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# Surgical left cardiac sympathetic denervation for long QT syndrome: effects on QT interval and heart rate

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**Abstract** The primary aim of the present study was to investigate the short-term effects of surgical left cardiac sympathetic denervation (LCSD) on the QT interval and heart rate in patients with congenital long QT syndrome (LQTS). Left cardiac sympathetic denervation was performed in five LQTS patients who had a history of syncope. The patients' 12-lead and 24-h Holter monitoring ECG was recorded 24 h before and 24 h after LCSD. Treadmill exercise tests were also performed before and 6 days after surgery to assess changes in heart rate and the QT interval after surgery. Left cardiac sympathetic denervation was successful in all patients. The mean value of the corrected QT interval (QTc) in the five patients decreased from 0.59 ± 0.05 to 0.48 ± 0.04 s ($P = 0.006$) immediately after the procedure and remained short (0.47 ± 0.04, $P < 0.05$) after a 21-month follow-up. The mean value of QTc on the 24-h Holter monitoring ECG also decreased in all patients (0.67 ± 0.07 vs 0.60 ± 0.05 s, $P < 0.01$). The mean, maximum, and minimum heart rate on the 24-h ECG remained unchanged ($P > 0.05$). The maximum heart rate during the exercise tests decreased from 162 ± 4 beats/min before surgery to 129 ± 10 beats/min ($P < 0.01$). The exercise-induced increase in QTc remained unchanged after the surgery ($P > 0.05$). Although four of the five patients were syncope-free until 21 months postoperatively, the remaining patient had a recurrence of syncope, requiring an increased dose of β blocker. These findings indicate that LCSD shortens QTc and diminishes the exercise-induced increase in heart rate whereas the resting heart rate and exercise-induced increase in QTc remain unchanged. These results may have implications for the effectiveness and limitations of LCSD.

**Key words** Long QT syndrome · Left cardiac sympathetic denervation · QT interval · Arrhythmia · Cardiac electrophysiology

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## Introduction

Congenital long QT syndrome (LQTS) is a cardiovascular disorder characterized by prolongation of the QT interval on the body surface ECG and the presence of syncope, seizures, and sudden cardiac death.[1] The incidence of LQTS is approximately one in 5000–7000,[2] and the 15-year mortality in untreated symptomatic patients is as high as 53%.[3] The young age of most patients and the high mortality in untreated symptomatic patients stress the importance of developing novel therapies for this life-threatening disorder.

Long QT syndrome is a genetic disease with more than five genes identified as being responsible for its occurrence.[4] Antiadrenergic therapy with β-blockers prevents syncope and cardiac arrest in 75%–80% of patients,[5–7] but more than 20% of patients continue to have syncopal episodes and remain at high risk for sudden cardiac death despite receiving a full dose of β-blockers. For such patients, implantable cardioverter defibrillators are often considered or recommended to prevent sudden death although they cannot prevent the recurrence of ventricular arrhythmia. Left cardiac sympathetic denervation (LCSD) may be useful for preventing cardiac events associated with LQTS.[6,8] Although LCSD appears to shorten the QT interval on the resting ECG without changing the heart rate,[1,8] its effect on the heart rate or T-wave morphology during exercise is less certain. The primary purpose of the study was to evaluate the immediate and short-term follow-up results of LCSD

from the resting and exercise ECG features in patients with congenital LQTS.

## Patients and methods

### Patient selection

In 2002, LCSD was performed on five patients at Tongren Hospital, Peking with congenital LQTS and a history of annual syncopal attacks for more than 5 years (Table 1). There were three female and two male patients, aged between 15 and 33 years. All patients were treated with oral β-blockers before the surgery. The resting heart rate in these patients before the operation ranged from 50 to 71 beats/min. The study was approved by the Institutional Review Board and informed consent was obtained from each patient before the study.

