Video-Assisted Thoracoscopic Left Cardiac Sympathetic Denervation in Chinese Patients with Long QT Syndrome

Kun Li, Jing Yang, Wenjia Guo, Tingting Lv, Jihong Guo, Jianfeng Li and Ping Zhang

Summary

Long QT syndrome is a rare but potentially lethal cardiac channelopathy. The primary aim of the study was to investigate the long-term effects of video-assisted thoracoscopic (VATS) left cardiac sympathetic denervation (LCSD) in Chinese patients with long QT syndrome.

VATS-LCSD was performed in eight Chinese patients with LQTS. Twelve-lead ECGs and 24-hour Holter monitoring ECGs were recorded before and after surgery. The medical charts were reviewed to obtain patient data, and the patients who had been lost to follow-up were contacted through telephone.

The average QTc was shortened from 534 ± 52.7 to 503 ± 43.7 ms (P = 0.030) 24 hours post-surgery and down to 486 ± 34.8 ms (P = 0.021) 1 week post-surgery, with the heart rate unchanged. The average QT dispersion was reduced from 67 ± 17.5 to 21 ± 3.9 ms (P < 0.001) 24 hours post-surgery and remained shortened 1 week later (30 ± 8.1 ms, P < 0.001). Moreover, the 24-hour ECG showed that the QTc was shortened from 552 ± 95.9 to 497 ± 19.7 ms at the minimum heart rate (P = 0.008), and was decreased from 594 ± 144 to 495 ± 74.1 ms at the maximum heart rate (P = 0.04), while the minimum and maximum heart rates were comparable before and after surgery. No death was observed during the follow-up period and the clinical symptoms improved in all patients. The annual event rate decreased from 4 ± 3.5 to 0.63 ± 1.37 events/year (P = 0.034) after surgery.

These findings indicate that LCSD shortens the QTc, with the heart rate remaining unchanged. QTd might be a useful parameter for evaluating the efficacy of VATS-LCSD. LCSD could improve patients’ quality of life by reducing cardiac events.

Key words: Channelopathy, ECG, QT interval, Syncope, Arrhythmia, Therapy

Congenital long QT syndrome (LQTS) is an inherited channelopathy that can cause syncope, seizures, and sudden cardiac death (SCD) even in otherwise healthy individuals. Most cardiac events are triggered by increased sympathetic activity occurring during physical or emotional stress in LQT1, at rest, or in association with sudden noises in LQT2 patients.

In order to prevent cardiac events, the current mainstay of treatment for LQTS patients is beta-blocker pharmacotherapy. Beta-blockers have proven effective in preventing syncope in about 75% of LQTS patients. Nevertheless, certain patients (20%-25%) continue to experience cardiac events despite high doses of betablockers. Additionally, many patients fail to respond or do not tolerate high dose beta-blockade. Implantable cardioverter defibrillators (ICDs) provide a more aggressive and effective SCD counterattack strategy in drug-refractory, highly symptomatic patients. However, ICDs do not prevent ventricular arrhythmias and sometimes can trigger norepinephrine release, subsequently resulting in electrical storms for significant morbidity and mortality as well as severely decreased quality of life and even death.

Video-assisted thoracoscopic (VATS) left cardiac sympathetic denervation (LCSD) is a less invasive surgical procedure with few complications that can bridge the therapeutic and comorbidity gap between the pharmacological and ICD therapies. In 1970s, Moss, et al. originally described LCSD, which reduces sympathetic activation by preventing norepinephrine release in the heart, and hence increases the threshold for fatal ventricular arrhythmias. The procedure involves surgical resection of the lower half of the stellate ganglion and the left sympathetic chain from T1 to T4. Previously, Schwartz, et al. showed that LCSD could shorten QTc by a mean of 39 ms at 6 months following-up in high-risk individuals.
Unfortunately, VATS-LCSD has been severely underutilized globally, especially in China, and its long-term effects remain uncertain. In the present report, we describe our institutional long-term follow-up experience with VATS-LCSD for Chinese LQTS patients.

**Method**

**Study design:** Patients who underwent VATS-LCSD at the Beijing Tsinghua Changgung Hospital and Peking University People’s Hospital between November 2007 and January 2016 were retrospectively enrolled in this study. A medical chart review was performed to obtain patient data, operative notes, and the perioperative course. All 12-lead ECGs, 24-hour Holter monitoring ECGs, and 24-hour Holter monitoring ECGs (SEER Light, GE Healthcare, Fairfield, America), medications, and development of cardiac events during the follow-up were reviewed. The QTc values were determined from standard 12-lead ECG data performed pre-LCSD and at 24 hours and 1 week post-surgery with Bazett’s equation. Twenty-four-hour Holter monitoring ECGs were recorded pre-LCSD and 1 week post-surgery. Patients who had been lost to follow-up were contacted through telephone. The institutional review boards of the Peking University People’s Hospital and Beijing Tsinghua Changgung Hospital approved the study protocol and all patients signed informed consents.

