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Cardiopulmonary effects following endoscopic thoracic sympathectomy for primary hyperhidrosis☆

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Abstract

Introduction: Endoscopic thoracic sympathectomy (ETS) is performed for the treatment of primary hyperhidrosis (PH). The second and third sympathetic thoracic ganglions excised in ETS also innervate the heart and lung. **Objective:** In the present work we studied the cardiopulmonary effects of ETS in a group of patients with PH. **Methods:** We performed a prospective study in 38 patients with severe PH. Pulmonary function, echocardiographic assessment of left ventricular function and myocardial contractility and maximal, symptom-limited, incremental exercise tests were evaluated 2 weeks before, and 6 months after ETS. Data were analysed with the paired *t*-test. Differences were considered significant when $p < 0.05$. **Results:** In pulmonary function tests, we found a statistically significant decrease forced expiratory flow in small airways and an increase of residual volume, a significant decrease in heart rate and ejection fraction, a significant decrease of 'rest' and 'peak' heart rate, and a significant increase of oxygen pulse (O_2 pulse) and oxygen peak uptake (V_{O_2} peak) after ETS ($p < 0.05$). **Conclusions:** These cardiopulmonary effects observed 6 months after ETS in the treatment of patients with PH are all in normal ranges and are not relevant in cardiopulmonary function. We concluded that ETS in patients with PH is a safe procedure. Patients must be informed about these cardiopulmonary effects before the operation.

Keywords: Primary hyperhidrosis; Endoscopic thoracic sympathectomy; Autonomous nervous system; Prospective study

1. Introduction

Primary hyperhidrosis (PH) is a disorder characterised by excessive sweating of the palms and often the armpits and soles of the feet. It is not known whether PH is a systemic or local disease. Presently, there is no consensus over the aetiology of PH. Although sweating is a normal function of an organism, its contribution to the regulation of body temperature being an essential mechanism of haemostasis, in this specific case and as far as we understand, sweating apparently has no homeostatic function.

Endoscopic thoracic sympathectomy (ETS) is performed for the treatment of primary hyperhidrosis [1]. This surgery is a minimally invasive procedure of thoracic sympathetic blockage and consists of the bilateral ablation of the second and third thoracic sympathetic ganglion, affecting the sympathetic nervous outflow to the arms and elsewhere. The results of this procedure have revealed a high degree of patient satisfaction [1—6].

The second and third sympathetic thoracic ganglions excised in ETS also innervate the heart and lungs. A few studies have shown a decrease of heart rate and significant effects on pulmonary function variables obtained 6 weeks after ETS. Small but significant decreases in forced expiratory volume in 1 s (−3%) and total lung capacity (−3%) were observed whereas forced expiratory flow at 75% of vital capacity decreased disproportionately (−8%) and airway resistance increased by 12% [7—10].

Currently, thousands of patients with hyperhidrosis are submitted to ETS and we believe it is important to know the degree of cardiac and pulmonary effects of this operation.

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To answer these questions we have studied the pulmonary function, left ventricular function and myocardial contractility with M mode, two-dimensional (2D), flow and tissue Doppler echocardiography and performed cardiopulmonary exercise testing in a sample of 38 patients with PH, 2 weeks before and 6 months after ETS.

2. Patients and methods

Thirty-eight consecutive patients referred for bilateral thoracic sympathectomy for PH were included in this prospective study. None of the patients was under medication at the time of the study.

Bilateral video-assisted thoracic sympathectomy was performed under general anaesthesia. All surgeries were performed by the same surgeon (JC), who had an experience of over 400 operations at the time of study initiation. The lung was excluded with a double-lumen tube. We used two incisions on the fourth and fifth intercostal spaces, and in all cases the second and third sympathetic ganglions were destroyed by electrocautery. One chest drain was left in place about 8 h after the surgery. Patients were discharged from hospital the day after operation. The study had been approved by the Lisbon Medical School Ethics Committee and performed according the Declaration of Helsinki. All patients provided written informed consent.

The pulmonary function, echocardiography and cardiopulmonary exercise tests were performed 2 weeks before and 6 months after ETS.

