Efficacy of Percutaneous Radiofrequency Sympathectomy Versus Percutaneous Ethanol Sympatholysis in the Treatment of Primary Hyperhidrosis

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Background: At present, there are many surgical treatments for primary hyperhidrosis (PH), but their medium- and long-term effects remain unclear.

Objectives: To evaluate and compare the efficacy of radiofrequency sympathectomy (RFS) and percutaneous ethanol sympatholysis (PES) in the treatment of PH.

Study Design: A retrospective study.

Setting: This study was performed at the Affiliated Hospital of Jiaxing University, China.

Methods: Patients who underwent RFS and PES at The First Affiliated Hospital of Jiaxing University for PH were retrospectively reviewed from January 2016 through December 2018 and were divided into an RFS group and a PES group. The Hyperhidrosis Disease Severity Scale was evaluated at the following time points: before the operation, immediately after the operation, 12 months and 24 months after the operation. The effective rate, patient satisfaction, and compensatory hyperhidrosis were also evaluated.

Results: A total of 94 patients diagnosed with primary hyperhidrosis were included (RFS group, n = 45; PES group, n = 49). RFS yielded a postprocedure 24-month effective rate of 53.33% in treating hyperhidrosis compared to PES (24.49%, P < 0.05). There were no significant differences between the 2 groups regarding patient satisfaction (P = 0.927) and compensatory hyperhidrosis (P = 0.711).

Limitations: This was a single-center study.

Conclusion: This is the first clinical study to evaluate the efficacy of RFS and compare it with PES in treating primary hyperhidrosis. RFS significantly decreased hyperhidrosis and had a higher 2-year effective rate compared to PES.

Key words: Primary hyperhidrosis, percutaneous ethanol sympatholysis, radiofrequency sympathectomy, compensatory hyperhidrosis

Primary hyperhidrosis (PH) is a chronic disorder characterized by excessive sweating in certain body regions, including the head; palm; armpit; chest and back; and the soles of the feet, seriously affecting the quality of life (1-3). A diagnosis of hyperhidrosis is made when excessive sweating lasts for more than 6 months and 2 or more of the following criteria are met: excessive sweating more than once per week, under the age of 25, a family history of hyperhidrosis, bilateral and symmetric sweating, nonsweating during sleep, and severely interfered daily activities due to sweating (4). Most people begin to sweat excessively in childhood, and it intensifies with hormonal changes at puberty into sexual maturity.
This is the natural history of hyperhidrosis, but the exact cause is still unknown. One possible etiology has been attributed to functional impairment of the sympathetic nervous system.

Nonoperative treatment for PH includes iontophoresis, local application of aluminum salts, and anticholinergic drug usage. However, these measures are not to be permanently applied as they provide only partial and temporary relief (6). Currently, the gold standard treatment for severe PH cases is surgical resection of the sympathetic chain through video-assisted thorascopic surgery. However, sympathectomy is associated with a high incidence of complications, the most common of which is hyperhidrosis in previously unaffected areas, known as compensatory hyperhidrosis (CH). Up to 80% of the cases of CH occur after sympathectomy (7). Therefore, surgery is usually the last option in the treatment of hyperhidrosis (8); less invasive, safer, and more effective treatments are still sought.

Percutaneous radiofrequency sympathectomy (RFS) and percutaneous ethanol sympatholysis (PES) are regarded as safe and effective procedures for treating primary hyperhidrosis (9,10). In most cases, it is possible to tailor the therapy to each individual patient, achieving a satisfactory outcome (1). In order to improve prognosis, many researchers have searched for possible predictive factors that would indicate better surgical outcomes. The purpose of this study was to analyze the effects of the 2 surgical treatments on patients with PH, in order to provide them with better treatment options and reference for clinical practice.

METHODS

Clinical Data
We retrospectively reviewed the information of 94 patients who underwent PES or RFS for primary hyperhidrosis from January 2016 through December 2018 in the pain department of our hospital. After Institutional Review Board approval, data were collected from medical records. The requirement for informed consent was waived in view of the retrospective design of the study.

