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SHORT COMMUNICATION

# Endoscopic thoracic sympathectomy as a novel strategy for vasospastic angina refractory to medical treatments

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**Summary** Although vasospastic angina (VSA) is usually controlled by medications, refractory or lethal cases are occasionally encountered. We performed bilateral endoscopic thoracic sympathectomy (ETS) in 5 male patients with refractory VSA. Prior to ETS, stellate ganglion blockade was performed in 4 patients to reduce VSA attacks and to confirm the effect of sympathetic blockade. Under endoscopic guidance, the second to fourth thoracic sympathetic ganglia were ablated with a YAG-laser. No patient had complications after ETS, including major sweating abnormalities. In 4 of 5 patients, ETS relieved all VSA symptoms. ST-segment elevation often detected before ETS was absent on repeated ambulatory 24-h Holter monitoring after ETS. ETS is an effective strategy for the treatment of refractory VSA.


Vasospastic angina (VSA) is caused by the spasm of a coronary artery even without organic stenosis. The incidence of VSA is higher in Japan than in Western countries. Although VSA is usually controllable by medications such as calcium channel blockers, we occasionally encounter cases refractory to medical treatment that often become lethal. The mechanism of coronary spasm has not been fully clarified; alternation of autonomic nervous tone is thought to be a major factor [1,2]. Although various trials to alter autonomic tone have been performed, there is no established treatment for refractory VSA cases. Since experimental studies have shown that stimulation of the sympathetic ganglion induces constriction of coronary arteries, stellate ganglion blockade (SGB) has been tried for refractory organic angina in some reports. However, the effects of SGB were transient in most cases. In the present

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study, we performed bilateral endoscopic thoracic sympathectomy (ETS) for high-risk patients with refractory VSA.

From 2001 to 2006, we experienced 5 male patients with VSA refractory to intensive medication therapies. In all patients, VSA was diagnosed based upon typical symptoms such as morning rest angina with ST-segment elevation in more than 2 leads of the 12-lead electrocardiogram, 2 leads with ST-elevation on the ambulatory 24-h Holter monitor, and/or coronary angiographic findings with a positive response to intracoronary acetylcholine (ACh) injection. None of the 5 patients had a significant organic stenotic lesion in any coronary artery. The patients were treated with calcium channel blockers, nitrates and/or nicorandil, and also with other coronary vasodilators including salpogrelate, quinapril, bunazosin, and/or denopamine, possibly effective for coronary vasospasm (Table 1). Nevertheless, their VSA symptoms could not be controlled. For these patients, we performed EST under the approval of our ethical committee. Written informed consent was given by each patient.

Prior to ETS, we first tried SGB by a standard method using the paratracheal technique with a 25-gauge needle inserted at the Chassaignac tubercle on the sixth cervical vertebra in 4 of the 5 patients. The concentration and volume of local anesthetics were carefully adjusted on an individual basis by each physician. Development of Horner's syndrome (ptosis and myosis) was confirmed as objective evidence of a successful block. The SGB was repeatedly performed for several days. Although SGB was effective in relieving angina symptoms, the effect was transient and we then performed ETS. In one patient (case 4 in Table 1), ETS was performed without prior SGB.

ETS was performed in all 5 patients based upon a previously described technique [3,4]. Briefly, patients were intubated with an endotracheal tube under general anesthesia and placed in a semi-reclining position with both arms in abduction. The pleural cavity was accessed via a Surgineedle in the axillary fossa, and approximately 2 l of carbon dioxide was insufflated into the pleural cavity. A modified urological electroresectoscope was introduced via the same incision in the axillary fossa to visualize the upper thoracic cavity. The sympathetic chain was identified in the immediate vicinity of the costovertebral joint. The second to fourth thoracic sympathetic ganglia, including the rami communicantes, were ablated by a YAG-laser. After exsufflation of gas, the procedure was repeated on the contralateral side. The operation time was less than 30 min in all 5 patients. No major complications occurred, except for the artificial pneumothorax caused by the thoracic endoscopic technique. No patients experienced sweating disorders such as dry hands with compensatory sweating, which is often a complication of the ETS procedure. Although transient exacerbation of VSA attacks occurred within a few days after ETS, 4 patients were completely free from VSA symptoms thereafter. In these patients, repeated ambulatory 24-h Holter monitoring did not detect ST-segment elevation and the number of medications for VSA was reduced. The remaining patient (case 4 in Table 1) sometimes complained of VSA symptoms after ETS, but no ST-T changes were documented at that time. This patient continued treatment with multiple medications. Overall, ETS reduced the average number of medications from 6.6 before ETS to 2.2 at 12 months after ETS (Fig. 1).