2.1. Pulmonary function tests

The pulmonary function tests (PFTs) were carried out using the commercially available Sensormedics Plethismograph. We measured the lung volumes and airway resistance and conductance 2 weeks before and 6 months after ETS. Pulmonary function was assessed by the forced vital capacity (FVC), total lung capacity (TLC), residual volume (RV), forced expiratory volume in 1 s (FEV1), forced expiratory flow (FEF) at 75%, 50% and 25% of the vital capacity, FEV1/FVC (Tiffeneau index), RV/TLC and airway resistance (Raw). All the parameters except RV/TLC, Tiffeneau index and Raw are expressed in percentage of predicted values. Raw units were expressed as kPa/l/s.

2.2. Echocardiography tests

A complete echocardiography study, including M mode and 2D (left atrium and left ventricular dimensions, with calculation of ejection fraction by the Simpson's rule), Doppler flow (transmitral: *e* and *a* waves, *e*/*a*, deceleration time; aortic velocities) and tissue Doppler (septal and lateral mitral annulus: e', a', e'/a', e/e', systolic velocity) was performed in each patient. All echocardiography measurements were recorded to allow posterior analysis.

2.3. Cardiopulmonary exercise tests

The gas exchange and exercise tolerance of the patients with hyperhidrosis before and after ETS were evaluated with the commercially available cycle ergometer equipment (Sensormedics-Ergometrics 900).

In this protocol, the work rate was increased continuously (ramp) until the maximum, symptom-limited (fatigue, dyspnoea or both) of the patients. The increment in watts/minute was selected according to the maximal work rate expected, considering the age, sex and height of the patient. We determined the heart rate at rest and during exercise.

The parameters analysed were the peak oxygen uptake (peak V_{O_2}), maximal work rate in watts (W_{max}), anaerobic threshold (AT), oxygen uptake at the anaerobic threshold (V_{O_2}/AT), the O_2 pulse, the heart rate at 'rest' and 'peak' (HR and HR 'peak'), the breathing reserve (BR) and the ventilator equivalents for CO_2 (VE/CO_2) and for O_2 (VE/V_{O_2}).

2.4. Statistical analysis

Data are expressed as mean ± SD and were compared with the paired *t*-test. All tests were two tailed.

3. Results

The study population consisted of 28 females and 10 males with an average age of 27.5 years (range: 15—42 years). No complications were recorded in any operated patient during or after surgery and symptoms of palmar and axilar hyperhidrosis disappeared completely after surgery in all subjects.

Table 1
Changes from baseline in lung function tests 6 months after ETS (*$p < 0.05$).

Parameters	Baseline		6 months		Difference			*p*-value
	Mean	SD	Mean	SD	Mean	95% CI		
FVC (%)	106.12	12.5	105.5	13.64	−0.62	−3.01	1.77	0.60
TLC (%)	101.82	9.50	101.6	10.41	−0.20	1.71	1.30	0.78
RV (%)	88.47	8.82	92.47	12.79	4	0.47	7.53	0.02 *
RV/TLC	22.79	4.22	23.59	4.19	0.79	−0.22	1.81	0.12
FEV1 (%)	102.74	11.6	101.5	12.72	−1.20	−3.66	1.25	0.32
FEV1/FVC	85.53	6.26	84.53	6.45	−1	−2.06	0.06	0.06
Raw (kPa/L/s)	0.22	0.10	0.24	0.08	0.02	−0.01	0.05	0.13
FEF 25%	98.65	16.1	96.38	17.56	−2.26	−6.14	1.61	0.24
FEF 50%	92.20	20.9	86.59	19.76	−5.62	−9.18	−2.06	0.003 *
FEF 75%	84.74	24.3	78.76	20.98	−5.97	−10.94	−1.00	0.02 *

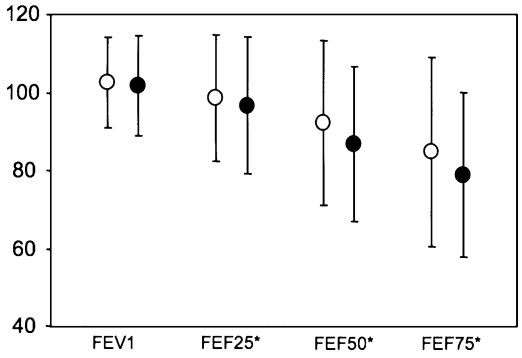

Fig. 1. FEV1, FEF25, FEF50* and FEF75* before ETS (open circles) and 6 months after surgery (closed circles). Units are percentage of predicted values (*$p < 0.05$).

