Efficacy and Safety of Radiofrequency Ablation Versus Video-assisted Thoracoscopic Sympathectomy in Palmar Hyperhidrosis: A Multicenter Cohort Study

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Research

Keywords: palmar hyperhidrosis, radiofrequency ablation, video-assisted thoracoscopic sympathectomy, efficacy, safety

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Abstract

Background: Radiofrequency ablation (RFA) was adopted as an alternative to surgical options for sympathectomy in patients with palmar hyperhidrosis (PHH), but the RFA comparative efficacy of treatments by video-assisted thoracoscopic sympathectomy (VATS) on long-term remains uncertain.

Methods: We recruited patients aged ≥14 years with diagnosed PHH from 14 centers in China. The treatment options of RFA or VATS were recruited in patient with informed consent. The primary outcome was the clinical efficacy in 1-year. Propensity scoring and multivariable models respectively were used to evaluate the clinical efficacy and inefficacy risk of treatment options.

Results: A total of 807 patients were enrolled, 351 patients underwent RFA, and 456 were VATS. After propensity score matching, the rate of complete remission was lower in RFA than in VATS (79.2% [247/312] versus 91.3% [285/312], 95% confidence intervals [CI] 0.21 to 0.57, p<0.001). However, the rate of palmar dryness (95% CI 0.38 to 0.92, p=0.020), of postoperative pain (95% CI 0.13 to 0.33, p<0.001), and of surgical-related complication (95% CI 0.19 to 0.85, p=0.020) is lower in RFA group than in VATS group, and radiofrequency ablation group of skin temperature rise is more common (95% CI 1.84 to 3.58, p<0.001).

Conclusion: Performing RFA had a lower success rate than VATS for the complete remission of palmar hyperhidrosis. However, RFA may be better reasonable treatment option for palmar hyperhidrosis before surgical sympathectomy, because it more possibly accepted and generalized due to lower symptomatic burden and costs than surgical sympathectomy in patients.

Trial Registration

ChiCTR2000039576, URL: http://www.chictr.org.cn/index.aspx

Summary Statement

Sympathectomy is the treatment of last resort in patients with palmar hyperhidrosis. Performing radiofrequency ablation may be better reasonable treatment option for palmar hyperhidrosis before surgical sympathectomy.

Review Articles and Special Articles

What We Already Know about This Topic

• Radiofrequency ablation (RFA) or video-assisted thoracoscopic sympathectomy (VATS) was adopted as an alternative to surgical options for sympathectomy in patients with palmar hyperhidrosis.

• A recent review and meta-analysis show that the RFA is effective for hyperhidrosis treatment. However, only two control studies with limited clinical data maybe cannot provided strong evidence for the management of hyperhidrosis.

What This Article Tells Us That Is New

• This study suggested that performing RFA had a lower success rate than VATS for the complete remission of palmar hyperhidrosis. However, RFA may be better reasonable treatment option for palmar hyperhidrosis before surgical sympathectomy.

• It should appear RFA is a reasonable first non-medical option for patients with palmar hyperhidrosis given the favourable safety and cost profile as well as reasonable efficacy.

Background

Hyperhidrosis refers to sweating exceeding physiological needs, and is considered to be a disease of the autonomic nervous system, with the specific pathogenesis unclear.[1-3] which the cholinergic receptor nicotinic alpha 1 subunit and activin a receptor type 1 maybe involvement of the pathogenesis of primary hyperhidrosis.[4, 5] The main involved symptom parts include hand, axilla, craniofacial region, and feet.[6, 7] Hyperhidrosis causes great troubles to patients' social life and work, and even depression in severe cases; severely affected patients have skin maceration and secondary microbial infections.[8-11] Hyperhidrosis condition can be primary or secondary.[12] Primary hyperhidrosis is excessive and uncontrollable sweating without any discernible cause.[8] Secondary hyperhidrosis can be caused by some diseases or drugs, which can affect all parts of the body.[9, 13] Two previous study reported that a prevalence of 2.8% in the United States and 2.08% in China, which would correspond to 7.8 million American and 29.1 million Chinese individuals with hyperhidrosis,[14, 15] more than half of hyperhidrosis symptom parts in the palms,[14] even more than that.[15]

For hyperhidrosis of treatment, the options are divided into surgical and non-surgical options.[16, 17] Non-surgical treatment includes injections of botulinum toxin,[8] topical antiperspirants (aluminum chloride hexahydrate),[18, 19] laser treatment,[20] and oral medications (anticholinergics, beta-blockers, and benzodiazepines),[17] and all these treatments have their limitations and higher the rate of recurrence. Therefore, surgery may be considered as a last resort when more conservative treatments have failed.[17] A video-assisted thoracoscopic sympathectomy (VATS) is the most common used surgical options for the treatment of hyperhidrosis.[18] However, more compensatory hyperhidrosis occurs after the VATS,[17] and it requires general anesthesia and has more tremendous trauma than other options.[11, 21-23]

As a minimally invasive therapies,[23] radiofrequency ablation (RFA) has many satisfactory advantages such as more minor trauma and quick recovery.[24, 25] The therapeutic mechanism of RFA is a thermal

effect, for tissue coagulation without causing neuromuscular excitation or pain[26]. At present, RFA has been widely used in the treatment of tumors and chronic pain, it has achieved remarkable results,[27] and RFA is has also been proved to be effective for hyperhidrosis treatment.[17] However, up to now, only two studies were designed to compared the effectiveness between RFA and VATS in the treatment of hyperhidrosis.[16, 28] One study reported that RFA has long-term patient satisfaction, which a success rate of 75% for treating palmar hyperhidrosis (PHH) in 46 patients.[16] Another non-randomized controlled clinical trial supports the view of surgical sympathectomy as the gold-standard treatment in severe cases of PHH in 31 patients.[28] These studies with limited clinical data have not provided strong evidence for the management of hyperhidrosis.[18] However, it is challenging to design a randomized controlled study to assess the effect and safety between the RFA and VATS in patients with PHH due to making randomization quite complex.[17]

Here, we conducted a nationwide multicenter cohort study to compare the efficacy and safety between RFA and VATS in patients with PHH, to improve clinical practice.

Methods

Study Design

The comparative efficacy research to assess the use of RFA and VATS for PHH was an investigator-initiated, controlled cohort study done at 14 centers in China between 2015 and 2019.