**LCSD:** All LCSD procedures were performed with VATS-LCSD. Patients were administered general anesthesia and placed on the operating table with their right side down. Three small incisions were made in the left chest along the mid-axillary line in order to accommodate a light source and camera, a grasper, and an electrocautery hook dissector. The denervation process included left sympathetic chain removal (the lower half of the stellate ganglion and T2-T4) with sympathetic nerve branch resection toward the heart, which has been described as high thoracic left sympathectomy. The cephalic portion of the left stellate ganglion was preserved to avoid Horner’s syndrome.

**Concomitant therapy:** Indications for LCSD included: 1) persistent symptoms (defined as arrhythmic events despite optimal medical therapy, or recurrent appropriate ICD shocks despite optimal medical therapy); 2) failure to tolerate medical therapy; and 3) prophylactic therapy. Arrhythmic events included recurrent syncope, frequent non-sustained VT, and aborted cardiac arrest.

**Statistical analysis:** Data are expressed as mean ± SD. Two-tailed Student’s t-test was used to compare the quantitative data before and after surgery. P < 0.05 was considered statistically significant. All data analysis was performed with SPSS 20.

**Results**

The demographics of this study cohort are summarized in Table I. There were five females (63%) and the average age at first syncope was 11 ± 6.94 years. Congenital deafness (Jervell and Lange-Nielsen syndrome) was present in two patients, and five had a family history of LQTS or SCD. An ICD had already been implanted before LCSD in one patient.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Patients</th>
<th>Age at first syncope, years</th>
<th>Treatment before LCSD</th>
<th>Treatment after LCSD</th>
<th>Indication for LCSD</th>
<th>Genetic Mutation</th>
<th>Follow-up, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>8</td>
<td>Atenolol, 50 mg/day, Propranolol 60 mg/day</td>
<td>Propranolol, 75 mg/day</td>
<td>Persistent symptoms</td>
<td>KCNQ1</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>21</td>
<td>Propranolol, 30 mg/day</td>
<td>Propranolol, 30 mg/day</td>
<td>Persistent symptoms</td>
<td>KCNQ1</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>16</td>
<td>Propranolol, 30 mg/day</td>
<td>Propranolol, 30 mg/day</td>
<td>Persistent symptoms</td>
<td>KCNQ1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>16</td>
<td>No</td>
<td>Propranolol, 30 mg/day</td>
<td>Persistent symptoms</td>
<td>Propranolol, 30 mg/day</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>2</td>
<td>Metoprolol, 12.5 mg/day</td>
<td>Propranolol, 60 mg/day</td>
<td>Persistent symptoms</td>
<td>Propranolol, 1.5 mg/kg/day</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>2</td>
<td>Propranolol, 30 mg/day</td>
<td>Propranolol, 30 mg/day</td>
<td>Persistent symptoms</td>
<td>Propranolol, 1.5 mg/kg/day</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>15</td>
<td>Metoprolol, 150 mg/day</td>
<td>Propranolol, 60 mg/day</td>
<td>Persistent symptoms</td>
<td>Propranolol, 1.5 mg/kg/day</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>10</td>
<td>Metoprolol, 150 mg/day</td>
<td>Metoprolol, 200 mg/day</td>
<td>Persistent symptoms</td>
<td>Metoprolol, 300 mg/day</td>
<td>4</td>
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</table>

Average 11 ± 6.94 20 ± 8.12 7 ± 3.20

LCSD indicates left cardiac sympathetic denervation; and ICD, implantable cardioverter-defibrillator.
surgery scars were very small compared with those of traditional LCSD surgery (Figure 1). No patients experienced arrhythmias before discharge. There was no mortality or serious postoperative complications. All patients experienced compensatory sweating, but no patient complained of discomfort caused by sweating. No patients developed Horner’s syndrome. Minor postoperative complications occurred in one (13%) of the patients. Patient no. 3 developed a small pneumothorax, necessitating chest tube suction. She was discharged 10 days later. Other patients were discharged 7 days after the procedure following completion of all postoperative investigations.

Twelve-lead ECG: The average QTc in the eight patients was shortened from 534 ± 52.7 to 503 ± 43.7 ms (P = 0.030) 24 hours post-LCSD, and down to 486 ± 34.8 ms (P = 0.021) 1 week post-LCSD (Table II and Figure 2). However, the mean heart rate value remained unchanged. Moreover, the average QT dispersion (QTd) was shortened from 67 ± 17.5 to 21 ± 3.9 ms (P < 0.001) 24 hours after surgery, and it remained shortened 1 week later (30 ± 8.1 ms, P < 0.001; Table II).