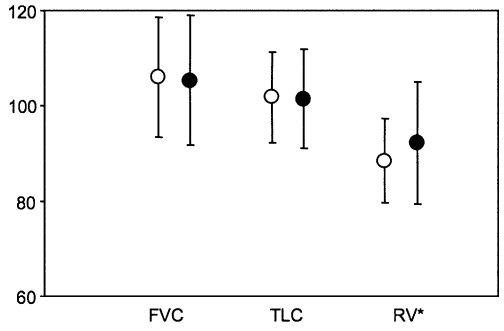

Fig. 2. FVC, TLC and RV* before ETS (open circles) and 6 months after surgery (closed circles). Units are percentage of predicted values (*$p < 0.05$).

The results of PFT (Table 1) revealed a statistically significant decrease of FEF 50% of −5.12 pp (95% confidence interval (CI): −9.18 to −2.06, Fig. 1) and FEF 75% of −5.97 pp (95% CI: −10.94 to −1.00, Fig. 1) and an increase in residual volume of 4 pp (95% CI: 0.47–7.53, Fig. 2) measured 2 weeks before and 6 months after ETS. We did not find any statistical difference after surgery in FEF 25%, FVC, TPC, FEV1, Tiffeneau index, RV/TLC and Raw (Table 1).

Concerning echocardiography tests (Table 2), we did not find statistically significant differences in the parameters analysed by M mode except in the heart rate (−5.15 bpm, 95% CI: −9.63 to −0.67 bpm). Using 2D echocardiography, we observed a statistically significant decrease in ejection fraction of −3.67 pp (95% CI: −1.46 to −5.9 pp, $p < 0.0019$). We did not find statistically significant differences in the other parameters analysed. Using Doppler flow we observed a statistically significant decrease of e/a of −0.28 pp (95% CI: −0.03 to −0.53 pp, $p < 0.029$). We did not find statistically significant differences in the other parameters analysed. In tissue Doppler we did not find statistically significant differences in the parameters analysed.

In cardiopulmonary exercise tests the results before and after ETS are summarised in Table 3. We observed a statistically significant decrease of heart rate at rest of −6.24 pp (95% CI: −2.39 to −10.08 p/m, $p < 0.0023$, Fig. 3) and peak heart rate of −5 pp (95% CI: −2.63 to 7.37 pp, $p < 0.0001$, Fig. 3). Concerning the 'V_{O_2}peak' we observed a statistically significant increase of 4.8 pp (95% CI: 0.29–8.06 pp, $p < 0.0359$, Fig. 4) and a statistically significant increase of O_2/pulse of 9.24 pp (95% CI: 4.79–13.68 pp, $p < 0.0002$, Fig. 4). We did not find any statistically significant differences in AT, V_{O_2}/AT, BR, VE/CO_2 and VE/V_{O_2} and W_{max}.

Table 2
Changes from baseline in M mode echocardiography, two-dimensional (2D), Doppler flow, tissue Doppler tests 6 months after ETS (*$p < 0.05$).