### Surgical procedures

Under single-lumen tracheal incubation anesthesia, the supraclavicular approach was used. Following a small incision in the left subclavicular region, the anterior scalene muscle was divided and the phrenic nerve was retracted medially.[1] The pleural ligamentum was cut and the stellate ganglion was exposed. After the lower part of the ganglion was resected, the left sympathetic chain between T2 and T3 was isolated and cut. Left cardiac sympathetic denervation was performed by an extrapleural approach, which makes thoracotomy unnecessary.[1] The cephalic portion of the left stellate ganglion was preserved to avoid Horner's syndrome.[1]

### ECG assessment

A standard 12-lead ECG and a 24-h Holter monitoring ECG (MS8000, Marquette, Danbury, CT, USA) were obtained 2 days before surgery and again on the second day after surgery. The treadmill exercise test (Q4500, Quinton, Bothell, WA, USA) was also conducted 2 days before and 7 days after the LCSD.

The QT interval was measured from the 12-lead ECG obtained before and after the LCSD. The QT interval was measured on the ECG lead in which the end of the T wave was the clearest, in most cases, on lead II or V5. For a comparison of the QTc before and after surgery, the same lead was always chosen for the QT assessment. The corrected QT interval (QTc) was calculated according to Bazett's formula ($QTc = QT/RR^{1/2}$), and reported in seconds. The RR interval was measured during sinus rhythm, taking the mean for at least 5 beats.

An average QTc was also obtained on 24-h Holter monitoring ECG by averaging all QTc of the 24-h recording, before and after the surgery. The maximum and minimum heart rate were calculated before and during exercise tests. QTc was measured immediately before and after the exercise, and the exercise-induced increase in QTc was calculated.

### 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.

## Results

Left cardiac sympathetic denervation was successful in all patients. The duration of surgery for each patient was between 30 and 40 min. There was no mortality or serious complications associated with the procedures. None of the patients experienced Horner's syndrome after the procedure. The patients were allowed to walk around in the ward 24 h after the surgery, when oral β-blocker therapy was resumed on the preoperation dose regimen. They were discharged 7 days after the surgery after completing all postoperative investigations.

### 12-lead ECG

The average QTc in the five patients was shortened from 0.59 ± 0.05 to 0.48 ± 0.04 s ($P = 0.006$) immediately after surgery (Fig. 1). The average QTc remained shortened 24 h and 21 months after surgery (Table 3). The QTc reduction

**Table 1.** Patients' clinical and ECG features before surgery

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Sex | F | F | F | M | M |
| Age at surgery (years) | 23 | 15 | 18 | 33 | 19 |
| Age at first syncope (years) | 13 | 2 | 2 | 1 | 6 |
| Syncope | + | + | + | + | + |
| Cardiac arrest | − | − | − | − | − |
| Average number of syncope episodes/year | 0.5 | 2 | 4 | 3 | 1 |
| Heart rate (beats/min) | 70 | 55 | 71 | 50 | 61 |
| QTc (s) | 0.59 | 0.60 | 0.67 | 0.66 | 0.62 |

