

# Associated with Ischemic Stroke Risk Reduction after Endoscopic Thoracic Sympathectomy for Palmar Sweating

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*Background:* Endoscopic thoracic sympathectomy (ETS) was performed to cure palmar hyperhidrosis (PH). After ETS, blood pressure decreased, and cerebral flow velocity increased within 1 month. However, no studies distinguish between subsequent ischemic and hemorrhagic stroke following ETS for PH. The association between stroke type and PH after ETS must be evaluated. *Methods:* We surveyed newly diagnosed patients with PH using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic code 708.8 from the Taiwan Longitudinal National Health Insurance Database. We matched patients with PH who underwent ETS (procedure code 05.29) and without surgery in the database between 2000 and 2010. We defined events as ischemic stroke (ICD-9-CM codes from 433 to 437) or hemorrhagic stroke (ICD-9-CM codes from 430 to 432). Patients were followed up until the first event or December 31, 2010. Risk factors for ischemic stroke and hemorrhagic stroke were analyzed using multivariable Cox proportional hazard regression. *Results:* The incidence of ischemic stroke was significantly lower in patients who underwent ETS (.22%) than in patients without surgery (.65%). The patients with PH who received ETS exhibited a reduced risk of ischemic stroke (adjusted hazard ratio [HR] .3; 95% confidence interval [CI] .12-.77). ETS treatment was not associated with a reduction in hemorrhagic stroke (adjusted HR .81; 95% CI .22-3;  $P = .755$ ). *Conclusions:* ETS in patients with PH was associated with reduced subsequent ischemic stroke risk. This additional ischemic stroke preventive effect should encourage health-care supporters to perform ETS in patients with severe PH. **Key Words:** Ischemic stroke—palmar hyperhidrosis—endoscopic thoracic sympathectomy—sympathetic withdrawal.  
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## Introduction

Palmar hyperhidrosis (PH) presents as an idiopathic excessive sweating of the palms with sympathetic overactivity. Patients with PH are treated with topical antiperspirants, anticholinergic agents, and botulinum. However, patients with severe PH experience a miserable quality of life that interferes with social activities, and these patients may undergo endoscopic thoracic sympathectomy (ETS) to improve excessive palmar perspiration.<sup>1</sup> ETS is performed via minimally invasive videothoracoscopy, but a fraction of patients experience compensatory sweating below the breast level and exercise intolerance after ETS.<sup>2</sup> Intolerance to compensatory sweating reduced the willingness of some patients with PH to undergo ETS in recent years. The present study provides evidence of a new benefit that enhances ETS treatment of PH.

Patients with PH exhibit decreased sympathetic tone, increased parasympathetic tone, and heart rate variability after ETS.<sup>3,4</sup> Extracranial and intracranial sonography revealed increased carotid artery flow volume and middle cerebral artery flow velocity and reduced blood pressure within 1 month after ETS.<sup>5</sup> Long-term risks of major cardiovascular events were reduced after ETS,<sup>6</sup> but the predominance of ischemic stroke (IS) or hemorrhagic stroke after ETS was not clarified.

We hypothesized that patients with PH who underwent ETS with sympathetic activity withdrawal will exhibit reduced occurrence of IS in a long-term follow-up study. We used the Taiwanese National Health Insurance Research Database (NHIRD) to evaluate the risk of stroke after ETS in patients with PH. We also assessed other risk factors for stroke for clinical use to reduce potential stroke risk in this condition. We observed that patients with PH exhibited a lower risk of long-term subsequent IS after ETS. The risk factors for subsequent IS included advanced age, no ETS, and presence of hypertension, hyperlipidemia, or coronary artery disease. Our findings suggest that controlling risk factors and undergoing ETS reduce IS risk in patients with PH.