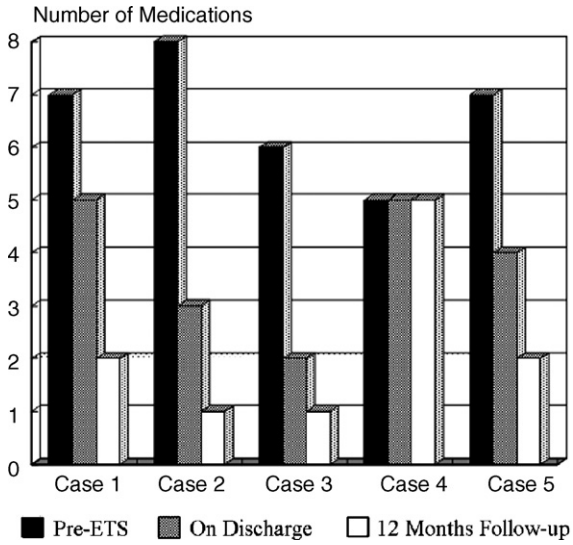


**Figure 1** The number of medications for vasospastic angina (VSA) before ETS, on discharge, and 12 months after ETS. The ETS successfully reduced the medications used in 4 of 5 patients.

Many reports suggested that the alternation of the autonomic nervous regulation participated in coronary artery spasm [1,2]. Although the precise role of the parasympathetic and sympathetic nerves in coronary spasm has not been clarified, it is well known that VSA attacks are often induced by sympathetic activation [2]. Since the heart and coronary arteries are regulated by the lower cervical and upper thoracic sympathetic ganglia [5], SGB is sometimes performed to treat patients with refractory angina due to organic coronary stenosis [6]. Therefore, we first applied SGB in our refractory VSA patients and succeeded in relieving their VSA symptoms. Although repeated SGB for several days could prevent coronary artery spasm, the effect was transient in our VSA patients. We hypothesized

**Table 1** Patients' characteristics

| Case | Age | Gender | ST elevation at attack | CAG | ACh test | Complication | Medications |
|---|---|---|---|---|---|---|---|
| 1 | 41 | M | II, III, aVF on 12 lead-ECG | No stenosis | LAD 100%, LCX 90% | Vf, AV block | Diltiazem, amlodipine, nicorandil, ISMN, TNG, sarpogrelate, denopamine |
| 2 | 69 | M | I, aVL, V1-6 on 12 lead-ECG | No stenosis | No operation | | Diltiazem, amlodipine, nicorandil, ISMN, TNG, sarpogrelate, denopamine, bunazocine, quinapril |
| 3 | 71 | M | II, III, aVF on 12 lead-ECG | No stenosis | No operation | AMI | Diltiazem, amlodipine, nicorandil, ISMN, TNG, sarpogrelate, simvastatin |
| 4 | 65 | M | II, III, aVF on 12 lead-ECG | No stenosis | RCA 100% | Vf | Diltiazem, amlodipine, nicorandil, ISMN, TNG, trandolapril |
| 5 | 40 | M | CM5, NASA on ambulatory 24 h ECG | No stenosis | No operation | CPR | Diltiazem, amlodipine, nicorandil, ISDN, ISMN, TNG, sarpogrelate, bunazocine |

M, male; LAD, left anterior descending artery; LCX, left circumflex artery; Vf, ventricular fibrilation; AV block, atrioventricular block; AMI, acute myocardial infarction; CPR, cardiopulmonary resuscitation; ISMN, isosorbide mononitrate; TNG, nitroglycerine; ISDN, isosorbide dinitrate.

that methods producing more sustained sympathetic blockade might produce long-term relief of symptoms if the patients responded to SGB. A previous report showed that ETS had a long-term effect on cardiac autonomic tone [7]. ETS is a therapeutic tool for palmer hyperhidrosis, reflex sympathetic dystrophy, circulatory disturbances of the upper extremities, and refractory angina in the presence of organic coronary stenosis [3,4,8,9]. To our knowledge, this is the first report describing the application of ETS for refractory VSA. In our experience, ETS showed long-term efficacy for VSA. However, there was concern that ETS reduced only VSA symptom, but did not suppress coronary artery spasm. Silent coronary spasm might increase the risk of sudden major events. Therefore, we carefully performed electrocardiographic monitoring and repeated ambulatory 24-h Holter monitoring, but there were no evidences of silent ischemic ST-T changes in any of the patients. Thus, ETS might reduce not only symptoms but also the frequency and degree of coronary vasospasm.