+, yes; −, no

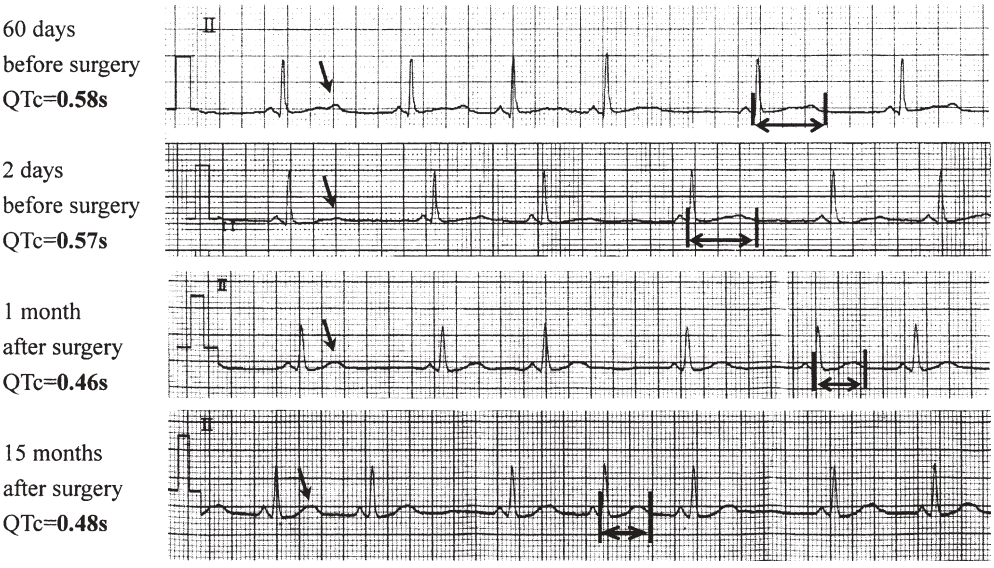


**Fig. 1.** Body surface ECG of a 15-year-old female patient. The QTc was shortened after left cardiac sympathectomy. The preoperative bifid T wave was also normalized after the procedure (*arrow*)

**Table 2.** Results of 24-h Holter monitoring and exercise tests before and after surgery

| | Before surgery | After surgery |
|---|---|---|
| 24-h Holter ECG | | |
| HR (beats/min) | 60 ± 6 | 61 ± 3 |
| Maximum HR (beats/min) | 103 ± 17 | 96 ± 15 |
| Minimum HR (beats/min) | 42 ± 7 | 46 ± 5 |
| Mean QTc (s) | 0.67 ± 0.07 | 0.60 ± 0.05** |
| During exercise tests | | |
| Maximum HR (beats/min) | 162 ± 4 | 129 ± 10** |
| Exercise grade | 4 ± 1 | 4 ± 1 |
| Duration of exercise (min) | 9.4 ± 3.6 | 10.4 ± 2.0 |
| QTc increase (s) | 0.02 ± 0.02 | 0.02 ± 0.01 |

HR, heart rate
** $P < 0.01$ compared with that before surgery

**Table 3.** Corrected QT interval (QTc) before and after left cardiac sympathectomy

| Patients | Before | 24 h after | 21 months after |
|---|---|---|---|
| 1 | 0.51 | 0.45 | 0.41 |
| 2 | 0.63 | 0.52 | 0.48 |
| 3 | 0.60 | 0.49 | 0.50 |
| 4 | 0.59 | 0.53 | 0.49 |
| 5 | 0.46 | 0.44 | 0.45 |
| Average | 0.56 ± 0.03 | 0.49 ± 0.04* | 0.47 ± 0.04* |

* $P < 0.05$ compared with the QTc before surgery

and normalization of T wave after the LCSD is shown in Fig. 1.

## 24-h Holter monitoring ECG

The 24-h Holter monitoring ECG showed that the mean value of QTc in 24 h was decreased in all patients (Table 2). The mean value of the heart rate remained unchanged, but the maximum heart rate was slightly decreased from 103 ± 17 to 96 ± 15 beats/min, and the minimum heart rate was increased from 42 ± 7 to 46 ± 5 beats/min ($P > 0.05$, Table 2).

One patient had frequent ventricular ectopics before surgery. The average ventricular ectopics decreased from 59 beats/h to 1 beat/h ($P < 0.001$) after surgery.

## Exercise tests

The exercise test was completed in four patients. One patient experienced minor foot injuries before surgery and was unable to complete the preoperative treadmill test. After surgery, the maximum heart rate during exercise was 129 ± 10 beats/min, which was significantly lower than that before LCSD ($P < 0.01$, Table 2).

Before LCSD, there was a 20-ms increase in QTc on average immediately after the exercise test. A similar degree of QTc increase was also observed after LCSD ($P > 0.05$, Table 2).

## Follow-up

The five patients were discharged within a week after the procedure on β-blockers. They were followed up for 21 months, during which time three of the five patients were administered propranolol at a dose ranging from 20 to 40 mg/day. Two other patients stopped taking propranolol within weeks after their hospital discharge because they did not feel there was a need to take β-blockers after the surgery.

Four patients were symptom-free during the follow up. One patient (patient no. 2, Table 3), who had an average of two syncopal attacks per year before the surgery, experienced two episodes of syncope during the 21-month follow-up. This patient was on a small dose of propranolol (20 mg once daily) during the follow-up and the QTc remained short.

