British Heart Journal, 1979, **42**, 396–401

Angina in cold environment
Reactions to exercise

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SUMMARY Seventeen male patients with angina pectoris, and a history of increased severity of angina in the cold, performed submaximal bicycle exercise tests in a normal (20°C) and a cold environment (–10°C, 2·2 m/s wind velocity) wearing standardised clothing. Observations were made during and after serial short-term exercise periods each starting at 50 W, with continuous load increase of 10 to 30 W per minute, separated by 30-minute rest intervals.

In the group as a whole, maximal work load decreased by 7 per cent during exposure to cold. Heart rate, systolic blood pressure, and rate-pressure product were significantly higher during submaximal exercise in the cold, but at maximal work load there was no difference in heart rate, rate-pressure product, or magnitude of ST segment depression. The decrease in maximal work load exceeded 5 per cent (mean 11%) in 10 patients, who were described as cold-susceptible, while the decrease averaged 1 per cent in the seven non-susceptible patients. The cold-induced reduction in maximal work load showed a significant correlation with the increase in heart rate, blood pressure, and rate-pressure product during submaximal exercise.

After exercise, heart rate was significantly lower and blood pressure and rate-pressure product significantly higher in the cold than at normal temperature in all patients. In cold-susceptible patients, blood pressure was significantly higher at two and four minutes after exercise, and rate-pressure product at two minutes after exercise, than in non-susceptible patients, but in spite of this angina disappeared more quickly in cold-susceptible patients.

In conclusion, subjective cold intolerance was objectively demonstrated in 10 out of 17 patients with angina pectoris, by exercise in a room at –10°C. Susceptibility to cold was explained by a higher heart rate and blood pressure during exercise in the cold room, than during exercise in the room at normal temperature.

Patients with angina pectoris often experience a worsening of their symptoms in cold weather. The physiological explanation of this has been said to be the earlier appearance of myocardial oxygen deficit during exercise in the cold, which may be caused by increased work done by the heart (Epstein *et al.*, 1969), by nervous reflexes to the heart causing coronary vasoconstriction (Freedberg *et al.*, 1944; Mudge *et al.*, 1976), by release of sympatheticoadrenal hormones (Wilkerson *et al.*, 1974), or by cooling of the blood in the heart chambers and coronary arteries (Leon *et al.*, 1970).

However, not all patients with angina are susceptible to cold. The reason for this is not clear, but Neill *et al.* (1974), claimed that those patients with a low exercise tolerance are most affected, because of a relatively greater decrease in work performance. This conclusion was based on studies at rest, and there has been no study of the effects of cold on angina during exercise. We therefore studied the effects of exposure to cold on effort angina during standardised conditions, in order to see whether cold intolerance could be explained by changes which could be measured non-invasively.

Received for publication 5 January 1979

Subjects

A questionnaire about the relation of their symptoms to cold was given to 50 consecutive patients with typical angina pectoris and electrocardiographic abnormalities during a routine bicycle ergometer test. All but two had observed worsening of

symptoms at temperatures below 10°C. Seventeen of the patients with subjective cold intolerance (all men and all non-smokers, mean age 52 years, range 45 to 60 years) were invited to participate in the study and gave informed consent. The study was approved by the ethical committee of the hospital. All 17 patients gave a history of typical stable angina for at least 12 months. Six had had one or more myocardial infarctions and all had exercise-induced anginal pain and 0·2 to 0·6 mV horizontal or downward sloping ST depression on the electrocardiogram at the end of exercise. On a standardised stepwise ergometer test their work capacity, expressed as $W_{max\ 6\ min}$ (Strandell, 1964), was on average 105 W (range 70 to 150 W) and in all was limited by angina. None had hypertension, but one patient had signs of obstructive lung disease. Eight patients were taking beta-adrenergic receptor blocking agents in constant dosage. No other treatment except short-acting glyceryl trinitrate was allowed. Several patients had occasional unifocal ventricular premature beats at rest, without any increase during exercise.