Recently, several case reports indicates stent implantation for diffuse and multiple coronary spasm with VSA refractory to optimal therapy, [10] but stenting for spastic coronary artery without organic stenotic lesion is still controversial. It has been reported that an oral β1-adrenoreceptor selective antagonist denopamine, which was also administered in one of our cases (case 1 in Table 1), is effective in VSA refractory to conventional medical therapies [11]. Sympathetic denervation by ETS for VSA seems to be contradictory to denopamine therapy that accelerates sympathetic nerve activity. However, denopamine for VSA is relatively low dose, and the mechanism of the effect is coronary vasodilatory action by a weak stimulation of β1-adrenoreceptor that is predominantly found in the conduit coronary artery possibly without sympathetic nerve activation [12].

To establish the ETS as an effective therapeutic strategy for refractory VSA, we should try more effort. Since the ETS causes a shift of sympathovagal balance toward parasympathetic tone, simultaneous assessment of autonomic response by heart rate variability would be rational, although we have no such data in these 5 cases. However, we believe that our 5 cases provide evidence that the ETS is a sound therapeutic option for VSA refractory to any medical treatments.

## References

[1] Tsuchiya T, Okumura K, Yasue H, Kugiyama K, Ogawa H. Heart period variability in patients with variant angina. Am J Cardiol 1996;77:932—6.
[2] Yoshida K, Utsunomiya T, Morooka T, Yazawa M, Kido K, Ogawa T, et al. Mental stress test is an effective inducer of vasospastic angina pectoris: comparison with cold pressor, hyperventilation and master two-step exercise test. Int J Cardiol 1999;70:155—63.
[3] Moya J, Ramos R, Morea R, Villalonga R, Perna V, Macia I, et al. Thoracic symapathicolysis for primary hyperhidrosis: a review of 918 procedures. Surg Endosc 2006;20:598—602.
[4] Nakamura Y, Yoshizawa H, Hirasawa M, Kida H, Matsumoto Y, Ueyama T. Effect of endoscopic transthoracic sympathectomy on plasma natriuretic peptide concentrations in humans. Circ J 2005;69:1079—83.
[5] Kawashima T. The autonomic nervous system of the human heart with special reference to its origin, course, and peripheral distribution. Anat Embryol 2005;209:425—38.
[6] Chester M, Hammond C, Leach A. Long-term benefits of stellate ganglion block in severe chronic refractory angina. Pain 2000;87:103—5.
[7] Tygesen H, Wettervik C, Claes G, Drott C, Emanuelsson H, Solem J, et al. Long-term effect of endoscopic transthoracic sympathectomy on heart rate variability and QT dispersion in severe angina pectoris. Int J Cardiol 1999;70:283—92.
[8] Drott C. Results of endoscopic thoracic sympathectomy (ETS) on hyperhidrosis, facial blushing, angina pectoris, vascular disorders and pain syndromes of the hand and arm. Clin Auton Res 2003;13:I20—30.
[9] Wittervik C, Claes G, Drott C, Emauelsson H, Lomsky M, Radberg G, et al. Endoscopic transthoracic sympathectomy for severe angina. Lancet 1995;345:97—8.
[10] Sugimoto A, Morino Y, Ikari Y. Stent implantation for diffuse and multiple coronary spasm with variant angina refractory to optimal therapy. J Invasive Cardiol 2007;19:E330—3.
[11] Shimizu H, Lee JD, Ogawa KB, Shimizu K, Yamamoto M, Hara A, et al. Efficacy of denopamine, a beta 1 adrenoreceptor agonist, in preventing coronary artery spasm. Jpn Circ J 1993;57:175—82.
[12] Ishide T. Denopamine, a selective beta-1-receptor agonist and a new coronary vasodilator. Curr Med Res Opin 2002;18:407—13.