Twenty-four-hour Holter monitoring ECG: The 24-hour Holter monitoring ECG showed that the mean value of the heart rate remained unchanged, as well as the QTc value at the average heart rate. However, the QTc was shortened from 552 ± 95.9 to 497 ± 19.7 ms at the minimum heart rate (P = 0.008), and was decreased from 594 ± 144 to 495 ± 74.1 ms at the maximum heart rate (P = 0.04), while the minimum and maximum heart rates were comparable before and after surgery.

Patient follow-up: The eight patients were discharged after the procedure on beta-blockers. The mean follow-up duration was 7 ± 3.20 years (1-10 years), during which time seven of the eight patients were administered propranolol at a dose ranging from 30 to 60 mg/day, and one was prescribed metoprolol 200 mg/day and mexiletine 300 mg/day. No death occurred during the follow-up period and the clinical symptoms and quality of life were im-

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**Table II.** ECG Features Before and After Surgery

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>24 hours after surgery</th>
<th>1 week after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>66 ± 13.8</td>
<td>73 ± 15.0</td>
<td>69 ± 15.4</td>
</tr>
<tr>
<td>QT</td>
<td>515 ± 49.6</td>
<td>461 ± 67.0</td>
<td>470 ± 36.2</td>
</tr>
<tr>
<td>QTc</td>
<td>534 ± 52.7</td>
<td>503 ± 43.7*</td>
<td>486 ± 34.8*</td>
</tr>
<tr>
<td>QTd</td>
<td>67 ± 17.5</td>
<td>21 ± 3.9*</td>
<td>30 ± 8.1*</td>
</tr>
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</table>

*P < 0.05 compared with the value before surgery.

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**Figure 1.** Small scar after VATS-LCSD (Arrow).

**Figure 2.** Body surface ECG of a 22-year-old female patient. The QTc was shortened after LCSD.
Figure 3. Comparison of cardiac events before and after LSCD.

**Table III.** Results of 24-Hour Holter Monitoring Before and After Surgery

<table>
<thead>
<tr>
<th>Holter</th>
<th>Pre-LSCD</th>
<th>Post-LSCD</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Recording time</td>
<td>23.34 ± 0.49</td>
<td>23.18 ± 0.64</td>
<td></td>
</tr>
<tr>
<td>Total beats</td>
<td>93,923 ± 13,426</td>
<td>86,325 ± 10,137</td>
<td></td>
</tr>
<tr>
<td>Average HR</td>
<td>70 ± 9.9</td>
<td>71 ± 10.2</td>
<td></td>
</tr>
<tr>
<td>QT</td>
<td>480 ± 60</td>
<td>520 ± 104</td>
<td></td>
</tr>
<tr>
<td>QTc</td>
<td>527 ± 49</td>
<td>516 ± 81.8</td>
<td></td>
</tr>
<tr>
<td>Minimum HR</td>
<td>50 ± 7.0</td>
<td>54 ± 8.9</td>
<td></td>
</tr>
<tr>
<td>QT</td>
<td>575 ± 97.2</td>
<td>528 ± 75.7</td>
<td></td>
</tr>
<tr>
<td>QTc</td>
<td>552 ± 95.9</td>
<td>497 ± 19.7</td>
<td>*</td>
</tr>
<tr>
<td>Maximum HR</td>
<td>115 ± 12.2</td>
<td>111 ± 16.4</td>
<td></td>
</tr>
<tr>
<td>QT</td>
<td>365 ± 35.0</td>
<td>387 ± 54.7</td>
<td></td>
</tr>
<tr>
<td>QTc</td>
<td>594 ± 144</td>
<td>495 ± 74.1</td>
<td>*</td>
</tr>
</tbody>
</table>

*P < 0.05 compared with the value before surgery

Discussion

The rationale of LSCD for LQTS lies in the vast experimental experience which has confirmed its convincing antifibrillatory effect in various conditions.\(^{16,23}\) Animal experiments have revealed that left stellectomy raises the ventricular fibrillation threshold, whereas right stellectomy decreases it.\(^{14,22}\) Nowadays, VATS-LCS is becoming increasingly recognized as a safe and viable adjunctive therapy in LQTS patients, but it is rarely performed in China. Herein, we describe our single-center experience using the minimally invasive VATS-LCS approach in Chinese LQTS patients. No serious complications, including Horner’s syndrome, postoperative bleeding or severe pain, developed after VATS-LCS in this study. Overall, we demonstrate that VATS-LCS is a low-morbidity procedure that achieves a marked response in Chinese LQTS patients, which is consistent with previous reports.