Methods

ENVIRONMENT

Observations were made both in a cold environment in a special chamber and at normal room temperature. In the cold chamber the temperature of the air and walls was −10°C (SD ±0·4) and the relative humidity was 75 per cent; wind was directed toward the face and trunk at a velocity of 2·2 m/s (±0·1). Normal room temperature was set at 20°C (±1), with no wind and a relative humidity of 40 per cent (±8). Temperature was measured with thermocouples (copper/constantan) and the wind speed with a warm-wire anemometer. The calculated wind chill indices (Burton and Edholm, 1955) were 950 (cold) at −10°C, which causes an equivalent thermal wind decrement of about 18°C on unprotected skin (LeBlanc *et al.*, 1976), and 150 (normal) at 20°C. Clothing was carefully standardised. In the normal room the patients were dressed in short underwear, long summer trousers, shirt, socks, and ordinary shoes. In the cold chamber at −10°C a woollen cardigan, a pilot's summer overall, gloves, and a knitted woollen cap were added. The clothing was not windproof and the face and neck were uncovered.

To observe the changes in rectal and skin temperatures two patients exercised at 20°C and −10°C, with a 30-minute rest interval. The temperature was measured with thermocouples in the rectum 7 cm from the anus, and on 10 skin sites. Mean skin temperature was calculated by weighting the skin temperatures in the following manner: medial foot, 0·05; medial calf, 0·15; outer and inner thigh, back, chest, each 0·125; upper and lower arm, each 0·07; hand (thumb grip), 0·06; and forehead, 0·10. The rectal temperature increased slightly (0·1°C) after the first exercise period, and then remained unchanged, as was noted in an earlier investigation (Lassvik, 1978). Mean skin temperature decreased by 5·2 ±0·1°C at the end of exercise. The greatest local temperature changes were −18·0 ±0·7°C on the forehead, −6·0 ±1·1°C on the hand and foot, and −5·5 ±0·7°C on the chest. Both patients then exercised for a third time, one in the room at normal temperature and the other in the cold room, with resulting changes in body temperature identical with those observed in the corresponding earlier exercise period.

TEST PROCEDURE

The patients exercised in the cold chamber and in the room at normal temperature, with randomisation of the order of tests, the procedure being repeated on a second day with reversal of the test order. On each test day, the patients performed an initial 'trial' test at normal room temperature, so that each patient did three periods of exercise each day. As the 'trial' test was identical to the randomised test in the room at normal temperature, the occurrence of carry-over effects of exposure to cold on subsequent exercise at normal room temperature could be observed; no consistent carry-over effects were seen.

The exercise tests were performed on an electrically braked bicycle (Siemens-Elema 380) in which (according to the manufacturer) pedalling resistance did not change at low temperatures. The bicycle was not exposed to cold until immediately before the exercise and all electronic equipment was kept at normal room temperature. Sitting exercise was performed with an initial load of 50 W and thereafter a continuous load increase of 10 to 30 W per minute by use of a ramp generator (Lassvik, 1978). The rate at which load was increased was such that the patients experienced moderately severe angina, which was taken as the endpoint of the exercise period, after an exercise time of four to eight minutes. The patients rested sitting on the bicycle for five minutes before and after the exercise, but were then allowed to move around freely at normal room temperature between tests. The rest intervals between tests were 30 minutes. Each cold exposure lasted for 17 ±1 minutes.

A six lead praecordial electrocardiogram was recorded continuously at a paper speed of 10 mm/s with a forehead electrode as a reference (CH leads), and heart rate was calculated from the recordings.

Mean ST depression was measured at the appearance of angina and at maximal work load, at a paper speed of 50 mm/s, from five consecutive complexes in one of the leads CH 4-6. Systolic blood pressure was measured using a cuff on the upper arm and an ultrasound Doppler device, with the cuff and a flat probe beneath the clothing.

Heart rate and blood pressure were measured after five minutes of sitting on the bicycle before exercise, every minute during exercise, just before stopping exercise, and every minute for four minutes after exercise. The rate-pressure product (heart rate x systolic blood pressure) was calculated. Peak expiratory flow rate was measured 4·5 minutes after exercise, with a Wright peak flow meter. During exercise, the work load at appearance of pain and the maximal work load were noted. Measurements were also made at three minutes when most of the patients had no pain, and at approximately 4·5 minutes when all patients had angina. After exercise, the time for disappearance of angina was noted.

All tests were performed at the same time of day. Patients were not allowed to take food, nitrites, or muscular exercise for two hours before the tests. All patients had previously performed five serial exercise tests at normal temperature to establish reproducibility (Lassvik, 1978).