Study Participants

Eligible participants were aged 14 years or older, were diagnosed as primary PHH who are undergone treatment options with RFA or VATS. Exclusions included patients who are non-palmar hyperhidrosis, and non-interventional treatment for hyperhidrosis.[16] The study was approved by institutional ethics committees at the principal investigator center in September 16, 2020, and it was being recognized in other 13 centers. This study was registered with the China Clinical Trials Registry in November 1, 2020 (ChiCTR2000039576). All patient’s provided written informed consent before RFA or VATS for treatment PHH. The study was done per the Declaration of Helsinki and Good Clinical Practice principles.

Study Cohort

The treatment options were done according to a prespecified analysis plan within between RFA and VATS framework. Per a prospective exposure factor definition, patients excluded who were secondary hyperhidrosis before RFA or VATS.

Patients of this study cohort included two distinct groups: The RFA group, which comprised patients who underwent RFA applied unilaterally, and the control (VATS) group, which the VATS were performed

sympathectomy (Thoracic 4 and or Thoracic 3 ganglia according to actual condition) by video-assisted thoracoscopic, under general anesthesia with double-lumen endotracheal intubation.[16, 18, 29] In the RFA group, the operation technique of RFA for PHH according to local practice at the study centers because there are no authoritative practical guidelines. Rejoice, in fact, we find that the patients underwent a homogeneity technique protocol at participate centers, which following subcutaneous local anesthetic infiltration, a 5 mm active cannula of the RFA device was advanced to the thoracic 4 sympathetic ganglions under fluoroscopic guidance (X-ray Computed Tomography). When the probe reached the desired point, the level of the cannula was tested by 3-Dimension's image reconstruction. After neurophysiological testing,[16] RFA thermal coagulation was applied at 90 degree C for 180 seconds, and 2 ml of 2% lidocaine was spread through the cannula after thermal coagulation in necessary. The decision to treatment options for PHH was not determined by study design, but instead was based on the decision of the physician and the patient, and may be influenced by regional health policy practices (Social Security fund policy and Medical Insurance Policy).

Variables

Control variables included the demographic data, clinical disease (Hyperhidrosis Disease Severity Scale [HDSS]),[1] quality of life (QOL) questionnaire,[28] and family history were collected at preoperative from the medical charts each of participation center. The HDSS questionnaire are consists of four statements, each receiving a score of 1 to 4, with 1 being the mildest grade and 4 the worst.[30] The QOL questionnaire is consists of twenty statements, each receiving a score of 1 to 5, with 20 being the mildest grade and 100 the worst. Outcomes variable included the clinical efficacy,[16] safety (intraoperative and postoperative complication),[31, 32] patient satisfaction, HDSS and QOL questionnaire,[33] compensatory hyperhidrosis,[33] and symptom recurrence[6] follow-up data of postoperative months 1, 3, 6, and 12 (1 year), as previously reported.[16, 33] For patient satisfaction is used the chief complaint of patients by phone call and return follow-up to respectively evaluated. To evaluate the postoperative QOL is used the last data of follow-up questionnaire. All follow-up was implemented by an external blinded endpoint committee (setting at the principal investigator institution).

Outcomes

The primary outcome was the clinical efficacy in 1-year. The success of clinical efficacy was defined as complete remission after treatment for PHH, and the ineffective treatment was defined as no remission or a few partial remissions after treatment for PHH. Surgical failure was defined as nothing improvement for hyperhidrosis symptoms in postoperative. The HDSS and QOL were assessed respectively in preoperative and postoperative as a component of the primary outcome were determined. The secondary outcomes were including symptom recurrence, complication, compensatory hyperhidrosis, patient satisfaction, length of stay, and hospital costs.

Sample size calculation

The study sample included patients aged ≥14 year who received RFA or VATS for PPH. Assuming an efficacy rate of 68%-100% with VATS by a report of published literature.[18] Per a power analysis of equivalence tests of two independent proportions using PASS 11 software (NCSS, LLC. Kaysville, Utah, USA.). Sample sizes of 150 in the treatment group and 150 in the control group achieve 90% power to detect equivalence. The margin of equivalence, given in terms of the difference, extends from 0.20 to 0.20. The calculations assume that two, one-sided Z tests are used. The significance level is Alpha targeted at 0.05.

Statistical Analysis

The RFA and VATS cohorts were analyzed separately for HDSS and QOL in preoperative and postoperative. The patients with the loss to follow-up will be excluded from the study analysis. In patients with PHH, baseline characteristics were compared between patients receiving RFA and VATS using standardized mean differences (SMD). The propensity score for receiving RFA was estimated using a logistic regression model. Covariates included in the model were demographics (age and sex), family history, HDSS and QOL in preoperative. Propensity-score matching was implemented using a nearest-neighbor strategy, with a minimum caliper of 0.1.[34, 35] The ratio was one patient receiving RFA matched with one patient receiving VATS. The SMD was used to assess the balance of baseline covariates between the RFA and VATS groups in the matched cohort. An SMD of less than 0.10 indicated a good balance.[36] In the matched cohort, the non-normally distributed of the length of stay and hospitalization costs were converted to categorical variables based on the median. The primary outcome and secondary outcomes for compared the distributions of categorical variables using the chi-square test in the unmatched cohort and a logistic-regression models in the matched cohort, which is reported with odds ratios (OR) and 95% confidence intervals (CI) for two treatment group. To test whether the findings of the patient-level analysis might be due to a causal effect of RFA, we used a further adjusted time-varying Cox proportional hazard model to estimate the hazard ratio for ineffective treatment in the matched cohort.

Statistical analyses were carried out using R 3.6.3 software.

Results

Baseline Characteristics

Between March 4, 2015 and December 31, 2019 at 14 centers in China, 853 patients were enrolled, and 46 patients were excluded on account of who was missing follow-up and thus the population for our study of the clinical efficacy included 807 patients: 351 in the RFA group and 456 in the VATS group (Figure 1) (Figure 2) (Table S1 in the Supplementary Appendix). Median follow-up was 1.5 years (IQR 1.4–1.7) in

the RFA group and 1.7 (IQR 1.4-2.3) in the VATS group. 19 (5.4%) patients in the RFA group and 27 (5.9%) in the control group were lost to follow-up. Because the proportion of patients with missing items was moderate, complete case analyses were done. In the baseline cohort, despite patients in the RFA and VATS groups were well matched for disease severity (HDSS), however, compare with the VATS group, patients underwent RFA who were older (mean, 25.1 years (SD 6.7) versus 23.0 years (SD 5.7), SMD 34.5%), more female (187/351 [53.3%] versus 215/456 [47.2%], SMD 12.3%), and they had lower QOL scores (SMD 19.1%) (Table1). After propensity-score matching, all baseline characteristics of patients who received RFA and VATS were well balanced with SMD less than 0.10 (Table 1).

