Evaluation of cardiac sympathetic nerve function by myocardial 123I-metaiodobenzylguanidine scintigraphy before and after endoscopic sympathectomy

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Object. The purpose of this study was to analyze the change in cardiac sympathetic function by performing a 123I-metaiodobenzylguanidine (MIBG) imaging study after endoscopic upper thoracic sympathectomy (EUTS) in patients with palmar hyperhidrosis before and after surgery.

Methods. Between February 1999 and February 2002, 135 patients underwent bilateral EUTS to treat palmar hyperhidrosis. Between September 2001 and February 2002, 12 of these consecutively enrolled patients were also included in a 123I-MIBG imaging study. These patients underwent cardiac 123I-MIBG imaging 1 day before and 7 days after they had undergone EUTS. The heart/mediastinum (H/M) ratio and the washout rate were calculated for both early and late phases, and single-photon emission computed tomography (SPECT) imaging of the early phase was performed.

Excessive perspiration from the palms disappeared immediately after EUTS in all patients, and they showed no symptoms of a circulatory condition following the procedure. On the 123I-MIBG imaging studies, the early H/M ratio before EUTS was 2.35 ± 0.26 and postoperatively it was 2.29 ± 0.23. The delayed H/M ratio before EUTS was 2.59 ± 0.3 and after the procedure it was 2.66 ± 0.27. There was no significant difference between the H/M ratio before and after EUTS.

The washout rate after EUTS (14.27 ± 4.71%) was significantly lower than that measured before EUTS (18.36 ± 5.13%; \( p < 0.01 \)). No apparent local defects of accumulation of MIBG were found on SPECT images obtained post-EUTS.

Conclusions. Endoscopic upper thoracic sympathectomy is a minimally invasive procedure; no local denervation was found after EUTS. Findings on 123I-MIBG imaging studies indicate that EUTS suppresses the activation of the sympathetic nervous system slightly, similar to beta-blocker therapy.

Key Words • hyperhidrosis • sympathectomy • cardiac sympathetic function • 123I-metaiodobenzylguanidine imaging study

Endoscopic upper thoracic sympathectomy is a minimally invasive procedure that is performed for thoracic sympathetic blockage and has been used for hyperhidrosis of the palm, peripheral vascular insufficiency, and Raynaud phenomenon. Because the cardiac autonomic nervous system can be influenced to a certain degree by the upper thoracic sympathetic nerve, the effect of EUTS on the heart has been closely investigated. Recently, a norepinephrine analog, MIBG, has become available. This MIBG accumulates in the endings of sympathetic nerves through a type 1 uptake mechanism and reflects the function of the cardiac sympathetic nerve. To assess the effect of EUTS on cardiac sympathetic nerve function, a myocardial 123I-MIBG scintigraphy study was performed on patients with essential hyperhidrosis before and after they underwent EUTS.

Materials and Methods

Patient Population

Between September 1998 and February 2002, 135 patients (63 men and 72 women, with a mean age of 24.5 ± 9.5 years) underwent EUTS to treat bilateral hyperhidrosis. Of all these patients, 12 consecutively enrolled patients (five men and seven women with a mean age of 26.5 ± 11.6 years) were selected for the 123I-MIBG imaging study, which took place between September 2001 and February 2002. All patients were well informed about these procedures and consented to participate in this study. None of the patients had a medical history or clinical signs indicative of any cardiac or pulmonary disease.

Symptom Assessment

All patients were interviewed and asked whether they experienced symptoms of a circulatory condition (palpitations, subjective arrhythmia, chest pain, or breathlessness in response to exercise during their daily life), compensatory hyperhidrosis, or Horner syndrome during a postoperative follow-up period by an independent observer who was not involved in the treatment.

Perspiration in nondenervated portions of the body, mostly over the trunk and upper thighs, after EUTS was defined as compensatory hyperhidrosis. Compensatory hyperhidrosis was graded in the following manner: severe (patients who experienced disabling perspiration that required changes of clothing throughout the day during a postoperative follow-up period); and mild (patients who did not experience disabling perspiration).

The EUTS Procedure

A brief description of the EUTS procedure following the patient follows. The patient was placed in a semisitting position. After single-lumen endotracheal intubation and the induction of general anes-
thesis, a small incision was made on the preaxillary line at the second intercostal space. After the pleural cavity had been entered, a thoracoscope was inserted. The pleural cavity was inflated with air, causing the lung to collapse gradually, and the upper ribs were identified. Once the sympathetic nerve trunk overlying the pleura close to the neck of the ribs had been identified, laser radiation was used for the ablation of the targeted T2–4 ganglia. After successful sympathectomy, the collapsed lung was reinflated and the gas in the pleural cavity was released through the endoscope. Following evacuation of the gas, the wound was closed without an insertion of drainage tubes. The same procedure was then repeated on the contralateral side.

