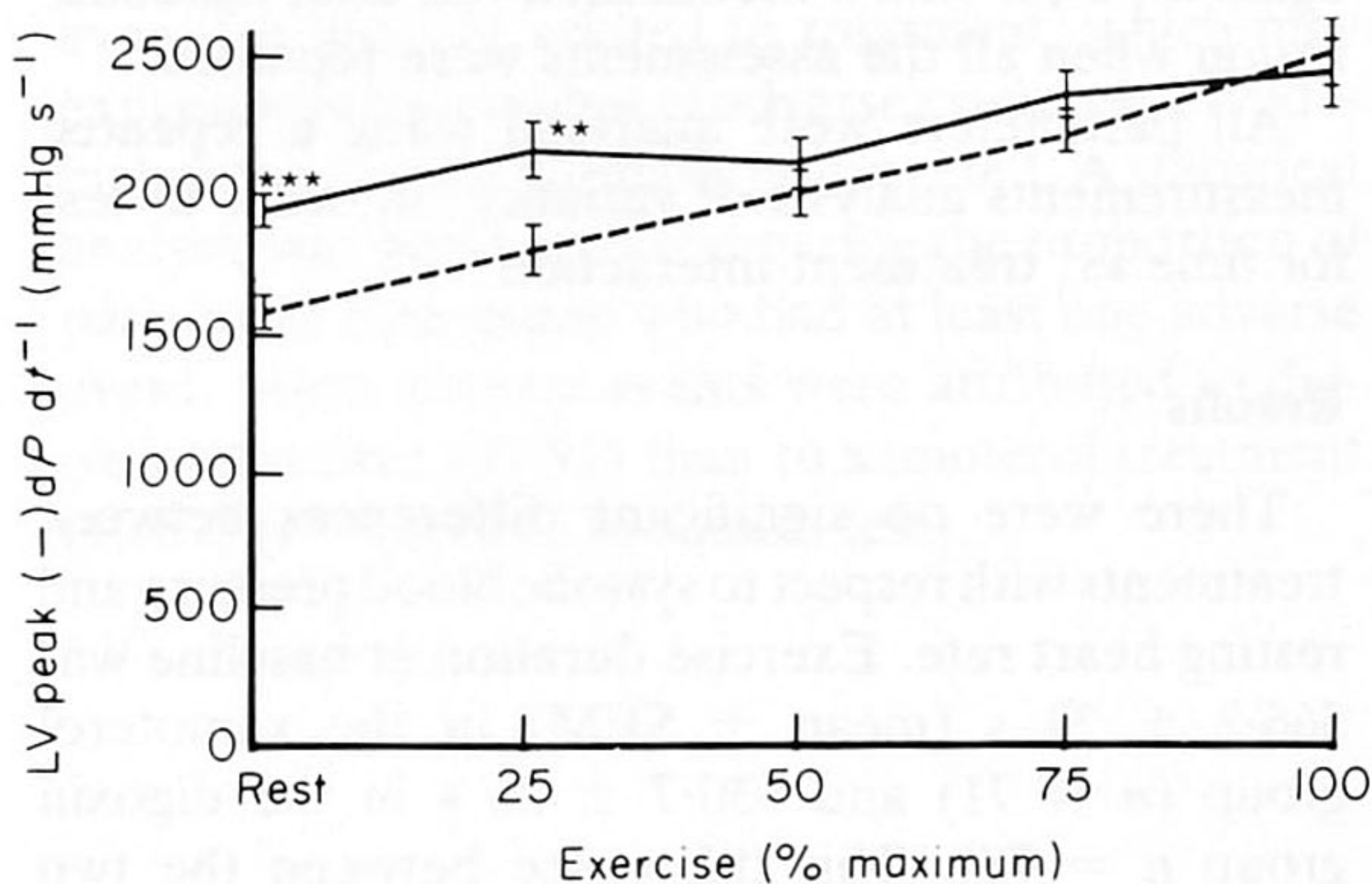


Figure 2 Effect of xamoterol (-; $n = 120$) on left ventricular relaxation during exercise and that of placebo (---; $n = 12$) (** $P < 0.02$; *** $P < 0.01$).

relaxation (Tau 1) at rest and up to 50% maximum exercise ($P < 0.05$) (Fig. 2). There were no significant differences between xamoterol and placebo at rest and on exercise in heart rate, blood pressure, cardiac index, stroke volume index, left ventricular end-diastolic pressure, ST segment change or in plasma noradrenaline or adrenaline concentrations.

Conclusions

In patients with left ventricular dysfunction, xamoterol improved indices of contractility and relaxation at rest and during submaximal exercise. These improvements in myocardial performance occurred without any evidence of worsening myocardial ischaemia.

Xamoterol may be a useful addition for the treatment of left ventricular dysfunction, and may particularly benefit patients with an ischaemic basis to their cardiac impairment.

References

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