Table 1

Baseline characteristics, according to treatment with radiofrequency ablation (RFA) and video-assisted thoracoscopic sympathectomy (VATS), in Propensity-Score–Matched Patients with primary hyperhidrosis.

	Unmatched			Matched		
	RFA (n=351)	VATS (n=456)	SMD	RFA (n=312)	VATS (n=312)	SMD
Age, mean (SD), year	22.99(5.65)	25.13(6.69)	0.345	24.16(5.94)	24.45(6.18)	0.048
Female, sex, n (%)	215(47.1)	187(53.3)	0.123	175(56.1)	164(52.6)	0.071
Family history, n (%)	195(42.8)	141(40.2)	0.053	122(39.1)	129(41.3)	0.046
HDSS in Preoperative, n (%) *			0.174			0.075
1	0(0.0)	0(0.0)		0(0.0)	0(0.0)	
2	16(3.5)	26(7.4)		14 (4.5)	19 (6.1)	
3	223(48.9)	161(45.9)		143(45.8)	144(46.2)	
4	217(47.6)	164(46.7)		155(49.7)	149(47.8)	
QOL in Preoperative, n (%)			0.113			0.011
20-35	0(0.0)	0(0.0)		0(0.0)	0(0.0)	
36-51	0(0.0)	0(0.0)		0(0.0)	0(0.0)	
52-68	41(9.0)	38(10.8)		33(10.6)	34(10.9)	
69-84	210(46.1)	174(49.6)		153(49.0)	152(48.7)	
85-100	205(45.0)	139(39.6)		126 (40.4)	126(40.4)	

* 1: My sweating is never noticeable and does not interfere with my daily activities; 2: My sweating is tolerable but sometimes it interferes with my daily activities; 3: My sweating is barely tolerable and frequently interferes with my daily activities; 4: My sweating is intolerable and always interferes with my daily activities.

Abbreviation: VATS, video-assisted thoracoscopic sympathectomy; RFA, radiofrequency ablation; HDSS, Hyperhidrosis Disease Severity Scale; QOL, quality of life questionnaire; SMD, standardized mean differences.

Primary Outcome

The postoperative association between treatment option and outcomes are presented in Table 2. In the matched cohort between 312 underwent RFA and 312 underwent VATS, the surgical failure rate was not found significant differences between RFA and VATS in hospital (0.3% [1/312] versus 1.0% [3/312], OR 2.84, 95% CI 0.26 to 72.59, P=0.428). However, the rate of complete remission was 79.2% (247/312) for treating PHH in the RFA group and 91.3% (285/312) in the VATS group (OR 0.35, 95%CI 0.21-0.57, P<0.001) in postoperative 1-year. The multivariable Cox model shows that the risk of ineffective treatment was higher in the RFA group than in the VATS group (HR 2.61, 95%CI 1.61-4.23, P <0.001), and

in with family history than in without (HR 1.84, 95%CI 1.21-2.81, P =0.004). However, the risk of ineffective treatment was lower with worse quality of life (QOL>84) than without (HR 0.41, 95%CI 0.19-0.91, P =0.027), and in with skin temperature rise than in without (HR 0.58, 95%CI 0.38-0.90, P =0.014) (Figure 3).

As a component of the primary outcome was determined, the HDSS was a significant reduction in two groups between preoperative and postoperative (P<0.001), and quality of life (QOL questionnaire) were significantly improved in two groups (P<0.0001) (Table 3). However, compared with the RFA group, the postoperative HDSS (1) assessment improved more significantly in the VATS group at the endpoint of follow-up (275/312 [88.1%] versus 245/312[78.5%], OR 0.46, 95% CI 0.29-0.73, P=0.001); likewise, the postoperative QOL questionnaire (20-35) improved also more significantly in the VATS group (251/312[80.4%] versus 217/312[69.6%], OR 0.54, 95% CI 0.37-0.78, P=0.001) (Table 2).

Table 2

Primary and secondary outcomes according to treatment with radiofrequency ablation (RFA) and video-assisted thoracoscopic sympathectomy (VATS), in Propensity-Score–Matched patients with palmar hyperhidrosis.

	RFA (n=312)	VATS (n=312)	Odds ratios (95% CI)	P Value
Primary outcomes				
Clinical efficacy in discharge, n (%)				
Surgical failure	3 (1.0)	1 (0.3)	2.84 (0.26 to 72.59)	0.428
Partial remission	57 (18.3)	66 (21.2)	0.82 (0.55 to 1.22)	0.319
Complete remission	252 (80.8)	245 (78.5)	1.18 (0.79 to 1.75)	0.420
Clinical efficacy in 1 year, n (%)				
Ineffective treatment	65 (20.8)	27 (8.7)	2.83 (1.76 to 4.67)	<0.001
Complete remission	247 (79.2)	285 (91.3)	0.35 (0.21 to 0.57)	<0.001
HDSS in Postoperative, n (%) *				
1	245 (78.5)	275 (88.1)	0.46 (0.29 to 0.73)	0.001
2	30 (9.6)	16 (5.1)	2.00 (1.08 to 3.85)	0.032
3	25(8.0)	9 (2.9)	3.26 (1.52 to 7.63)	0.004
4	12 (3.8)	12 (3.8)	1.00 (0.43 to 2.33)	0.996
QOL in Postoperative, n (%)				
20-35	217 (69.6)	251 (80.4)	0.54 (0.37 to 0.78)	0.001
36-51	50 (16.0)	42 (13.5)	1.26 (0.80 to 1.97)	0.321
52-68	35 (11.2)	17 (5.4)	2.20 (1.21 to 4.13)	0.011
69-84	7 (2.2)	2 (0.6)	3.76 (0.89 to 25.54)	0.103
85-100	3 (1.0)	0 (0.0)	-	0.997
Secondary outcomes				
Symptom recurrence, n (%)	62 (19.9)	26 (8.3)	2.78 (1.71 to 4.63)	<0.001
Compensatory hyperhidrosis, n (%)	208 (66.7)	204 (65.4)	1.11 (0.82 to 1.50)	0.487
Palmar dryness, n (%)	39 (12.5)	61 (19.6)	0.59 (0.38 to 0.92)	0.020
Postoperative pain, n (%)	27 (8.7)	96 (30.8)	0.21 (0.13 to 0.33)	<0.001
Skin temperature rise, n (%)	221 (70.8)	153 (49.0)	2.56 (1.84 to 3.58)	<0.001
Patient satisfaction, n (%)				
Dissatisfaction	14 (4.5)	9 (2.9)	1.63 (0.69 to 4.01)	0.269