Inclusion and Exclusion Criteria

Inclusion Criteria:
1) The patients met the clinical diagnostic criteria of primary hyperhidrosis; 2) The age of the patients was greater than and/or equal to 14 years; and 3) The patients underwent RFS or PES.

Exclusion Criteria
1) Patients who had received immunosuppressive therapy; 2) Uncooperative patients or those with mental illness, intellectual disability, or confusion; 3) Patients who had severe liver, kidney, heart, or lung diseases; 4) Patients that study conductors lacked basic information about and could not be followed up after the operation.

Patients were selected according to the inclusion and exclusion criteria, and all patients were divided into either the RFS group (n = 45) or the PES group (n = 49) by reviewing their intraoperative imaging data.

Follow-up
The baseline data characteristics included age, gender, family history, main site, palmar plus, craniofacial region, and preoperative Hyperhidrosis Disease Severity Scale (HDSS). The primary outcome was the postprocedure 24-month effective rate. The severity of hyperhidrosis was evaluated with the Hyperhidrosis Disease Severity Scale (HDSS) questionnaire. The postoperative data included effective rate, patient satisfaction, CH, and HDSS score 12 months and 24 months postoperation, all of which were evaluated by telephone follow-up.

The questionnaire consisted of 4 statements. Each was scored from one to 4, with one being the mildest degree and 4 being the worst grade (11). The secondary outcomes included incidence of compensation and the patient satisfaction score. Patient satisfaction was scored into 3 grades: 8–10 highly satisfied, 5–7 satisfied, and 1–4 dissatisfied.

Surgical Methods

Percutaneous Ethanol Sympatholysis
After an 8-hour fast, the patient was admitted to the operating room, venous access was opened, and SPO2 and noninvasive blood pressure were monitored. The patient lay prone on the treatment bed with a soft pillow under the abdomen to keep the patient in a comfortable position. Then the surgeon performed a chest computed tomography (CT) scan with a 3 mm slice distance. After scanning, the optimal puncture surface and skin puncture point were selected, the puncture path was drawn by software (Vitrea version:4.0.693), the puncture depth and angle were determined, and the body surface puncture point was marked with infrared ray. After disinfection, a No. 7 blunt needle was inserted according to the proposed puncture path under the guidance of CT, and...
the needle slowly entered the anterolateral margin of the vertebral body through the T3-T4 paraspinal space. After confirming that the needle was not in the blood vessels or the chest, the test dose of 1% lidocaine + 30% iohexol was injected through the puncture needle, and the surgeon observed the distribution of the mixture. Sitting for 15 minutes, after the mixture was completely absorbed, about 4 mL 90% ethanol (containing 3.5 mL of absolute ethanol and 0.5 mL of 30% iohexol) was injected into the left and right sides respectively. After injection, another chest CT scan showed that the solution was confined to the anterolateral side of the target vertebral body (10) (Figs. 1A, 1B). Finally, the surgeon removed the puncture needle and applied an adhesive bandage topically to the puncture point. After vital signs showed the patient to be stable, the patient was safely sent back to the ward.

Radiofrequency Sympathectomy (RFS)

The preoperative procedure and the insertion of the needle into the anterolateral margin of the vertebral body were performed as described above. Then the surgeon pulled out the needle core and inserted the matching electrode along the intubation. The position of the RF tip was determined by sensory and motor electrical stimulation tests, and the RF parameters were set to 90°C for 120 seconds (12-14). After treatment, the RF electrode and puncture needle were taken out, and an adhesive bandage was locally affixed to the puncture point. The patient safely returned to the ward after showing stable vital signs (Fig. 1C).

Power of the Study

Analysis of the clinical data of the patients show that the postprocedure 2-year effective rate was 24.49% for the PFS group and 53.33% for the RFS group. The power of the study was estimated to be 80%, with a 95%CI and a 2-sided Type I error of 5%. Therefore, the present study required 44 patients in each group. To compensate for patients who might be lost to follow-up, 94 patients were reviewed for the 2 groups. Among them, 49 patients were included in the PES group and 45 patients were in the RFS group.