Parameters	Baseline		6 months		Difference			p-value
	Mean	SD	Mean	SD	Mean	95%CI		
M Mode echocardiography								
Heart rate (bpm)	69.85	12.2	64.7	8.74	−5.15	−9.63	−0.67	0.02 *
Left atrium (mm)	33.18	5.04	32.97	4.67	−0.21	−1.38	0.97	0.72
LVEDV (mm)	46.29	7.97	46.59	4.89	0.30	−2.97	3.56	0.85
LVESV (mm)	29.76	5.65	29.5	4.09	−0.26	−2.09	1.56	0.77
IVSd (mm)	7.91	1.29	7.97	1.34	0.06	−0.43	0.55	0.80
LVPWd (mm)	7.73	1.59	9.12	8.32	1.39	−1.36	4.15	0.31
IVSs (mm)	11.23	2.45	11.03	1.98	−0.2	−1.05	0.63	0.62
LVPWs (mm)	13.76	2.29	13.73	1.87	−0.03	−0.85	0.79	0.94
Fractional shortening (%)	39.97	8.78	36.82	4.65	−3.15	−6.61	0.31	0.07
Two-dimensional (2D)								
L.A.	43.26	4.86	43.15	6.1	−0.11	−2.06	1.82	0.90
R.A.	41.26	3.97	40.68	6.03	−0.58	−2.56	1.38	0.54
Ejection fraction (%)	76.23	5.86	72.56	5.16	−3.67	−5.9	−1.46	0.002*
Doppler flow								
e (cm/s)	91.15	15.91	85.47	19.84	−5.68	−12.01	0.66	0.07
a (cm/s)	42.35	9.84	43.88	9.76	1.53	−3.49	6.55	0.53
e/a	2.25	0.60	1.97	0.41	−0.28	−0.53	−0.030	0.03 *
Deceleration time	194.75	64.31	190	44.22	−4.75	−35.35	25.85	0.74
Aortic velocities (cm/s)	122.55	17.69	123.03	24.2	0.48	−7.44	8.41	0.90
Tissue Doppler								
Sistolic velocity	0.10	0.02	0.1	0.02	0.01	0.00	0.02	0.09
e'	0.16	0.03	0.17	0.03	0.01	−0.002	0.2	0.09
a'	0.08	0.01	0.09	0.02	0.00	−0.005	0.01	0.49
e'/a'	1.94	0.47	2.05	0.54	0.11	−0.1	0.32	0.29

Table 3
Changes from baseline in cardiopulmonary exercise tests 6 months after ETS (*$p < 0.05$).

Parameters	Baseline		6 months		Difference			p-value
	Mean	SD	Mean	SD	Mean	95% CI		
Peak V_{O_2} (%)	74.85	14.15	79.03	15.01	4.18	0.29	8.06	0.04 *
W_{max} (%)	80.53	18.10	80.94	15.89	0.41	−2.35	3.17	0.76
AT (%)	45.53	12.73	47.74	12.73	2.20	−0.13	4.54	0.06
V_{O_2}/AT	16	4.58	16.38	4.44	0.38	−0.40	1.15	0.32
O_2 pulse (%)	90.91	19.01	100.15	23.47	9.24	4.79	13.68	0.0002 *
HR (bpm)	84.68	15.01	78.44	14.59	−6.24	−10.08	−2.39	0.002 *
Peak HR (%)	93.18	7.30	88.18	6.15	−5.00	−7.37	−2.63	0.0001 *
BR (%)	44.65	11.63	41.76	14.30	−2.88	−6.94	1.18	0.15
VE/V_{O_2}	30.94	4.65	29.94	4.98	−1.00	−2.38	0.38	0.15
VE/V_{CO_2}	31.32	5.57	30.56	5.19	−0.76	−1.84	0.31	0.15

4. Discussion

In lung function we observed a mean FEF decrease in small airways and a RV increase 6 months after ETS, but we did not observed changes in FEV1, FVC and TLC 6 months after ETS. Noppen and Vincken [7], Noppen et al. [9] and Gonzalez et al. [10] observed changes in these pulmonary volumes in periods varying from 4 weeks to 3 months after ETS, but these changes decreased substantially after 6 months of follow-up. In our opinion, those differences are consequence of the surgical procedure that determine postoperative changes of pulmonary function lasting at least 4 months as demonstrated by Furrer et al. [11]. However, if the modulation of bronchial tone is mainly vagal and, in current opinion, the bronchial adrenergic innervations are sparse or non-existent, how can we explain the pulmonary changes we verified after ETS? It is difficult to explain this ETS-decreased sympathetic bronchial activity relationship as a consequence of T2 and T3 adrenergic pulmonary efferent or afferent section during the surgery, but we can conclude that, probably, the bronchial adrenergic modulation is more important than was previously thought.