Moderate	38 (12.2)	34 (10.9)	1.11 (0.67 to 1.84)	0.684
Satisfaction	98 (31.4)	107 (34.3)	0.88 (0.63 to 1.23)	0.463
Complete satisfaction	162 (51.9)	162 (51.9)	1.00 (0.73 to 1.38)	0.985
Complication, n (%)	11 (3.5)	24 (7.7)	0.41 (0.19 to 0.85)	0.020
Length of stay >2 days, n (%)	71 (22.8)	198 (63.5)	0.21 (0.13 to 0.33)	<0.001
Hospital costs > 1260, $, n (%)	18 (5.8)	269 (86.2)	0.01 (0.00 to 0.01)	<0.001

* 1: My sweating is never noticeable and does not interfere with my daily activities; 2: My sweating is tolerable but sometimes it interferes with my daily activities; 3: My sweating is barely tolerable and frequently interferes with my daily activities; 4: My sweating is intolerable and always interferes with my daily activities.

Abbreviation: VATS, video-assisted thoracoscopic sympathectomy; RFA, radiofrequency ablation; CI, confidence interval; HDSS, Hyperhidrosis Disease Severity Scale; QOL, quality of life questionnaire; SMD, standardized mean differences.

Secondary Outcome

In the matched cohort, we found that PHH who underwent RFA were higher than those who underwent VATS in terms of symptom recurrence (OR 2.78, 95% CI 1.71 to 4.63, p<0.001). On the contrary, the rate of clinical symptoms after treatment shows that the rate of palmar dryness, postoperative pain, skin temperature rise, and surgical-related complication is lower in the RFA group than in the VATS group (Table 2). The common complication of VATS was pneumothorax (11/312 [3.5%]), pleural effusion (6/312 [1.9%]), and incisional pain (4/312 [1.3%]) (Table S1 in the Supplementary Appendix). The length of stay was a shorter period in the RFA group than in the VATS group (OR 0.21, 95% CI 0.13-0.33, P<0.001). The hospital costs were lower in the RFA group than in the VATS group (OR 0.01, 95% CI 0.00-0.01, P<0.001). For the compensatory hyperhidrosis and the chief complaint of patient satisfaction, we were not found significant differences between RFA and VATS (Table 2).

Table 3

Comparison of radiofrequency ablation (RFA) versus video-assisted thoracoscopic sympathectomy (VATS) for primary hyperhidrosis according to the HDSS and QOL in preoperative and postoperative with matched cohort.

	RFA (n=312)			VATS (n=312)		
	Preoperative	Postoperative	P-value	Preoperative	Postoperative	P-value
HDSS*						
1	0 (0.0)	245 (78.5)	<0.001	0 (0.0)	275 (88.1)	<0.001
2	19 (6.1)	30 (9.6)	0.102	14 (4.5)	16 (5.1)	0.708
3	144 (46.2)	25 (8.0)	<0.001	143 (45.8)	9 (2.9)	<0.001
4	149 (47.8)	12 (3.8)	<0.001	155 (49.7)	12 (3.8)	<0.001
QOL						
20-35	0 (0.0)	217 (69.6)	<0.001	0 (0.0)	251 (80.4)	<0.001
36-51	0 (0.0)	50 (16.0)	<0.001	0 (0.0)	42 (13.5)	<0.001
52-68	34 (10.9)	35 (11.2)	0.898	33 (10.6)	17 (5.4)	0.018
69-84	152 (48.7)	7 (2.2)	<0.001	153 (49.0)	2 (0.6)	<0.001
85-100	126 (40.4)	3 (1.0)	<0.001	126 (40.4)	0 (0.0)	<0.001

* 1: My sweating is never noticeable and does not interfere with my daily activities; 2: My sweating is tolerable but sometimes it interferes with my daily activities; 3: My sweating is barely tolerable and frequently interferes with my daily activities; 4: My sweating is intolerable and always interferes with my daily activities.

Abbreviation: VATS: video-assisted thoracoscopic sympathectomy; RFA: radiofrequency ablation; HDSS: Hyperhidrosis Disease Severity Scale; QOL: quality of life questionnaire.

Discussion

Both performing RFA and VATS is considered a success procedure for PHH to complete remission. However, performing RFA (79.3%), compared with VATS (91.2%), was a lower rate of complete remission for PHH in postoperative 1-year. This may due to the reason that the operator to excise the sympathetic nerve more precisely under direct vision on the screen through video-assisted thoracoscopic.[37] and not just because of the operator was relatively less experience in eliciting this block.[16]

The surgical-related complication was appeared at a lower level in the two groups, in keeping with several prior studies demonstrating that destruction of these nerves is safe and effective to stops hyperhidrosis of the palmar.[17, 18, 21, 23] Complications have been described in two aspects. On the one hand, complications related to performing surgical procedures commonly occur during the perioperative period, such as dyspnea, acute chest syndrome, incisional pain, pneumothorax, pleural effusion. Another, it is caused by excision of the sympathetic nerve, which commonly appears after hospital discharge, such as axillary pain, shoulder-back pain, compensatory hyperhidrosis, bradycardia, nasal obstruction, nerve injury, and intercostal neuralgia.[31, 32] In this large sample of a cohort study, although not all

complications were observed, these complications were considered could tolerable, which to the relative merits of improved hyperhidrosis symptoms and improved quality of life, and patient satisfaction in each patient with chief complaints.