Statistical Analysis

Statistical analyses were conducted using SPSS 25.0 (IBM). The normality of the distribution of data was tested by Kolmogorov-Smirnov test. The variables with nonnormal distribution were presented by median (quartile spacing) and were compared by the Mann-Whitney U test. The variables with normal distribution were analyzed and compared by one-way analysis of variance (ANOVA) and the values were expressed as mean ± SD. The analysis of effective rate was performed using the Pearson’s χ²-squared test. Bilateral P < 0.05 indicated that the difference was statistically significant.

RESULTS

Patients’ Data Characteristics

A total of 94 patients were diagnosed with primary hyperhidrosis during the study period. According to the different surgical methods, they were divided into 2 groups: RFS (n = 45) and PES (n = 49).

The patients’ characteristics in both groups are summarized in Table 1. Family history was elicited in 20 of 94 patients (21.3%). The mean age of the enrolled patients was 28.53 ± 11.27. Demographic data, including age and gender, indicated no significant differences between the 2 groups (P (age) = 0.214; P (gender) = 0.811). A

Fig. 1. Computed Tomography (CT) example images of percutaneous puncture thoracic blockade. A: The puncture needle is in place. B: CT scan – the red arrow displays the ideal liquid distribution of lidocaine and iohexol. The contrast agents are distributed in the compartment of the anterior part of the rib head on the outer surface of the pleura displayed by 3-dimensional reconstruction during percutaneous sympathectomy. C: Lateral intraoperative fluoroscopic view, exhibiting the cannula position (white arrow). The sympathetic ganglia are not visible on CT.
A comparison of these 2 groups showed no significant differences in family history, main site, course, and HDSS preprocedure ($P_{(\text{family history})} = 0.429$, $P_{(\text{main site})} = 0.179$, $P_{(\text{course})} = 0.539$, $P_{(\text{HDSS preprocedure})} = 0.242$).

**Analysis of HDSS**

**Analysis of the HDSS Score in the RFS Group**
The preoperative and postoperative one-day, one-year and 2-year HDSS scores in the RFS group are shown in Table 2. The postoperative HDSS score at each time point was lower than prior to the operation. The difference was significant ($P_{(1 \text{ day})} < 0.001$, $P_{(1 \text{ year})} < 0.001$, $P_{(2 \text{ years})} < 0.001$).

**Analysis of the HDSS Score in the PES Group**
The preoperative and postoperative one-day, one-year and 2-year HDSS scores in the PES group are shown in Table 2. The postoperative HDSS score at each time point was lower than prior to the operation. The difference was significant ($P_{(1 \text{ day})} < 0.001$, $P_{(1 \text{ year})} < 0.001$, $P_{(2 \text{ years})} = 0.006$).

**Analysis of HDSS Scores Between the RFS and PES Groups**
No significant differences were noted in the HDSS scores between the RFS and PES groups prior to the operation and one day, one year and 2 years following the operation ($P_{(\text{before operation})} = 0.234$, $P_{(1 \text{ day})} = 0.732$, $P_{(1 \text{ year})} = 0.381$, $P_{(2 \text{ years})} = 0.173$).

In our follow-up results, in each group the hyperhidrosis symptom was significantly relieved after their respective operation compared with the preoperation symptom. However, there was no statistically significant difference in the scores of hyperhidrosis symptoms at each time point when comparing the 2 operations.

**Analysis of Follow-up Data Between the Groups**
Based on the follow-up data in Table 3, RFS successfully treated 75.56% of patients with hyperhidrosis, which was higher than the PES success rate (73.47%). Meanwhile, RFS had a higher postprocedure 2-year effective rate compared to PES ($P = 0.004$).

Patient satisfaction and occurrence of compensatory hyperhidrosis were similar in both groups ($P_{(\text{satisfaction})} = 0.927$, $P_{(\text{compensatory hyperhidrosis})} = 0.711$). We found no significant difference between RFS and PES for the treatment of primary palmar hyperhidrosis in terms of initial surgery results, compensatory hyperhidrosis, and patient satisfaction (Table 3).

**DISCUSSION**
This is the first clinical study to evaluate the role of radiofrequency sympathectomy and compare it with the percutaneous ethanol sympatholysis treatment option in primary hyperhidrosis.