Concerning the left ventricular function and myocardial contractility effects after ETS we verified a significant statistically decrease of heart rate, ejection fraction and e/a ratio. The heart rate and ejection fraction decrease are probably the result of a decrease in rest adrenergic activity. The e/a ratio decrease is probably a consequence of a mild alteration of diastolic relaxation, caused by decreased heart rate after ETS. Nevertheless, the echocardiography differences before and after surgery does not seem to suggest significant cardiac function effects after ETS. It is difficult to explain these results as a consequence of cardiac adrenergic efferent section, considering the anatomic variability of the cardiac sympathetic efferent innervations of T2 and T3 ganglions, which are usually rare [12–14]. Based on the work of Malliani, Ruscone and Bishop who demonstrated in their experimental works the importance of cardiac sympathetic afferents in the autonomic modulation of the heart, we considered the hypothesis that it could be a consequence of cardiac adrenergic afferent section [15–18].

In the cardiopulmonary exercise effects after ETS we verified a decrease in 'rest' and 'peak' heart rate, suggesting a decreased adrenergic activity, and an increase in oxygen pulse caused by the negative chronotrophic effect after ETS, already verified by other authors [8,9]. However, the increase of the oxygen 'peak' uptake (V_{O_2} 'peak') demonstrated in our investigation is, to our knowledge, the first report in the literature assessing the ETS cardiopulmonary effects in PH patients. On the other hand, we did not observe any increase in work rate and therefore we concluded that the V_{O_2} peak increase was 'not efficient', without chemical or mechanical energy production.

The increase in V_{O_2} peak is not caused by increased ventilation, because the mean forced expiratory flow decreased, and also because we did not observe any changes regarding the ventilatory reserve and the respiratory efficiency (VE/V_{O_2}). These facts exclude a better external respiration as a cause of the V_{O_2} peak increase demonstrated in this investigation. There is no evidence suggesting that the

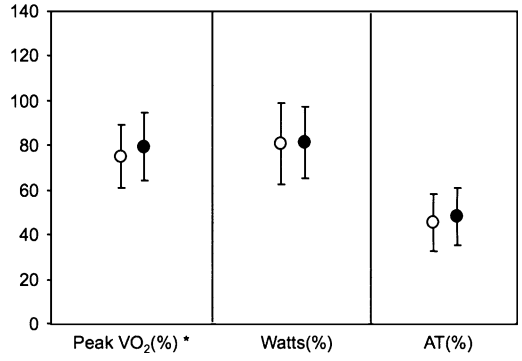

Fig. 3. Peak V_{O_2}*, Watts and AT* before ETS (open circles) and 6 months after surgery (closed circles). Units are percentage of predicted values (*$p < 0.05$).

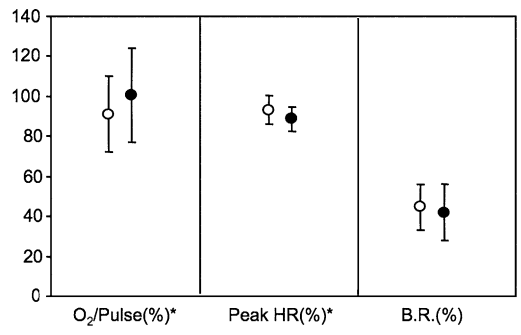

Fig. 4. O_2/pulse*, peak HR* and BR before ETS (open circles) and 6 months after surgery (closed circles). Units are percentage of predicted values (*$p < 0.05$).

V_{O_2} increase could be the result of a possible cardiac output increase and, in fact, we observed a decrease in the ejection fraction.

The theoretical increase of nitric oxide (NO) after ETS [19,20] and the NO capacity of blunting alpha-adrenergic vasoconstriction in contracting skeletal muscles during the maximal exercise, the functional sympatholysis, could be a consistent explanation of the V_{O_2} peak increase, but we cannot prove this hypothesis [21—25].

In summary, based on the anatomical variability of the cardiac sympathetic efferent innervations of T2 and T3 ganglions that usually are rare and the supposedly sparse or non-existent adrenergic bronchial activity, it is difficult to explain these results suggesting a decreased adrenergic activity, as a consequence of adrenergic efferent section [12—14]. We cannot explain the pulmonary effects, but we consider the hypothesis that the bronchial adrenergic modulation is more important that we thought before.

Concerning the cardiac effects, also suggesting a decreased adrenergic activity, the hypothesis that they could be a consequence of cardiac adrenergic afferent section must be investigated.

It is important to underline that our study population composed of patients already suffering from an autonomic dysfunction disorder and this means that our sample has specific clinical characteristics, which makes us believe that the observed cardiac effects in PH patients of ETS probably would not be observed in healthy individuals.