In this study, the advantages of RFA were more minimally invasive,[24] fewer postoperative pain,[26] shorter lengths of stay, and lower hospital cost. These advantages are reasonable and deserve positive recognition, which the RFA was used as a Lesion Generator for thermal ablation under fluoroscopic guidance by a 5 mm active cannula.[6, 16] A more minimally invasive procedure that it is no require general anesthesia and greater trauma procedures,[11, 21-23] leads to less postoperative pain,[26] possibly is the unnecessary longer length of stay, and reduced hospitalization costs for in RFA procedures than in VATS procedures. In addition, we did find a higher rate of skin temperature rises in the RFA group, which maybe because it has a more extensive impact on surrounding nerve tissue or because it is un-annihilated for sympathetic nerve, leading to a higher the rate of symptoms recurrent in RFA than in VATS. This study shows that a negative correlation between palmar temperature rise and inefficacy treatment. However, palmar temperature change may cannot be used to predict cure or guide surgical approach.[38] In general, RFA options brings lower symptomatic burden, which is more possible to be accepted for patients, and there will be more treatment options (one more RFA, or VATS) in patients who underwent RFA when symptoms recurrent.[33]

In comparison, the advantage of VATS treatment for hyperhidrosis is that the sympathetic nerve could be excision more thoroughgoing, lead to being improved more significantly in the symptoms of hyperhidrosis and quality of life, and the rate of symptom recurrence is lower in VATS than in RFA. A pathogenesis study of PHH shows that the cholinergic receptor nicotinic alpha 1 subunit and activin a receptor type 1 maybe involvement of the pathogenesis of primary hyperhidrosis.[4, 5] Another genome-wide analysis of families with PHH shows that variants or mutations located outside the coding regions might be involved in the molecular pathogenesis of PHH.[3] In the Cox proportional hazard model for ineffective treatment show that higher risk in patients with family history than without, which the reason may from variants or mutations located outside the coding regions.[4, 15]

This study has several limitations. First, an observational study to evaluating the clinical efficacy of RFA and VATS are potentially subjected to selection bias.[39] Even though the balance was achieved in each cohort by propensity matching score, but it is still possible that patients selected for RFA differed in terms of treatment history compared with patients receiving VATS, and seven centers did not perform RFA for PHH. However, sympathectomy is the last resort of treatment when conservative treatments are a failure or intolerable,[18] which treatment history did not affect the clinical outcome of sympathectomy.[3, 4] Second, the proposed different follow-up times were observed for RFA or VATS treatment effect with HDSS and QOL needs to be independently assessed.[33] In this context, it is essential to note that the endpoint assessment for treatment of clinical efficacy for long-term outcomes might need more concerned.[17] Third, this study lack data were indicating ethnicity. Although ethnicity could potentially affect the study results, the study population only is yellow. Finally, missing data possibly influence

results, we are not sure whether the inclusion of lost to follow-up data will affect the final analysis results in this study.

Conclusions

This study suggests that performing RFA had a lower success rate than VATS for the complete remission of PHH. However, RFA may be better reasonable treatment option for palmar hyperhidrosis before surgical sympathectomy, because it more possibly accepted and generalized due to lower symptomatic burden and costs than sympathectomy in patients.

Abbreviations

PHH, Palmar Hyperhidrosis; RFA, Radiofrequency Ablation; VATS, Video-assisted Thoracoscopic Sympathectomy; CI, Confidence interval; OR, odds ratios; HR, Hazard Rati; HDSS, Hyperhidrosis Disease Severity Scale; QOL, quality of life questionnaire; SD: standard deviation; SMD: standardized mean differences

Declarations

Author contributions:

Professor Jing Tang had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

Study concept and design: Jing Tang, Yiyue Zhong, Bing Huang, Liangqing Zhang.

Acquisition, analysis, or interpretation of data: Jing Tang, Yiyue Zhong, Yanwen Zhu, Bing Huang.

Drafting of the manuscript: Yiyue Zhong, Jing Tang.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Yiyue Zhong, Jing Tang.

Administrative, technical, or material support: Yiyue Zhong, Jing Tang.

Study supervision: Jing Tang.

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The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Conflicts of Interest

The writing committee declares that they have no conflicts of interest.

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References

1. Gabes M, Jourdan C, Schramm K, Masur C, Abels C, Kamudoni P, Salek S, Apfelbacher C: **Hyperhidrosis Quality of Life Index (HidroQoL©): further validation and clinical application in patients with axillary hyperhidrosis using data from a phase III randomized controlled trial**. *The British journal of dermatology*2020.
2. Wade R, Llewellyn A, Jones-Diette J, Wright K, Rice S, Layton AM, Levell NJ, Craig D, Woolacott N: **Interventional management of hyperhidrosis in secondary care: a systematic review**. *The British journal of dermatology*2018, **179**(3):599-608.
3. Schote AB, Schiel F, Schmitt B, Winnikes U, Frank N, Gross K, Croyé MA, Tarragon E, Bekhit A, Bobbili DR*et al*: **Genome-wide linkage analysis of families with primary hyperhidrosis**. *PLoS One*2020, **15**(12):e0244565.
4. Lin JB, Kang MQ, Huang LP, Zhuo Y, Li X, Lai FC: **CHRNA1 promotes the pathogenesis of primary focal hyperhidrosis**. *Molecular and cellular neurosciences*2021:103598.
5. Lin JB, Chen JF, Lai FC, Li X, Xie JB, Tu YR, Kang MQ: **Involvement of activin a receptor type 1 (ACVR1) in the pathogenesis of primary focal hyperhidrosis**. *Biochem Biophys Res Commun*2020, **528**(2):299-304.