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**Table 1. Basic characteristics of hyperhidrosis patients.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>RFS</th>
<th>PES</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean ± SD)</td>
<td>30.0 ± 12.5</td>
<td>27.1 ± 10.0</td>
<td>0.214</td>
</tr>
<tr>
<td>Age, group (n, %)</td>
<td>0.228</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>9 (20.0)</td>
<td>14 (28.6)</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>20 (44.4)</td>
<td>19 (38.8)</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>6 (13.3)</td>
<td>10 (20.4)</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>4 (8.9)</td>
<td>5 (10.2)</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>6 (13.3)</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Gender (n, %)</td>
<td></td>
<td>0.811</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>20 (44.4)</td>
<td>24 (49.0)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>25 (55.6)</td>
<td>25 (51.0)</td>
<td></td>
</tr>
<tr>
<td>Family history (n, %)</td>
<td>12 (24.5)</td>
<td>8 (16.3)</td>
<td>0.429</td>
</tr>
<tr>
<td>Main site (n, %)</td>
<td></td>
<td>0.179</td>
<td></td>
</tr>
<tr>
<td>Palmar</td>
<td>10 (22.2)</td>
<td>19 (38.8)</td>
<td></td>
</tr>
<tr>
<td>Planter</td>
<td>1 (2.2)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Craniofacial region (n, %)</td>
<td>11 (24.4)</td>
<td>9 (18.5)</td>
<td></td>
</tr>
<tr>
<td>Course (n, %)</td>
<td></td>
<td>0.953</td>
<td></td>
</tr>
<tr>
<td>0-10</td>
<td>20 (44.4)</td>
<td>19 (38.8)</td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>19 (42.2)</td>
<td>22 (44.9)</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>5 (11.1)</td>
<td>6 (12.2)</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>1 (2.2)</td>
<td>2 (4.1)</td>
<td></td>
</tr>
<tr>
<td>HDSS score preprocedure (mean ± SD)</td>
<td>3.42 ± 0.58</td>
<td>3.29 ± 0.54</td>
<td>0.243</td>
</tr>
</tbody>
</table>

**Table 2. Differences in the HDSS scores during long-term follow-up.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Before Operation</th>
<th>One Day After Operation</th>
<th>One Year After Operation</th>
<th>2 years After Operation</th>
<th>Comparison within groups</th>
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<tr>
<td>RFS</td>
<td>3.42 ± 0.58</td>
<td>1.87 ± 1.06</td>
<td>2.18 ± 1.09</td>
<td>2.62 ± 0.94</td>
<td>$&lt;0.001 &lt;0.001 &lt;0.001$</td>
</tr>
<tr>
<td>PES</td>
<td>3.29 ± 0.54</td>
<td>1.94 ± 0.97</td>
<td>2.37 ± 0.99</td>
<td>2.88 ± 0.86</td>
<td>$&lt;0.001 &lt;0.001 0.006$</td>
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</tr>
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In the follow-up data, younger people (aged from 10 to 30) accounted for 66% of the total number of included patients, indicating that this population is more likely to seek treatment for hyperhidrosis. Earlier studies have established the relationship between age and the effects of sympathectomy in treating hyperhidrosis, suggesting the older the better (15). This may explain why the improvement rate of hyperhidrosis in this cohort was lower than that reported in the literature.

Regardless of gender, the quality of life of patients with hand hyperhidrosis improved after video-assisted thoracoscopic surgery. No significant difference was detected in the proportion of men and women patients, which may indicate that there was no particularly obvious gender tendency for hyperhidrosis susceptibility. It is worth noting that in our follow-up conversation, some patients mentioned the problem of postoperative pain, which lasted for a short time and basically disappeared one day after the operation, without a serious impact. This was not included in these results.

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In general, both RFS and PES therapy successfully stopped refractory hyperhidrosis. In both the RFS and PES groups, significant decreases were established in the HDSS scores 2 years after the treatment, compared with the scores recorded before the treatment. We found no significant difference between RFS and PES for the treatment of primary hyperhidrosis in terms of initial surgery outcomes, complications, and patient satisfaction.