Myocardial \textsuperscript{123}I-MIBG Imaging Study

Twelve patients underwent cardiac \textsuperscript{123}I-MIBG imaging 1 day before and 7 days after the EUTS. Anterior planar imaging was performed 30 minutes after (early imaging) and 3 hours after (delayed imaging) the injection of 111 MBq of \textsuperscript{123}I-MIBG. The H/M ratio was calculated as the ratio between the mean count in the region of interest surrounding the entire left ventricular region and the mean count in the region of interest in the upper mediastinum; this was used as an index of myocardial MIBG uptake on early and delayed anterior images.

The washout rate was obtained as follows: washout rate = \[\frac{H_{\text{initial}} - H_{\text{delayed}}}{H_{\text{initial}}}\] where $H_{\text{initial}}$ is the initial averaged heart pixel count and $H_{\text{delayed}}$ is the delayed averaged heart pixel count.

A triple-headed SPECT system (Neurocam; General Electric Medical Systems, Milwaukee, WI) with low-energy parallel hole collimators was used to perform SPECT imaging in all patients to obtain early short-axis images and early long-axis images. Accumulation of \textsuperscript{123}I-MIBG was visually graded as absent, severely reduced, reduced, or normal by three independent observers who were unaware of the data on individual patients.

Statistical Analysis

All data are expressed as means $\pm$ standard deviations. The Student paired t-test was used for comparisons of the H/M ratio and washout rate before and after EUTS. Differences were considered significant at a probability level lower than 0.05.

Results

Postoperative Course

Excessive perspiration from the palms disappeared immediately after EUTS in all 135 patients. No symptoms of a circulatory condition were identified in these patients during a mean postoperative follow-up period of 18 months (range 6–48 months). Compensatory hyperhidrosis after EUTS was observed in 87 patients, 85 of whom considered it to be mild and two of whom considered it to be severe. There was no development of Horner syndrome in any patient. Four patients required a chest tube because of pneumothorax and two patients experienced recurrent hyperhidrosis during the follow-up period (Table 1). Nevertheless, more than 95% of the patients were satisfied with their treatment, and stated that they would undergo the procedure again in similar circumstances, given the option.

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>symptom(s) of a circulatory condition</td>
<td>0 (0)</td>
</tr>
<tr>
<td>compensatory hyperhidrosis</td>
<td></td>
</tr>
<tr>
<td>mild</td>
<td>85 (63)</td>
</tr>
<tr>
<td>severe</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>pneumothorax requiring postop</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Horner syndrome</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

FIG. 1. Graphs showing changes in \textsuperscript{123}I-MIBG imaging parameters before and after EUTS. NS = not significant.
discovered on early short-axis images and early long-axis images before and after EUTS by three dependent observers who were unaware of individual patient data (Fig. 2).

Discussion

Endoscopic upper thoracic sympathectomy for hyperhidrosis can be performed using a number of surgical approaches. Traditionally, this procedure was performed via an open thoracic approach through the supraclavicular, transaxillary, or posterior pathways. These open procedures were associated with significant tissue trauma and postoperative pain, however, and were therefore only performed very selectively. The development of the minimally invasive thoracoscopic technique, which is associated with minimal postoperative pain, rapid recovery, and excellent cosmetic results, has led to a renewed interest in the treatment of hyperhidrosis by transection of the sympathetic nerve chain.

The EUTS procedure has been associated with a high success rate (> 90%) in decreasing hyperhidrosis in many studies including this one. The standard procedure of EUTS performed in patients with hyperhidrosis involves resection of the T-2 and T-3 sympathetic ganglia, as well as the T-4 ganglia, and many surgeons, including us, prefer resecting the T2–4 sympathetic ganglia because it has been suggested that the severity of the compensatory hyperhidrosis is correlated with the extent of the sympathectomy. The level at which the sympathectomy should be performed is not yet well established.

Sympathetic cardiopulmonary nerves arise from the cervical sympathetic nerve trunks and travel alongside the great arteries to innervate the ventricles. It has been suggested that EUTS affects the autonomic cardiocirculatory function because the T-2, T-3, and T-4 ganglia are in the direct path of the sympathetic innervation of the heart. Indeed, some authors have reported that the heart rate decreases after EUTS. After this procedure, the heart rate is usually slightly reduced, although one case has been reported in which the patient presented with intractable bradycardia with permanent pacing. It has been reported that influences on the cardiac autonomic nerve in patients without cardiac disease were less at rest, despite the suppressed response to sympathetic stimulation after surgery. Jeng and colleagues reported that there is a significant reduction in the diastolic pressure after EUTS, but not in the systolic pressure or in the heart rate. Using Holter electrocardiographic recordings, Abraham, et al., recently reported that the heart rate was significantly decreased after bilateral EUTS and cautioned that patients should be informed of the bradycardia that can result from sympathectomy. These authors also showed that there was no decrease in the heart rate after unilateral right-sided EUTS. We therefore believe that careful monitoring is necessary after bilateral EUTS in a patient with cardiac disease.