## Materials and Methods

Taiwan National Health Insurance began in 1995, and it covers 99% of Taiwan's 23 million citizens. The NHIRD provides health-care information data for all Taiwanese citizens.<sup>7</sup> All medical units submit computerized claims data for medical payments. The longitudinal National Health Insurance claim database randomly selects patients from the population. The database contains patient identification numbers, outpatient visiting and admission dates, and up to 5 diagnostic and procedure codes from the International Classification of Diseases Ninth Revision, Clinical Modification (ICD-9-CM) in the inpatient database and up to 3 diagnostic and procedure codes in the outpatient database. The obtained data included the patient's age, gender, comorbidities, and the dates of ETS and IS. The Ethics Institutional Review Board of the Tri-Service General Hospital approved this study.

We identified PH cases (ICD-9-CM diagnostic code 708.8) that were entered from January 1, 2000, to December 31, 2010 in Taiwan from the outpatient dataset of longitudinal National Health Insurance claim database. Patients who received an ETS procedure under general anesthesia are hospitalized to observe recovery conditions. Therefore, we retrieved patients with PH who received ETS (ICD-9-CM procedure code 05.29) from the inpatient database. The ETS procedure was not performed in children because the potential risks and benefits are not justified.<sup>8</sup> The incidence of PH was lower with advanced age in NHIRD.<sup>9</sup> Therefore, we excluded patients who were younger than 18 years and older than 65 years

of age, patients with unidentified genders, and patients in whom PH and stroke were diagnosed before 2000. The date of the first diagnosis of PH was defined as the index date. We designed the study and control groups using one-fold propensity scores and matched the patients by age, gender, index date, and comorbidities to correct for baseline selection bias. Figure 1 shows a flowchart of the study design.

We defined an event as IS (ICD-9-CM codes from 433 to 437) after the index date. Patients were followed up until the first event or December 31, 2010. We also analyzed hemorrhagic strokes (430-432) for comparison. Comorbidities identified by the ICD-9-CM codes included diabetes mellitus (250), hypertension (401-405), coronary artery disease (410-414), depression (296.2-296.3, 296.82, 330.4, 331), anxiety (ICD-9-CM 300.1-300.3, 300.5-300.9), atrial fibrillation (427.31), pneumonia (480-486), hyperlipidemia (272), congestive heart failure (428), renal disease (580-589), liver disease (571), injury (800-999), and tumors (140-208).

Descriptive statistics were assessed in the IS and IS-free groups. The chi-square test was used for categorical variables, and Student's *t* test was performed for continuous variables. Risk factors were assessed using a multivariate Cox proportional hazard regression model, and a *P* < .05 indicated statistical significance. The risks of IS and hemorrhagic stroke are presented using the hazard ratio (HR) after adjusting for factors, including the season, area, urbanization level, hospital type, and income. All statistical analyses were performed using SPSS software version 21 (International Business Machine company, Armonk, New York).

## Results

A total of 5580 patients with PH were enrolled. A total of 2790 of patients with PH received ETS, and 2790 of the patients did not receive ETS. Table 1 presents the characteristics of the IS and IS-free groups. IS in patients with PH occurred in those with more advanced age, coronary artery disease, diabetes mellitus, hypertension, hyperlipidemia, liver disease, and patients residing in the least urbanized area. The incidence of IS was significantly lower in patients who underwent ETS (.22%) than patients who did not undergo the surgery (.65%), with an absolute risk reduction of 66.67%. The median follow-ups were 2.73 years in the ETS group and 2.64 years in the ETS-free group. The cumulative incidence of IS was higher in the ETS group (Fig 2, log-rank test *P* = .01).

Table 2 shows the risk factors for IS in patients with PH. ETS significantly reduced the risk of IS (adjusted HR .3; 95% confidence interval [CI] .12-0.77). Risk factors for IS in patients with PH included advanced age (adjusted HR 3.44; 95% CI 2.64-9.33 in aged 45-64 years), coronary artery disease (adjusted HR 1.53; 95% CI 1.12-2.44), hypertension (adjusted HR 3.42; 95% CI 1.03-11.64),

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