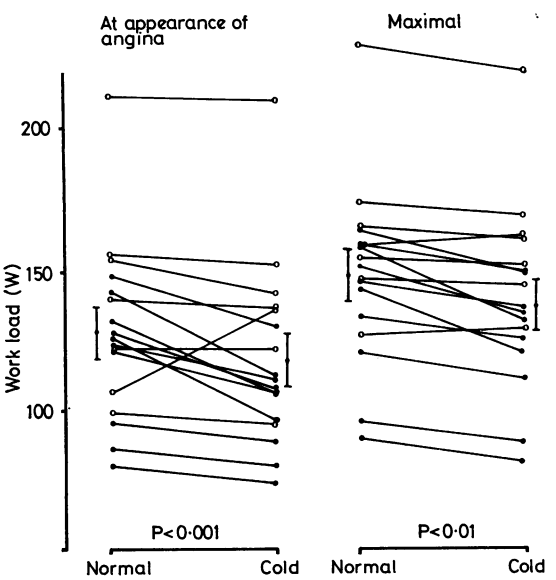

Fig. 1 *Angina and work performance in normal and cold environment. ●, cold-susceptible patients; ○, non-susceptible patients. Each symbol represents the mean of two exercise tests. Mean values ±SEM for all 17 patients are also shown.*

STATISTICS

For each patient the mean values were calculated for the two sets of randomised exercise periods and were evaluated with the t test for paired observations, and regression analysis. Multiple regression analysis was used for correlating cold-induced changes of exercise capacity with haemodynamic and clinical data (Draper and Smith, 1967). Patients in whom there was a more than 5 per cent decrease in maximal work load during exposure to cold were arbitrarily defined as cold-susceptible, and observations made in these patients were compared with those made in non-susceptible patients using the two-sample t test for unpaired data.

Results

The work load at appearance of pain decreased on exposure to cold by 8±1 per cent (mean± SEM) ($P < 0.001$), and the maximal work load by 7±1 per cent ($P < 0.01$) (Fig. 1). ST depression did not change between the normal and the cold

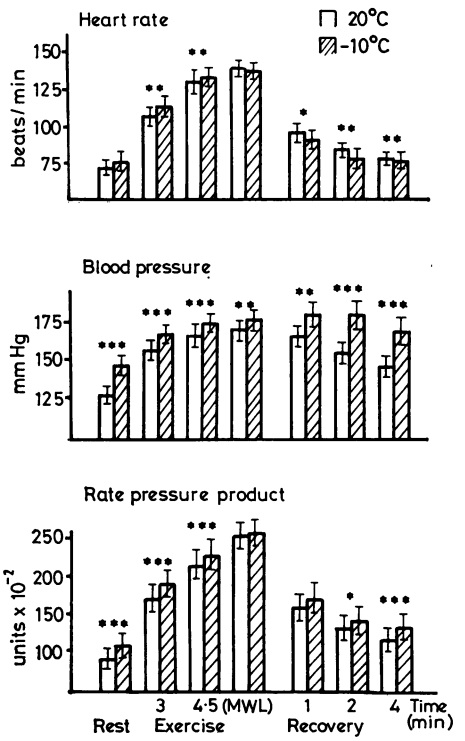

Fig. 2 *Heart rate, systolic blood pressure, and rate-pressure product in normal and cold environment before, during, and after exercise. Mean values ±SEM. Significance of differences: *P < 0·05; **P < 0·01, ***P < 0·001.*

room (0·1 ±0·02 mV at appearance of pain and 0·25 ±0·04 mV at maximal work load, in both environments). Time for disappearance of angina did not change (122 ±22s in normal and 111 ±27s in cold room).

On exposure to cold, the heart rate was significantly higher during exercise (at three and at 4·5 minutes ($P < 0·01$) (Fig. 2), but in contrast the heart rate after exercise was significantly lower ($P < 0·01$) (Fig. 2). Blood pressure was significantly higher throughout exposure to cold ($P < 0·001$) (Fig. 2). During the first two minutes after exercise in the cold, blood pressure tended to be higher than at maximal work load. The greatest individual rise in blood pressure was 45 mmHg, from 180 mmHg at maximal work load to 225 mmHg two minutes after exercise. In contrast, at normal room temperature blood pressure decreased gradually and significantly from maximal work load to four minutes after exercise ($P < 0·01$) (Fig. 2). Rate-pressure product was significantly higher at cold exposure ($P < 0·001$) except at maximal work load and at one minute after exercise (Fig. 2).