Metaiodobenzylguanidine is a guanethidine analog that accumulates in the norepinephrine storage granules of postganglionic sympathetic neurons. Radiolabeling of MIBG

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Fig. 2. Four 123I-MIBG SPECT images obtained in a 24-year-old woman with palmar hyperhidrosis who had undergone EUTS. No local defects of MIBG accumulation were found on the early short-axis image or on the long-axis image obtained before and after the procedure. Upper Left: Early short-axis image obtained before EUTS. Lower Left: Long-axis image obtained before EUTS. Upper Right: Short-axis image obtained after EUTS. Lower Right: Long-axis image obtained after EUTS.
allows visualization of functioning sympathetic nerve tissue in richly innervated organs such as the heart. To date, 123I-MIBG has been used in various physiological and pathological states to determine cardiac adrenergic activity, however, there has been little reference to the effect of EUTS on cardiac sympathetic nerve function evaluated by myocardial 123I-MIBG scintigraphy in the literature.

Cardiac sympathetic innervation is usually evaluated by determining the H/M ratio. Findings on images obtained during the 1st 30 minutes after injection of 123I-MIBG mainly reflect nonneuronal uptake, whereas findings on delayed images obtained 4 hours postinjection reflect cardiac sympathetic innervation. Dae, et al. reported finding negligible MIBG uptake in transplanted and denervated hearts on early images. Authors of previous reports have noted that 123I-MIBG washout from the heart commences 3 minutes postinjection. These findings support the concept that early images obtained at 30 minutes postinjection demonstrate neuronal uptake in the early phase.

The tracer washout rate reflects a spillover of norepinephrine into plasma and is thought to be an indicator of the excitation of adrenergic nerve activity, that is, the activation of the sympathetic nervous system. It has been suggested that a reduction in sympathetic nervous system activity causes a decrease in the washout rate. In the group of patients with dilated cardiomyopathy, the delayed H/M ratio is low and the washout rate in this group high; the delayed H/M ratio increases and the washout rate decreases in response to beta-blocker therapy. Therefore the H/M ratio and washout of tracer measured using 123I-MIBG scintigraphy are useful for examining the severity of dilated cardiomyopathy and determining the applicability of beta-blocker therapy. Even in patients with other diseases, such as diabetes mellitus, essential hypertension, and congenital long QT syndrome, 123I-MIBG scintigraphy can be used to evaluate the severity of the disease and the effectiveness of the therapy. In this study, 123I-MIBG SPECT images demonstrated no defects and the H/M ratio indicated no significant changes made by EUTS. These results indicate that the EUTS did not cause denervation and that cardiac sympathetic innervation was fully maintained. In our study, the washout rate was significantly decreased by the EUTS, probably due to the calming of adrenergic nerve activity. The decrease in the washout rate caused by EUTS in this study is similar to the effect of beta-blocker therapy. Noppen, et al. reported that patients with hyperhidrosis exhibit overfunctioning of the sympathetic nervous system and that EUTS corrects this hyperfunction and produces a partial beta blocker–like activity. Indeed, recently, EUTS has been performed for severe angina and for long QT syndrome. Wettervik, et al. have concluded that EUTS can be performed without major complications, alleviates angina, and increases the maximum working capacity in patients with advanced coronary disease. Reardon and colleagues have recommended a combination of EUTS and astellate ganglion block for the treatment of long QT syndrome. If additional studies of the change in cardiac sympathetic nerve function are advanced, the indication of EUTS for a variety of diseases requiring beta-blocker therapy may be supported.

In this study, we could not compare the sympathetic nerve activity of patients before EUTS with that of healthy individuals because we did not perform a control study with healthy volunteers. Compared with results obtained in healthy volunteers in past studies the H/M ratio and the washout rate obtained before EUTS in this study do not appear to differ.

Conclusions

We believe that EUTS is an effective therapy for essential hyperhidrosis; it is also a safe method for thoracic sympathetic nerve blockage, as shown by the absence of local denervation after the procedure. On the basis of 123I-MIBG imaging studies we suggest that EUTS suppresses the excitation of adrenergic nerve activity slightly, as does beta-blocker therapy.

References

16. Lai CL, Chen WJ, Liu YB, et al: Bradycardia and permanent pac-


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