6. Purtuloğlu T, Deniz S, Atım A, Tekindur Ş, Gürkök S, Kurt E: **A new target of percutaneus sympathic radiofrequency thermocoagulation for treatment of palmar hyperhidrosis: T4**. *Agri : Agri (Algoloji) Dernegi'nin Yayin organidir = The journal of the Turkish Society of Algology*2013, **25**(1):36-40.
7. Lecouflet M, Leux C, Fenot M, Célerier P, Maillard H: **Duration of efficacy increases with the repetition of botulinum toxin A injections in primary palmar hyperhidrosis: a study of 28 patients**. *J Am Acad Dermatol*2014, **70**(6):1083-1087.
8. Heckmann M, Ceballos-Baumann AO, Plewig G: **Botulinum toxin A for axillary hyperhidrosis (excessive sweating)**. *The New England journal of medicine*2001, **344**(7):488-493.
9. Walling HW: **Primary hyperhidrosis increases the risk of cutaneous infection: a case-control study of 387 patients**. *J Am Acad Dermatol*2009, **61**(2):242-246.
10. Hamm H, Naumann MK, Kowalski JW, Kütt S, Kozma C, Teale C: **Primary focal hyperhidrosis: disease characteristics and functional impairment**. *Dermatology*2006, **212**(4):343-353.
11. Nyamekye IK: **Current therapeutic options for treating primary hyperhidrosis**. *European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery*2004, **27**(6):571-576.
12. McConaghy JR, Fosselman D: **Hyperhidrosis: Management Options**. *Am Fam Physician*2018, **97**(11):729-734.
13. Galadari H, Galadari I, Smit R, Prygova I, Redaelli A: **Treatment approaches and outcomes associated with the use of abobotulinumtoxinA for the treatment of hyperhidrosis: a systematic review**. *J Am Acad Dermatol*2020.
14. Strutton DR, Kowalski JW, Glaser DA, Stang PE: **US prevalence of hyperhidrosis and impact on individuals with axillary hyperhidrosis: results from a national survey**. *J Am Acad Dermatol*2004, **51**(2):241-248.
15. Lai FC, Tu YR, Li YP, Li X, Lin M, Chen JF, Lin JB: **Nation wide epidemiological survey of primary palmar hyperhidrosis in the People's Republic of China**. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society*2015, **25**(2):105-108.
16. Purtuloglu T, Atim A, Deniz S, Kavakli K, Sapmaz E, Gurkok S, Kurt E, Turan A: **Effect of radiofrequency ablation and comparison with surgical sympathectomy in palmar hyperhidrosis**. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*2013, **43**(6):e151-154.
17. Hasimoto FN, Cataneo DC, Hasimoto EN, Ximenes AMG, Cataneo AJM: **Radiofrequency in the treatment of primary hyperhidrosis: systematic review and meta-analysis**. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society*2020, **30**(2):111-120.
18. Nawrocki S, Cha J: **The etiology, diagnosis, and management of hyperhidrosis: A comprehensive review: Therapeutic options**. *J Am Acad Dermatol*2019, **81**(3):669-680.
19. Gee S, Yamauchi PS: **Nonsurgical management of hyperhidrosis**. *Thoracic surgery clinics*2008, **18**(2):141-155.

20. Cervantes J, Perper M, Eber AE, Fertig RM, Tsatalis JP, Nouri K: **Laser treatment of primary axillary hyperhidrosis: a review of the literature**. *Lasers in medical science*2018, **33**(3):675-681.
21. Atkinson JL, Fode-Thomas NC, Fealey RD, Eisenach JH, Goerss SJ: **Endoscopic transthoracic limited sympathotomy for palmar-plantar hyperhidrosis: outcomes and complications during a 10-year period**. *Mayo Clin Proc*2011, **86**(8):721-729.
22. Cruddas L, Baker DM: **Treatment of primary hyperhidrosis with oral anticholinergic medications: a systematic review**. *Journal of the European Academy of Dermatology and Venereology : JEADV*2017, **31**(6):952-963.
23. Alric P, Branchereau P, Berthet JP, Léger P, Mary H, Mary-Ané C: **Video-assisted thoracoscopic sympathectomy for palmar hyperhidrosis: results in 102 cases**. *Annals of vascular surgery*2002, **16**(6):708-713.
24. Abd-Elsayed A, Nguyen S, Fiala K: **Radiofrequency Ablation for Treating Headache**. *Current pain and headache reports*2019, **23**(3):18.
25. Guo L, Kubat NJ, Nelson TR, Isenberg RA: **Meta-analysis of clinical efficacy of pulsed radio frequency energy treatment**. *Ann Surg*2012, **255**(3):457-467.
26. Starr JB, Gold L, McCormick Z, Suri P, Friedly J: **Trends in lumbar radiofrequency ablation utilization from 2007 to 2016**. *The spine journal : official journal of the North American Spine Society*2019, **19**(6):1019-1028.
27. Friedman M, Mikityansky I, Kam A, Libutti SK, Walther MM, Neeman Z, Locklin JK, Wood BJ: **Radiofrequency ablation of cancer**. *Cardiovascular and interventional radiology*2004, **27**(5):427-434.
28. Garcia Franco CE, Perez-Cajaraville J, Guillen-Grima F, España A: **Prospective study of percutaneous radiofrequency sympathicolysis in severe hyperhidrosis and facial blushing: efficacy and safety findings**. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*2011, **40**(4):e146-151.
29. Cerfolio RJ, De Campos JR, Bryant AS, Connery CP, Miller DL, DeCamp MM, McKenna RJ, Krasna MJ: **The Society of Thoracic Surgeons expert consensus for the surgical treatment of hyperhidrosis**. *The Annals of thoracic surgery*2011, **91**(5):1642-1648.
30. Solish N, Bertucci V, Dansereau A, Hong HC, Lynde C, Lupin M, Smith KC, Storwick G: **A comprehensive approach to the recognition, diagnosis, and severity-based treatment of focal hyperhidrosis: recommendations of the Canadian Hyperhidrosis Advisory Committee**. *Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al]*2007, **33**(8):908-923.
31. Lai YT, Yang LH, Chio CC, Chen HH: **Complications in patients with palmar hyperhidrosis treated with transthoracic endoscopic sympathectomy**. *Neurosurgery*1997, **41**(1):110-113; discussion 113-115.
32. Puffer RC, Bishop AT, Spinner RJ, Shin AY: **Bilateral brachial plexus injury after MiraDry® procedure for axillary hyperhidrosis: a case report**. *World neurosurgery*2019.
33. Romero FR, Cataneo DC, Cataneo AJM: **Outcome of Percutaneous Radiofrequency Thoracic Sympathectomy for Palmar Hyperhidrosis**. *Seminars in thoracic and cardiovascular surgery*2018,

30(3):362-366.

34. Austin PC: **Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies**. *Pharmaceutical statistics*2011, **10**(2):150-161.
35. Ouldali N, Toubiana J, Antona D, Javouhey E, Madhi F, Lorrot M, Léger PL, Galeotti C, Claude C, Wiedemann A*et al*: **Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children**. *Jama*2021.
36. Austin PC, Stuart EA: **Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies**. *Stat Med*2015, **34**(28):3661-3679.
37. Horslen LC, Wilshire CL, Louie BE, Vallières E: **Long-Term Impact of Endoscopic ThoracicSympathectomy for Primary Palmar Hyperhidrosis**. *The Annals of thoracic surgery*2018, **106**(4):1008-1012.
38. Liu Y, Li H, Zheng X, Li X, Li J, Jiang G, Wang J: **Sympathicotomy for palmar hyperhidrosis: the association between intraoperative palm temperature change and the curative effect**. *Annals of thoracic and cardiovascular surgery : official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia*2015, **21**(4):359-363.
39. Agoritsas T, Merglen A, Shah ND, O'Donnell M, Guyatt GH: **Adjusted Analyses in Studies Addressing Therapy and Harm: Users' Guides to the Medical Literature**. *Jama*2017, **317**(7):748-759.