5. Conclusions

In conclusion, the cardio pulmonary effects in primary hyperhidrosis patients after ETS are all in normal ranges and are not relevant in cardiopulmonary function. We concluded that ETS in patients with PH is a safe procedure. Patients must be informed about these cardiopulmonary effects before the operation.

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Appendix A. Conference discussion

Dr C. Choong (*Cambridge, United Kingdom*): I have two quick questions. First, do you think that the changes are clinically relevant? In other words, did your patients report difficulty in breathing or they are more tired? Do you think it's clinically relevant in terms of the findings? I know you found statistical significance; however, whether they are clinically relevant I think is very important too. That's question number one.

The second question is, based on your findings, have you changed or altered your surgical techniques at all?

Dr Cruz: No. The changes are all within normal values. We haven't seen any difference in the patients clinically. But I think that if you have a patient with asthma, you must be careful. You must clearly study the patient. If he's in stage I, you probably don't have any problem. I myself operated some patients with mild or moderate asthma. But if you have patients with serious asthma, I wouldn't say you should operate.

Yes, now I'm doing another technique, but this is not as a result of this investigation because I consider that this is safe. We all suspected that there were cardiac and pulmonary changes because everybody who performs sympathectomy knows that the patients are more bradycardic. So you must have some changes. Now I sometimes operate the third and the fourth, but this is not for this work. I do sympathectomies very often and I'm worried about

compensatory hyperhidrosis and my change of technique has to do with that. I don't know if you have a better result in terms of the complications, especially compensatory hyperhidrosis, but it's not for that. You can do the T2 and T3 operation without problems.

Dr R. Cerfolio (*Birmingham, Alabama, USA*): To go back to that question, have you noticed a difference on where you interrupt the chain and to what degree you get bradycardia or change in EF? So when you operate on someone, let's just say their hands are hyperhidrotic, where would you interrupt the chain for just hands?

Dr Cruz: I'm sorry, can you repeat?

Dr Cerfolio: Yes. Two questions. One, is there a difference in your level of bradycardia based on the number of interruptions of the chain or where you interrupt the chain? And I want to know where you are doing your sympathectomy, because we all do it a little bit differently, and even our definitions are different.

Dr Cruz: Yes. There are some works that pointed to that. If there is a difference in the number of ganglions, you do the ablation or the excision, and some authors have found a correlation between the number of ganglions we excise and the changes you can verify. But I didn't see that. I began to do the excision of the third and the fourth recently and I can't say that I see any difference for that.

Dr Cerfolio: So when you say the third, you mean you're going at the third rib and you're just interrupting the chain just below the third rib or on top of the third rib?

Dr Cruz: On top of the third to do the ablation of the third and the fourth.

Dr Cerfolio: So on top of the third rib and on top of the fourth rib?

Dr Cruz: No. On the top of the fifth rib.

Dr Cerfolio: And if they have an axillary component, do you go a little bit lower on the fourth rib?

Dr Cruz: No. On the top of the fifth rib.

Dr Cerfolio: Same operation?

Dr Cruz: Yes, I do the same.

Dr T. Dosios (*Athens, Greece*): There is no doubt that there is an effect of sympathectomy on the cardiovascular system. We tried to investigate the effect of sympathectomy on the mechanical properties of the aorta and the histology of the aorta. We performed a series of experiments in pigs and we performed bilateral sympathectomy from T2 to T5. We sacrificed the animals 2 months later and we found that the aorta has less elasticity; that is, the aorta is more stiff and loses the elastin histologically and increases the collagen. This means that definitely the sympathectomy has an effect on the cardiovascular system, and not only on these factors you described, but also on the mechanical properties of the vessels.

Dr Cruz: Yes, I agree with you. I didn't talk about that because it is not published, but I also studied in these patients the cardiac autonomic control, and I have utilized in all the patients a study of heart rate variability with 24-h Holter recordings before and after surgery, and I noticed that we demonstrated clearly in frequency and time that there was a clear decrease of adrenergic activity and a clear increase of vagal activity. This paper has already been accepted and will also be published in the Journal of Thoracic and Cardiovascular Surgery.