The cold-induced decrease in maximal work load was significantly correlated with the cold-induced increase in heart rate and rate-pressure product after three minutes of exercise ($P < 0·001$ and $P < 0·01$, respectively) and with the increase in heart rate, blood pressure, and rate-pressure product after 4·5 minutes of exercise ($P < 0·001$, $P < 0·05$, and $P < 0·01$, respectively) (Fig. 3). No correlation was found between cold-induced decrease in maximal work load and changes in heart rate or rate-pressure product at rest or at maximal work load, or blood pressure changes at rest, at three minutes of exercise, or at maximal work load. Cold-induced changes in time for disappearance of angina were not correlated with changes in heart rate, blood pressure, or rate-pressure product after exercise.

Cold-induced changes in maximal work load were not related to the patient's age, height, weight, duration of angina, or number of infarctions, medical treatment, maximal work load, maximal work time, performed work, time of the year for the investigation, or a rough estimate of the patient's outdoor activities.

Peak expiratory flow rate after exercise was not significantly different in the cold room and in the room at normal temperature (503 ±30 l/min and 501 ±30 l/min, respectively).

Occasional ventricular premature beats were seen in seven patients both at rest and during exercise, with no increase on exposure to cold.

COLD-SUSCEPTIBLE VS NON-SUSCEPTIBLE PATIENTS

In 10 cold-susceptible patients the cold-induced reductions of work load at appearance of pain and maximal work load were 14 ±2 per cent and 11 ±1 per cent, respectively (both $P < 0·001$). Time for disappearance of angina decreased by 14 ±6 per cent ($P < 0·05$). In seven non-susceptible patients, work load at appearance of pain and maximal work load did not change significantly (−1 ±0%). The time for disappearance of angina increased, but the change was not significant (10 ±9%). The differences between the groups were significant in respect not only of maximal work load but also work load at appearance of pain ($P < 0·001$) and time for disappearance of angina ($P < 0·05$). Five of the cold-susceptible patients and three of the non-susceptible patients were taking beta-adrenergic blocking drugs.

During exercise in the cold (at three and 4·5 minutes) cold-susceptible patients had significantly greater increases in heart rate ($P < 0·01$) and rate-pressure product ($P < 0·05$) than non-susceptible patients, averaging six beats/minute and 1400 units,

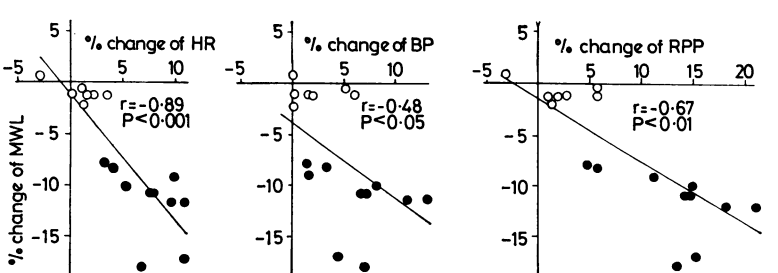

Fig. 3 *The correlation between percentage changes* of maximal work load (MWL) and heart rate (HR), systolic blood pressure (BP), and rate pressure product (RPP) after four and a half minutes of exercise in a cold room compared with room at normal temperature. *Percentage change calculated (e.g. for heart rate) as* $\frac{HR_{-10}^{\circ} - HR_{20}^{\circ}}{HR_{20}^{\circ}} \times 100$

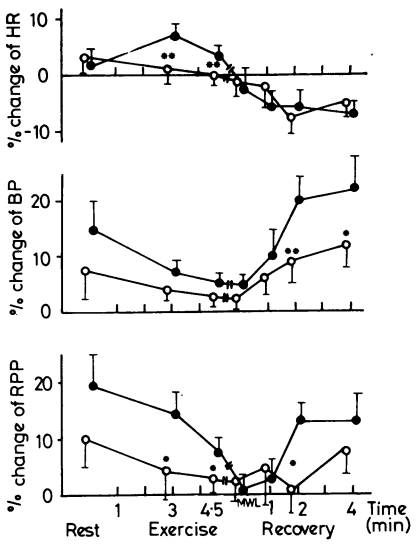

Fig. 4 *Percentage changes in heart rate (HR), blood pressure (BP), and rate-pressure product (RPP) in 10 cold-susceptible patients (●) and seven non-susceptible (○) patients, in cold room compared with room at normal temperature. Significance of differences: *P < 0·05, **P < 0·01.*

respectively (Fig. 4). Blood pressure tended to be higher in cold-susceptible patients (mean difference 6 mmHg) but the differences were not significant. After exercise, cold-susceptible patients had significantly greater increases in blood pressure at two minutes ($P < 0{\cdot}01$) and four minutes ($P < 0{\cdot}05$), and in rate-pressure product at two minutes ($P \pm 0{\cdot}05$) than non-susceptible patients during exposure to cold.