## Discussion

### Rationale of LCSD for LQTS

Long QT syndrome is caused by mutations in genes encoding cardiac ion channels involved in the control of repolarization. However, sympathetic innervation plays a major and critical role in initiating arrhythmic events.[9] T-wave alternans, one of the characteristics of long QT syndrome, can be reproduced by stimulation of the left stellate ganglion in animals[10] and in human subjects.[11] Animal experiments have shown that left stellectomy increases the ventricular fibrillation threshold, whereas right stellectomy decreases it.[12,13] In humans, left sympathectomy shortens the prolonged QT interval, thereby reducing the probability of malignant arrhythmia.[6] Currently, LCSD is being performed in only a limited number of centers and is reserved mainly for patients who have failed β-blocker therapy.[1,2]

### Techniques of LCSD

The earliest technique of left cardiac sympathectomy is a simple left stellectomy, which involves ablation of the left stellate ganglion and often results in Horner's syndrome as an adverse effect.[1] The drawback of this procedure is that it provides only limited cardiac denervation in humans.[1,6] The latest surgical technique of sympathectomy, as shown in the present study, is designed to remove the lower part of the left stellate ganglion and the first four or five thoracic ganglia.[1] This procedure produces adequate cardiac sympathetic denervation and an extremely low incidence of Horner's syndrome because the ocular sympathetic fibers are spared.[1,6] In our study no patient developed Horner's syndrome, indicating that this complication can be largely avoided through this procedure.

### ECG features after LCSD

A previous study has shown that LCSD may shorten QTc by an average of 41 ms.[6] The results in our five patients who successfully underwent LCSD demonstrated that LCSD shortens QTc without affecting the resting heart rate. The average QTc on 24-h Holter monitoring was also reduced after surgery in most patients. The average, maximum, and minimum heart rate within 24 h remained unchanged. These results indicate that LCSD does not result in a significant decrease in the resting heart rate and, therefore, can be used in LQTS patients with a wide range of the baseline heart rate.

Left cardiac sympathetic denervation attenuates exercise-induced increases in the heart rate. In canine models, sympathectomy did not affect the maximum heart rate during exercise tests.[14] In our patients who completed exercise testing before and after the surgery, the average maximum heart rate obtained during the exercise test was reduced by approximately 40 beats/min. The maximum heart rate during the exercise test did not reach the level before surgery. Although these patients were treated with postoperative β-blockers that are known to diminish the heart rate during exercise,[15] the subdued heart rate response to exercise was largely contributable to the LCSD, because the type and dosage of the drug remained unchanged after the procedures. Left cardiac sympathetic denervation did not change the exercise-induced increase in QTc.

It is interesting that after LCSD, the bifid T wave in one patient returned to a normal, smooth T wave. The electrophysiological mechanism and the clinical implications of these improvements in T-wave morphology need to be explored in future studies.

Although LCSD may largely reduce the sympathetic innervation to the heart, it is unlikely to completely abolish the influence of catecholamines on the heart because the circulating adrenaline or noradrenaline is not affected to a significant extent by the procedure. Therefore, the pathophysiology of myocyte membrane ionic channels responsible for LQTS may not be corrected completely through LCSD. As a result, LCSD decreases QTc in some patients but may not change QTc in others.[1] This may also explain the unchanged QTc increase during exercise testing in our patients. For these reasons, many patients who underwent successful LCSD were still advised to take β-blockers.[1] Whether LCSD alone leads to long-term symptom control in patients with congenital LQTS remains unclear, and further large-scale studies are warranted.

### Limitations

The major limitation of this study is that the number of patients enrolled was very small. Whether the observed benefits on QTc and syncopal attacks in this study also occur in a larger patient population remains uncertain. However, the results from these patients are encouraging and further studies in more patients with longer periods of follow-up are warranted.

In conclusion, our study in these patients indicated that LCSD has a significant and immediate effect on cardiac electrophysiology. It shortens the QTc on the 12-lead ECG and attenuates the exercise-induced increase in heart rate. However, LCSD has no significant effect on the resting heart rate and the exercise-induced increase in QTc in these patients. Whether these ECG changes translate into long-term prevention of ventricular arrhythmia in patients with long QT syndrome remains to be seen.

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