Compensatory hyperhidrosis is the most common side effect of surgery, and its pathogenesis is not clear. Researchers have proposed a mechanism for the production of growth hormone, according to which the negative feedback responsible for inhibiting sweating was blocked in the hypothalamus. The incidence of compensatory hyperhidrosis reported in the literature ranges from 60% to 90% (16). In our study, the incidence of compensatory hyperhidrosis was 53.3% in the RFS group and PES group, respectively, which was relatively lower than the results previously reported. This might be due to the selection of lower level paravertebral spaces for sympathectomy in our study (T4) compared to higher levels selected in previous reports (17). T4 sympathetic is a surgical method that has been associated with relatively shorter-term complications and better effects (18,19). Besides, previous examinations also reported that compensatory hyperhidrosis was the most important factor in determining a patient's satisfaction with the procedure (20). This may explain the lack of difference in patient satisfaction between the groups, although there seems to be a trend of positive response in patients who received RFS.

RFS, originally described by Wilkinson in 1984 (21), was used to treat various diseases, such as pain syndromes, Prinzmetal angina, complex regional pain syndrome type I, Raynaud disease, and hyperhidrosis (21-24).

The advantages of radiofrequency ablation include long-lasting pain relief, relatively high precision, as well as the ability to stimulate nervous system elements before the development of lesions, safeguarding against ablating a wrong target (25). However, RFS was performed without a direct view of the sympathetic chain, targeting sites using the adjacent bone reference. Therefore, the exact locations of the sympathetic chain and/or accessory fibers, such as the Kuntz nerve, cannot be visualized, so they could be missed. Due to the fluidity of anhydrous alcohol, the positioning accuracy was lower than that of the PES group. This may explain why the immediate success rate of the RFS treatment was lower than that of PES in this study. Besides, the nerve damage caused by anhydrous ethanol is often not severe enough. For this reason, the negative effects lasted from several months to several years, and the symptoms often recurred within a few months, which might be related to the regeneration and repair of the nerves.

Finally, we concluded that both RFS and PES are safe and effective treatments; the former seemed to cause less compensatory hyperhidrosis, and to some extent could improve the symptoms of hyperhidrosis patients for a longer time. Meanwhile, RFS has higher technical requirements for operators. Due to the fluid-
ity of anhydrous ethanol, PES has a higher immediate treatment effective rate. PES is recommended for use by novice surgeons, but at the same time, attention should be paid to the risk of a large sympathetic block caused by an excessive flow range.

There are several limitations in the current study. First, the sample size was not sufficient to complete the propensity score match. Thus, a propensity score matching study was used to minimize patient selection bias and eliminate potential confounding factors. Second, some authors have pointed out that axillary hyperhidrosis and plantar hyperhidrosis are not accompanied by hand hyperhidrosis, and the curative effect is uncertain (26). Interestingly, it was reported that patients with more than one preoperative hyperhidrosis site presented worse quality of life prior to surgery than those with a single hyperhidrosis site, but the number of hyperhidrosis sites before surgery did not affect the surgical outcomes (27). Unfortunately, the small number of patients with PH did not allow us to establish and discuss specifically whether the 2 treatments yielded different outcomes in the treatment of hyperhidrosis. Considering the limitations of this retrospective study, our research team will conduct further randomized prospective trials on this topic in the future, and continue to follow up the patients who received surgical treatment, hoping to remedy the above deficiencies in the near future.

As a whole, this study established that both percutaneous computed tomography-guided RFS ablation of sympathetic ganglia and percutaneous ethanol sympatholysis are promising treatment modalities for primary hyperhidrosis. However, percutaneous RFS ablation was more effective and associated with a longer effectiveness time compared with percutaneous ethanol sympatholysis.

Authors’ Contributions

KYX, JJJZ and MY conceived and designed the study. QLH, GL and LL performed the experiments. HDN and JCT coordinated and supervised the experiments. GL and JJJZ did the data analysis. QLH, JJJZ, and JCT wrote the article. All authors read and approved the final manuscript.

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