Effects of Endoscopic Transthoracic Sympathicotony on Hemodynamic and Neurohumoral Responses to Exercise in Humans

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Endoscopic transthoracic sympathicotony (ETS) is a minimal invasive procedure of thoracic sympathetic block and has been used successfully in the treatment of primary palmar hyperhidrosis. To examine the effect of Th 2-3 ETS on hemodynamic responses to submaximal upright treadmill exercise in humans, cardiac output, plasma noradrenaline and adrenaline at rest and during the last 40s of stage 2 in a modified Bruce protocol were measured before and after ETS in 21 patients with primary palmar hyperhidrosis. Heart rate, mean arterial pressure, rate-pressure product, and noradrenaline decreased at rest and at submaximal exercise after ETS. Cardiac index at rest did not change either before or after ETS, but decreased (8.9±0.6 vs 6.8±0.4L·min⁻¹·m⁻²; p<0.01, mean±SEM) at submaximal exercise after ETS. Stroke index and systemic vascular resistance were similar both at rest and at submaximal exercise before and after ETS. Thus, ETS reduces myocardial oxygen demand and plasma noradrenaline levels both at rest and during exercise without significantly depressing cardiac function in terms of stroke volume. (Circ J 2002; 66: 357–361)

Key Words: Autonomic nervous system; Cardiac function; Catecholamine; Endoscopic transthoracic sympathicotony; Exercise; Palmar hyperhidrosis

Methods

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Twenty-one patients with primary palmar hyperhidrosis (10 males and 11 females, mean age 28±3 years; mean±SEM) participated in the study. None of these patients had cardiac disease nor were receiving any drug that might affect autonomic function directly or indirectly. All patients gave their informed consent before participating.

Endoscopic Transthoracic Sympathicotony

The operative technique, which has been described in detail elsewhere,6 has been used in more than 400 patients with palmar hyperhidrosis at National Kanazawa Hospital since 1993. Patients were intubated with an endotracheal tube under general anesthesia and placed in a semireclining position with both arms in abduction. (In the semireclining position, the pneumothorax is located in the apical region.) Approximately 2 liters of carbon dioxide was insufflated into the pleural cavity through a Surgineedle entered via the axillary fossa. A modified urological electroresectoscope was introduced via the same incision into the axillary fossa, thus obtaining an excellent view of the upper thoracic cavity. The second and third thoracic sympathetic ganglia, including rami communicantes, were destroyed by electrocautery. After exsufflation of the gas, the procedure was repeated on the opposite side. Operation time was within 30min. The patient was discharged from hospital the day after operation and the hospital stay was 2 days. Most patients resumed work within a few days and resumed sports activities within 2 weeks.

Treadmill Exercise Test

Submaximal, graded, upright treadmill exercise was performed according to a modified Bruce protocol comprising...
Effects of ETS on percent changes in hemodynamic parameters

### Hemodynamic Measurements

At the end of stage 2, exercise was stopped. Systolic arterial pressure increased by 180±36%, the rate–pressure product increased by 135±27%, and systemic vascular resistance decreased by 66±3%. After ETS, heart rate increased by 64±6%, cardiac index increased by 0.7±1.0%, and systemic vascular resistance decreased by 66±3%

### Statistical Analysis

Values are expressed as the mean±SEM. Paired t tests were used to compare hemodynamic and neurohumoral variables. A p-value less than 0.05 was considered statistically significant.

### Results

#### Baseline

Hemodynamic responses to exercise before and after ETS are summarized in Table 1. At baseline after ETS, systolic, diastolic, and mean arterial pressures, heart rate, and the rate–pressure product decreased; whereas cardiac index, stroke index, and systemic vascular resistance remained unchanged compared with values before ETS.

#### Exercise Hemodynamics

At submaximal exercise after ETS, heart rate, diastolic and mean arterial pressures, cardiac index, and the rate–pressure product decreased; whereas systolic arterial pressure, stroke index, and systemic vascular resistance did not change compared to values before ETS.

Effects of ETS on percent changes in hemodynamic parameters are shown in Fig 1. With exercise before ETS, heart rate increased by 83±7%, cardiac index increased by 274±41%, the rate–pressure product increased by 135±12%, and systemic vascular resistance decreased by 66±3%. After ETS, heart rate increased by 64±6%, cardiac index increased by 180±36%, the rate–pressure product increased by...
by 110±12%, and systemic vascular resistance decreased by 53±4%. All these changes were less than those before ETS. Increases in mean arterial pressure and stroke index after ETS were similar to changes before ETS.

**Neurohumoral Response**

Effects of ETS on plasma catecholamine are shown in Fig 2. After ETS, plasma noradrenaline concentration at baseline decreased from 390±28 pg/ml to 269±19 pg/ml, whereas plasma adrenaline concentration remained unchanged. At submaximal exercise after ETS, plasma noradrenaline concentration decreased from 869±74 pg/ml to 673±63 pg/ml and plasma adrenaline concentration also decreased from 128±16 pg/ml to 91±9 pg/ml.