Figures

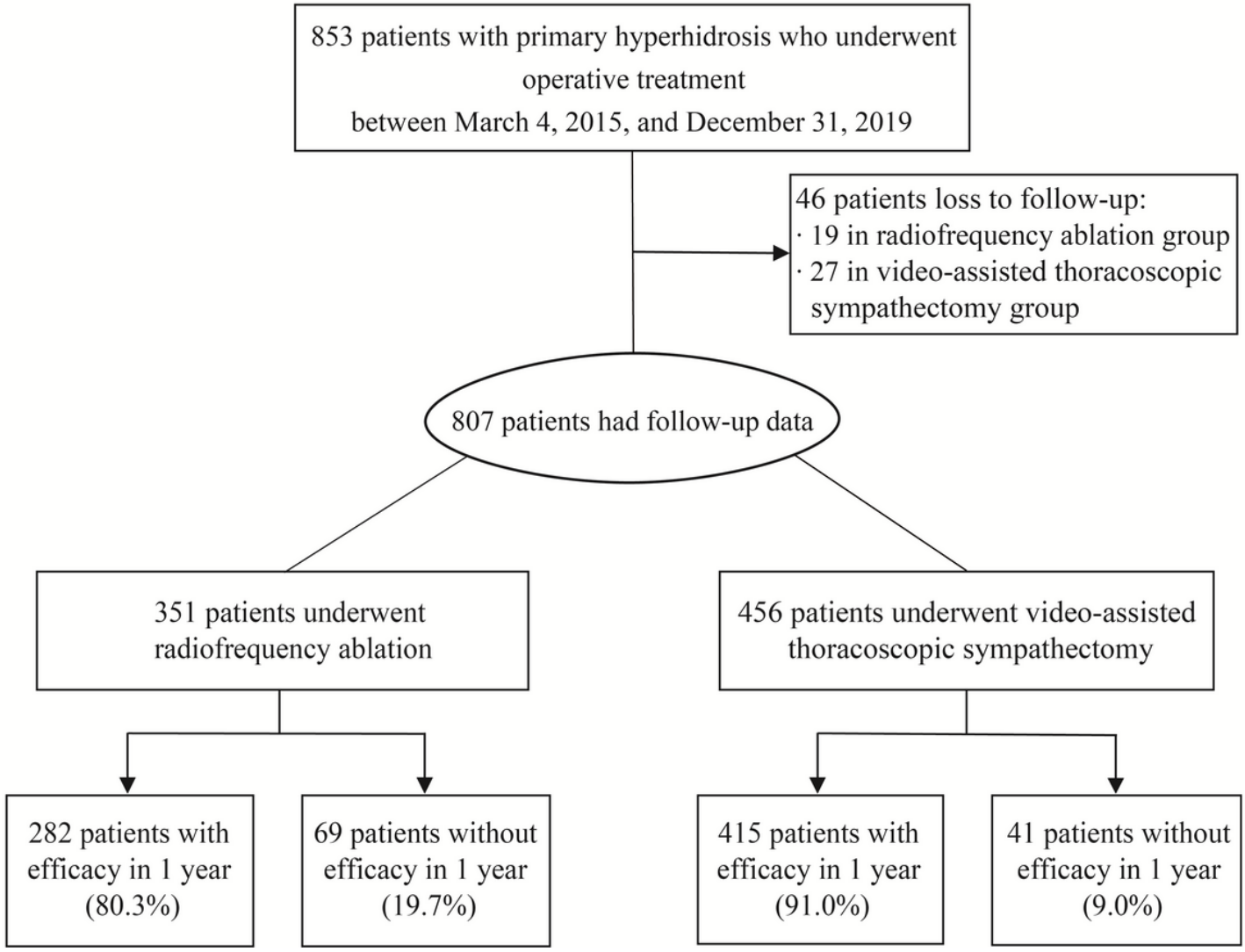

Figure 1

Study profile showing selection of study participants.