Discussion

Although all the patients investigated gave a history of reduced exercise tolerance in the cold, almost half the patients showed no decrease in working capacity on exposure to the cold (–10°C, 2 m/s wind velocity). As the exercise procedure included successive exercise periods on the same day, it was possible that the warming up effect of the first period of exercise, and carry-over effects of the cold exposure on the next exercise period, might decrease differences between tests. The design of the investigation however, excluded such effects (see also Lassvik, 1978). Another possibility is that the laboratory procedure failed to reproduce the real life situation which includes many uncontrolled circumstances. On the other hand, physical conditions, such as wind, rain, and snow, and psychological factors such as the expectation of untoward effects of cold in the real life situation, may make the laboratory experiment better for identifying the effects of cold exposure *per se*.

The levels of rate-pressure product at moderately severe angina were the same during exercise at normal temperature and in the cold chamber. This indicates that the constant relation between angina pectoris and rate-pressure product, reflecting myocardial oxygen demand (Robinson, 1967), still holds in a cold environment. The significant relation between cold-induced decrease of maximal work load and increases in heart rate, blood pressure, and rate-pressure product suggests that the observed reduction in maximal work load in cold-susceptible patients is probably the result of the increase in the work done by the heart.

We found a significantly greater increase in both heart rate and blood pressure in all patients during submaximal exercise in the cold chamber compared with the room at normal temperature. This suggests an increase in both cardiac output and peripheral resistance which has been shown to occur in healthy volunteers both during acute (Keatinge *et al.*, 1964) and long-term exposure to cold (Hanna *et al.*, 1975). In patients with angina pectoris, and in healthy controls, cold has been found to increase peripheral resistance and blood pressure at rest (Neill *et al.*, 1974). In addition, Epstein *et al.* (1969) found that during light exercise in the cold, peripheral resistance remains high. There is no increase in heart rate at rest, a finding which may be explained by the baroreceptor reflex reducing sympathetic cardio-acceleration (Sarnoff *et al.*, 1965). With local cooling of the face, heart rate may even decrease (Hayward *et al.*, 1976). During light exercise, baroreceptor reflex activity might likewise suppress cold-induced increase in heart rate as was seen in the study by Epstein *et al.* (1969). In our investigation the work load was greater and the environment considerably colder, probably resulting in increased sympathetic activity which could explain why the heart rate was higher during exercise in the cold chamber compared with the normal room temperature. The importance of heart rate for the development of ischaemia is shown by the favourable action of beta-adrenergic blocking agents in angina, and by atrial pacing studies.

Another observation in this study was that after exercise in the cold room, blood pressure did not fall normally but remained high, and in a few patients increased further. Heart rate fell more rapidly than at normal temperature, probably because of increased baroreceptor reflex activity resulting from the higher blood pressure. In spite of this, the rate-pressure product remained significantly higher in all patients. In cold-susceptible

patients, cold-induced increases in both blood pressure and rate-pressure product after exercise were significantly greater than in non-susceptible patients, but nevertheless angina disappeared more rapidly. An explanation of the faster disappearance of angina after exercise in cold-susceptible patients might be that the higher arterial pressure improved coronary perfusion; also a faster fall in heart rate during the first minute after exercise might reduce oxygen demand and also improve myocardial oxygen supply because of a longer diastole. On the other hand, a practical implication of the high post-exercise blood pressure during exposure to cold might be a further decrease in the angina threshold during subsequent exercise.

The rapid decrease in heart rate and disappearance of angina after exercise during exposure to cold might indicate that the haemodynamic changes are caused by nervous reflexes rather than by circulating catecholamines. Strong baroreceptor reflex activity could, however, be concealing sustained catecholamine effects on heart rate. Keatinge *et al.* (1964) found that there was only a small increase in plasma adrenaline even during very intense acute skin cooling, and it seems likely that the haemodynamic changes induced by the short-term exposure to cold in this study are caused mainly by direct sympathetic nervous reflexes.

In conclusion, differences in the behaviour of heart rate and blood pressure could explain the different effects of cold on the development of angina during exercise and recovery after exercise in a group of patients with angina pectoris, and objectively identify a subgroup of cold-susceptible patients.

This investigation was supported by grants from the Swedish National Association against Heart and Chest Diseases, the County Council of Östergötland, and 'Förenade Liv' Mutual Group Life Insurance Company, Stockholm, Sweden.

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