**Long-Term Effects**

Long-term effects of ETS on hemodynamic responses to exercise are summarized in Table 2. One year after ETS, both the heart rate and rate-pressure product at baseline and at submaximal exercise were less than before ETS.

**Discussion**

The present study demonstrated that, at rest after ETS, heart rate, arterial pressure, and the rate-pressure product decreased, whereas cardiac and stroke indices remained unchanged. The change induced by exercise for each of heart rate, cardiac index, systemic vascular resistance, and the rate-pressure product after ETS was less than that before ETS, whereas changes in the mean arterial pressure and stroke index were similar to responses before ETS. These findings suggest that ETS reduces myocardial oxygen demand both at rest and during exercise through a decrease in heart rate and arterial pressure without significantly depressing cardiac function in terms of stroke volume.

Papa et al have reported that heart rate at rest and after effort decreased and that blood pressure response to exercise was blunted after open thoracic sympathectomy.10 Drott et al have reported that after ETS, heart rate at rest, as well as during exercise, decreased, and that systolic arterial pressure was reduced at rest, but that diastolic arterial pressure was not significantly altered.11 In a study by Noppen and colleagues, after Th 2-3 ETS, heart rates at rest and at

**Table 2  Long-Term Effects of Endoscopic Transthoracic Sympathectomy (ETS) on Hemodynamic Responses to Exercise**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ETS</td>
<td>79±5</td>
<td>128±7**</td>
</tr>
<tr>
<td>1 year after ETS</td>
<td>72±4*</td>
<td>105±6***</td>
</tr>
<tr>
<td>Systolic arterial pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ETS</td>
<td>118±3</td>
<td>154±6**</td>
</tr>
<tr>
<td>1 year after ETS</td>
<td>112±5</td>
<td>138±7*</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ETS</td>
<td>69±5</td>
<td>68±7</td>
</tr>
<tr>
<td>1 year after ETS</td>
<td>66±3</td>
<td>57±6</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ETS</td>
<td>86±4</td>
<td>97±6</td>
</tr>
<tr>
<td>1 year after ETS</td>
<td>81±3</td>
<td>84±4</td>
</tr>
<tr>
<td>Rate–pressure product (10³ beats·mmHg/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ETS</td>
<td>9.4±0.8</td>
<td>19.6±1.0**</td>
</tr>
<tr>
<td>1 year after ETS</td>
<td>8.0±0.6*</td>
<td>14.5±0.9**</td>
</tr>
</tbody>
</table>

*p<0.05 vs baseline, **p<0.05 vs baseline, *p<0.05 vs before ETS. Values are mean±SEM.
peak exercise were reduced significantly, but systolic and diastolic arterial pressure responses to exercise remained unchanged:2 Thus, the effect of thoracic sympathectomy on heart rate is consistent, but that on blood pressure is controversial. In the present study, heart rate at rest and during exercise decreased after ETS, which is consistent with previous studies.10–12 Systolic, diastolic, and mean arterial pressures at rest decreased, but the increases in arterial pressure with exercise were not blunted after ETS. The different blood pressure responses to exercise after ETS may be partially explained by the differences in the extent of sympathetic or the severity of exercise.

The mechanism responsible for the decrease in arterial pressure at rest and during exercise after ETS is still unclear because the effect of ETS on cardiac output response to exercise has not yet been reported. In the present study, we measured cardiac output during exercise before and after ETS. At rest after ETS, systemic vascular resistance tended to decrease but cardiac output did not change. During exercise after ETS, systemic vascular resistance did not change, but cardiac output decreased because of the blunted heart rate response to exercise. Thus, the decrease in mean arterial pressure at rest after ETS is mainly due to the reduction of systemic vascular resistance, whereas the decrease in mean arterial pressure during exercise is due to the reduction of cardiac output.

Martin et al have reported that, normally, when heart rate response to isometric exercise was prevented by ß-blockade or combined ß-adrenergic and parasympathetic blockade, blood pressure was still raised to normal levels by vasoconstriction.13 In the study of Haskell and coworkers, a normal rise in blood pressure during isometric exercise also occurred in patients who had had heart transplants and, thus, had completely denervated heart.14 In the present study, the lack of an increase in systemic vascular resistance when a fall in cardiac output occurred was observed during exercise after ETS. The mechanism for this lack of increase in systemic vascular resistance is unclear; however, several possible explanations are suggested. First, ETS suppresses the reflex vasoconstriction in non-working muscles of both arms during treadmill exercise. Second, the level of treadmill exercise in the present study was mild. The cardiovascular effect by the central command is mainly due to the withdrawal of vagal tone both at the beginning of exercise and during mild exercise, and sympathetic activation through the metaboreflex of working muscle occurs during moderate to severe exercise.15,16 Therefore, the sympathetic activation by the central command and the metaboreflex of working muscle seems to have been small during exercise in the present study. Third, the cardiac sympathetic afferent reflex contributes to an increase in sympathetic outflow.17,18 It is possible that ETS diminished this reflex by partial blockade of cardiac sympathetic afferent fibers in the present study.