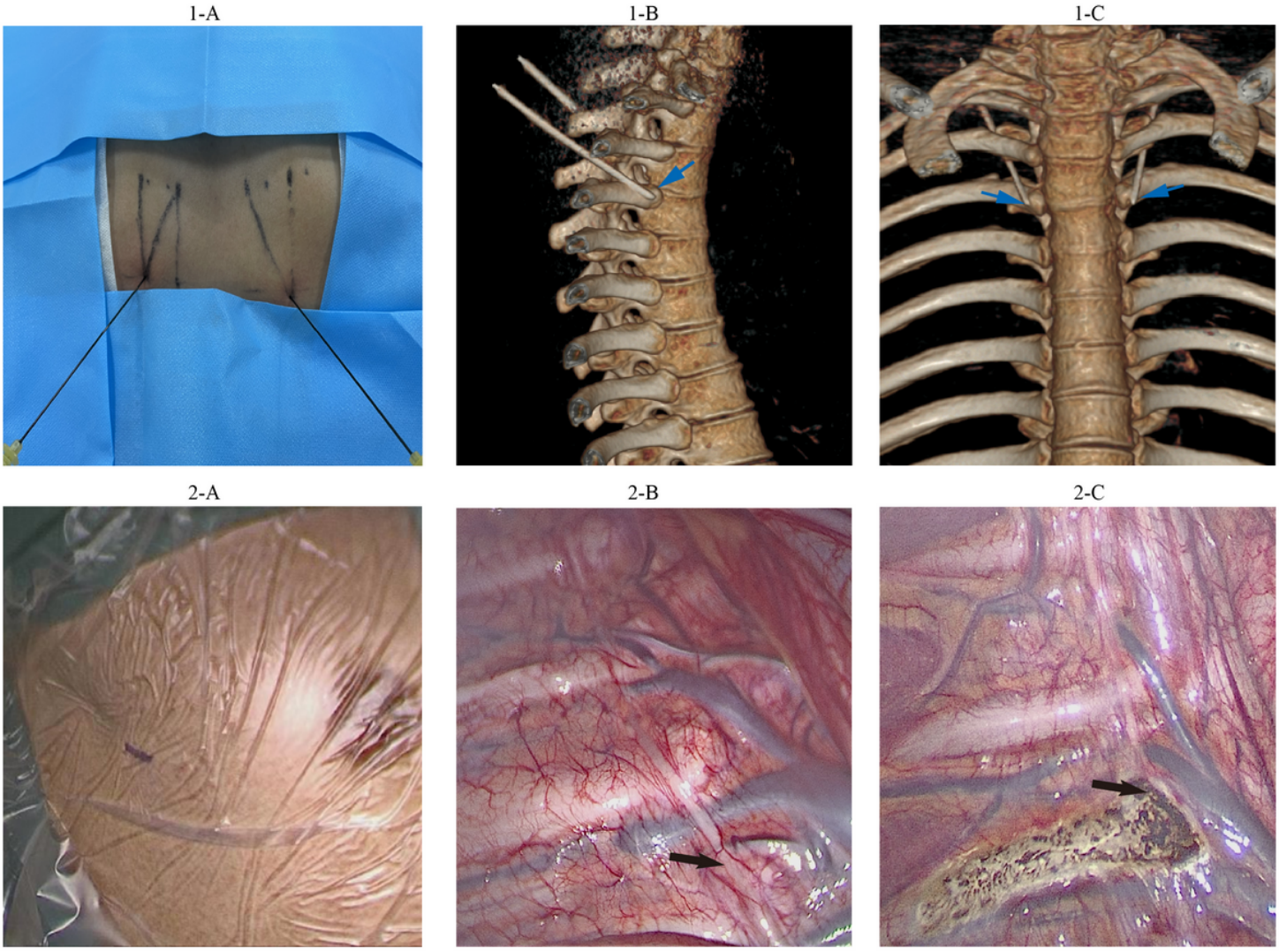

Figure 2

The radiofrequency ablation (RFA) and video-assisted thoracoscopic sympathectomy (VATS) for treatment with pathways and procedures at the level of fourth thoracic. R-1: Body surface for operative approach in RFA R-2: Lateral film for 3-Dimensions X-Ray Computed Tomography image in RFA R-3: Positive film for 3-Dimensions X-Ray Computed Tomography image in RFA V-1: Body surface for operative approach in VATS V-2: Straight view of the sympathetic nerve before surgery with VATS V-3: Straight view of the sympathetic nerve after surgery with VATS

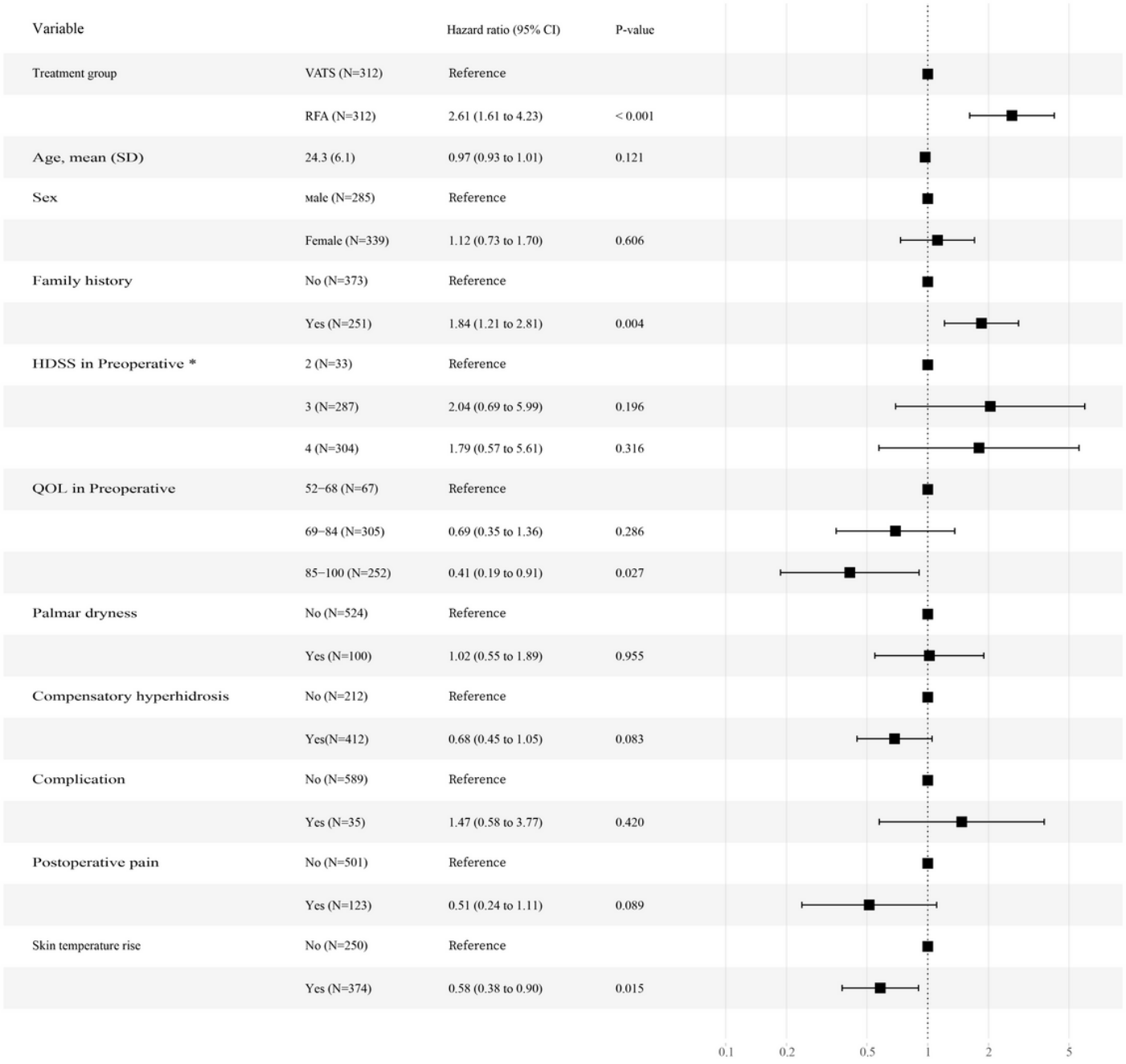

Figure 3

The multivariable models to estimate the hazard ratio of symptom recurrence by time-varying Cox proportional hazard model. * 1: My sweating is never noticeable and does not interfere with my daily activities; 2: My sweating is tolerable but sometimes it interferes with my daily activities; 3: My sweating is barely tolerable and frequently interferes with my daily activities; 4: My sweating is intolerable and always interferes with my daily activities. Abbreviation：RFA: radiofrequency ablation; VATS: video-assisted thoracoscopic sympathectomy; HDSS: Hyperhidrosis Disease Severity Scale; QOL: Quality of Life questionnaire

Supplementary Files

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