**LCSD and QT interval:** QTc prolongation is an important marker for increasing risk of ventricular arrhythmias and SCD in LQTS patients, therefore, it is of vital importance to evaluate QTc intervals before and after LSCD. Schwartz, et al.\(^{20}\) have observed a QT-attenuating effect after denervation, reporting a decrease in the QTc by an average of 39 ± 54 ms 6 months after LSCD. Similar results were observed in our research, which showed that QTc was shortened 32 ms 24 hours after LSCD and 48 ms 1 week after LSCD, respectively (Table III). In addition, our results in eight patients demonstrated that LSCD shortens QTc without affecting the resting heart rate. And 24-hour Holter monitoring also showed that QTc intervals were shortened by 89 and 55 ms at the maximum and minimum heart rates, respectively, after the procedure, with the maximum and minimum heart rates remaining...
unchanged. However, QTc shortening is not a completely reliable parameter for estimating the efficacy of LCSD or the prognosis of patients during long-term follow-up. Schwartz, et al. indicated that a change < 40 ms didn’t appear to significantly worsen the prognosis in terms of both event-free survival and rate of events. In our research, we found that QTd was reduced from 67 ± 17.5 ms before LCSD to 21 ± 3.9 ms 24 hours after LCSD and to 30 ± 8.1 ms 1 week after LCSD. Indeed, increased QTd is often detectable in LQTS patients, and a positive response to therapy may be associated with lower values. QTd might be a useful parameter for evaluating the efficacy of VATS-LCSD and further research is needed to assess the relationship between QTd and long-term prognosis. All these results indicate that LCSD is effective in reducing the risk of cardiac events in LQTS patients without resulting in a significant decrease in the heart rate and, therefore, can be used in LQTS patients with a wide range of baseline heart rates. **LCSd and cardiac event:** Schwartz, et al. pointed out the important fact that the efficacy of LCSD should not be based simply on QTc reduction alone but rather on a decrease in arrhythmia-related cardiac events. In their first series of 85 patients, Schwartz, et al. reported a significant decrease in cardiac event rates from 99% to 45%. In their follow-up study of 147 patients with LQTS, a 90% reduction in cardiac event rates was confirmed. Ackerman, et al. showed that among the 29 previously symptomatic patients with a reduction of cardiac events post-LCSD, 79% of them had no breakthrough cardiac events within the 3.6 years’ follow-up. Overall, our current data showed similar post-LCSD success with 100% of the patients experiencing a reduction of cardiac events post-LCSD (Figure 3). However, although the clinical symptoms attenuated, patient no. 6, who was recognized to be of high risk for SCD before the procedure, still has high annul cardiac event burden after surgery. This is consistent with the previous research of Schwartz, et al. showing that LCSD is not entirely effective in preventing cardiac events including SCD during long-term follow-up in high-risk patients. Thus, ICD is recommended as complementary treatment in such patients. In fact, LCSD and ICD are not mutually exclusive and may complement each other by improving the quality of life through reduction the number of cardiac events and reducing the risk of SCD. Furthermore, Bos, et al. confirmed that patients receiving denervation therapy as primary prevention were less likely to have a breakthrough cardiac event compared with patients having the procedure done for secondary prevention. In our research, patient no.4 (Table I), who underwent LCSD for primary prevention, did not experience cardiac events during the 9-year follow-up. Overall, this demonstrates that VATS-LCSD has a significant impact on reducing cardiac events, and therefore can effectively improve the life quality of patients. However, the high risk of LQTS patients cannot be abolished by LCSD alone and LCSD should certainly not be viewed as curative or an ICD alternative in high-risk patients. As for low risk patients, primary prevention may be considered as an effective therapy.

**Conclusion**

Our research indicates that VATS-LCSD has a significant effect on cardiac electrophysiology and presents a valuable therapeutic option for LQTS patients. It reduces the QTc level in Chinese LQTS patients without affecting the heart rate, and therefore can be used in patients with a wide range of the baseline heart rates. QTd might be a useful parameter for evaluating the efficacy of VATS-LCSD. Moreover, LCSD could prevent or reduce the occurrence of syncopal episodes or life-threatening arrhythmias in patients affected by LQTS.

**Limitations:** The major limitations of this study are due to the inherent nature of a retrospective design involving a limited patient number secondary to the rare prevalence of these diseases. However, the results from these patients are encouraging and further studies in more patients with longer periods of follow-up are warranted.

**Disclosures**

**Conflicts of interest:** None.

**References**

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