Several studies have found no difference between cardiac contractility at rest in transplanted denervated hearts and in normal subjects.19,20 Conversely, Bengel and colleagues have reported that the response by cardiac contractile function to exercise is impaired in heart-transplant recipients, but that the restoration of sympathetic innervation is associated with an improved response by contractile function to exercise.21 Thus, sympathetic drive seems to support cardiac contractility during exercise but not at rest. In the present study, stroke volume did not change either at rest or during exercise after ETS. No changes in stroke volume at rest either before or after ETS seems to be consistent with results of previous reports.9,20 In another study, we have observed that after ETS mean arterial pressure and heart rate decreased, but that left ventricular end-diastolic volume increased.22 Although in the present study we did not measure end-systolic elastance of the left ventricle, which is independent of loading condition, we believe that afterload reduction and preload increase via sinus bradycardia by ETS caused the stroke volume to remain unchanged during exercise therefore counterbalancing the depression of cardiac contractility.

Plasma noradrenaline concentration decreased both at rest and at submaximal exercise after ETS. Plasma adrenaline concentration remained unchanged at rest but decreased at submaximal exercise. A reduction in the amount of catecholamine released from the sympathetic nerve terminal in the upper extremities and the heart can account for decreases in the level of noradrenaline. However, the cause of decreased levels of adrenaline at submaximal exercise is uncertain because most of the plasma adrenaline is released from the adrenal medulla. The sympathetic ganglion is not a simple relay station but a site modulated by short interneurons and a variety of neurotransmitters and receptors.

Therefore, Th 2-3 ETS might have modified the sympathetic regulation of adrenaline secretion from the adrenal medulla. Th 2-3 ETS increases the plasma level of atrial natriuretic peptide,25 which has widespread sympatholytic activity.24 Th 2-3 ETS might have influenced the amount of adrenaline secreted from the adrenal medulla via changes in humoral factors such as atrial natriuretic peptide.

Many reports have shown that ETS for palmar hyperhidrosis is an efficient procedure, even after long-term follow-up periods ranging from 3 years to 16 years.25–29 However, for how long ETS affects the cardiovascular system is unclear. Tygesen et al have reported that changes in heart rate variability, which indicates significantly reduced sympathetic and increased vagal tone, and the reduction of QT dispersion both persisted for 2 years after ETS.30 The present study demonstrated that blunted heart rate and the rate–pressure product responses to exercise by ETS persisted for at least 1 year. Although we cannot draw definite conclusions regarding the lasting effects of ETS on the cardiovascular system because of the small number of patients studied, the effect of ETS on the cardiovascular system as well as on palmar hyperhidrosis seems to continue for several years.

The benefits of ETS have been reported in the treatment of patients with severe angina pectoris who are not eligible for coronary artery bypass grafting or angioplasty.3,4 Endoscopic transthoracic sympathectomy acts much like a selective cardiac ß-receptor blockade. Observations from the present study, which showed that ETS reduces the rate–pressure product during exercise without causing a significant fall in cardiac function in terms of stroke volume and that the effect of ETS on blunted heart rate responses to exercise persists for at least 1 year, support the benefits and safety of ETS for the treatment of selected patients with severe angina pectoris as well as for patients with palmar hyperhidrosis.

Several limitations of the study should be noted. First, the reproducibility of the hemodynamic and catecholamine responses to the treadmill exercise test was not examined in the present study. Studies have demonstrated that psychological and mental stress increases plasma adrenaline levels.31,32 In the present study, because plasma adrenaline
levels tended to decrease at baseline and decreased during exercise after ETS, we cannot discard the possibility that habituation to the treadmill exercise test affected the hemodynamic and neurohumoral responses to exercise.

Second, the rate–pressure product is an inaccurate and indirect method of assessing myocardial oxygen consumption. Other factors, such as wall tension and contractility, that contribute to myocardial oxygen consumption were difficult to measure during the treadmill exercise test and thus ignored.

Third, end-systolic elastance of the left ventricle, which is independent of loading condition, was not measured. Instead, we estimated cardiac function in terms of stroke volume; therefore, the exact effect of ETS on cardiac contractility during exercise remains unknown.

Fourth, cardiovascular deconditioning after prolonged bed rest has been attributed to inactivity, and this deconditioning has been observed substantially after 20 h of head-down tilt bed rest! Therefore, we cannot discard the possibility that the 2 days of hospital stay might have influenced the hemodynamic response to exercise in the present study because we did not have a control group for comparison.

Fifth, we evaluated the effectiveness of ETS by the extent of palmar sweating and did not confirm the effect of ETS on cardiac sympathetic nerve activity. However, in the preliminary study, we examined the effect of ETS on cardiac sympathetic nerve activity by myocardial 123I-metaiodobenzylguanidine imaging and observed that ETS decreased the myocardial clearance of 123I-metaiodobenzylguanidine, but did not induce the localized change of 123I-metaiodobenzylguanidine activity on single photon emission computed tomography imaging.

References