Physical and Psychological Consequences of Left Cardiac Sympathetic Denervation in Long-QT Syndrome and Catecholaminergic Polymorphic Ventricular Tachycardia

Kathryn E. Waddell-Smith, MBBS; Kjetil N. Ertresvaag, MD; Jian Li, BSc; Krish Chaudhuri, MBBS, MSurg, MBA, MEd; Jackie R. Crawford, NZCS; James K. Hamill; David Haydock; Jonathan R. Skinner, MBChB, MD; on behalf of the Cardiac Inherited Disease Group New Zealand*

Background—Left cardiac sympathetic denervation reduces risk in long-QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia. Side effects and patient satisfaction have not been systematically analyzed in patients who underwent left cardiac sympathetic denervation. Aims of this study included documenting physical and psychological consequences and patient satisfaction after left cardiac sympathetic denervation in LQTS or catecholaminergic polymorphic ventricular tachycardia.

Methods and Results—Patients with LQTS (N=40) and catecholaminergic polymorphic ventricular tachycardia (N=7) underwent video-assisted thoracoscopic left cardiac sympathetic denervation, with a median follow-up of 29 months (range, 1–67 months). Clinical records were reviewed; 44 patients completed a telephone survey. Of 47 patients (53%), 25 were preoperatively symptomatic (15 syncope, 7 near-drowning, and 3 resuscitated sudden death). Indications for left cardiac sympathetic denervation included β-blocker intolerance (15; 32%) or nonadherence (10; 21%) and disease factors (18; 38%; catecholaminergic polymorphic ventricular tachycardia [6], near-drowning [2], exertional syncope [1], symptoms on therapy [2], LQT3 [1], QTc>520 ms [6]). Other indications were competitive sports participation (2), family history of sudden death (1), and other (1). Median QTc did not change among patients with LQTS (461±60 to 476±54 ms; *P*=0.49). Side effects were reported by 42 of 44 (95%). Twenty-nine patients (66%) reported dryness on left side, 26 (59%) a Harlequin-type (unilateral) facial flush, 24 (55%) contralateral hyperhidrosis, 17 (39%) differential hand temperatures, 5 (11%) permanent and 4 (9%) transient ptosis, 5 (11%) thermoregulation difficulties, 4 (9%) a sensation of left arm paresthesia, and 3 (7%) sympathetic flight/fright response loss. Majority of the patients were satisfied postoperatively: 38 (86%) were happy with the procedure, 33 (75%) felt safer, 40 (91%) recommended the procedure to others, and 40 (91%) felt happy with their scar appearance.

Conclusions—Despite significant morbidity resulting from left cardiac sympathetic denervation, patients with LQTS and CPVT have high levels of postoperative satisfaction. **(*Circ Arrhythm Electrophysiol*. 2015;8:1151-1158. DOI: 10.1161/CIRCEP.115.003159.)**

Key Words: adverse effects ■ long-QT syndrome ■ polymorphic catecholergic ventricular tachycardia ■ sympathectomy ■ video-assisted thoracoscopic surgery

Video-assisted thoracoscopic sympathectomy is used to treat various disorders, most commonly focal hyperhidrosis and facial blushing.[1] The procedure (where the lower part of the left stellate ganglion and first 4–5 thoracic ganglia are ablated) also significantly reduces the occurrence and frequency of symptoms in long-QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), even in high-risk populations.[2–7]

Editorial see p 1007

Side effects of sympathectomy have been well documented in the hyperhidrosis and blushing populations and include compensatory/reflex hyperhidrosis, pain, gustatory sweating, and Horner syndrome.[8–10] However, there is scant acknowledgment of these symptoms in cardiology literature. To make a balanced decision regarding the risk–benefit ratio for this procedure and

Received February 19, 2015; accepted February 19, 2015.

From the Green Lane Paediatric and Congenital Cardiac Services (K.E.W.-S., J.R.C.) and Department of Paediatric Surgery (K.N.E., J.K.H.), Starship Children's Hospital, Auckland, New Zealand; Department of Child Health, The University of Auckland (K.E.W.-S., J.L., J.R.S.); and Department of Cardiothoracic Surgery, Auckland City Hospital, Auckland, New Zealand (K.C., D.H.).

*A list of Cardiac Inherited Disease Group New Zealand members is given in the Data Supplement.

The Data Supplement is available at http://circep.ahajournals.org/lookup/suppl/doi:10.1161/CIRCEP.115.003159/-/DC1.

Correspondence to Jonathan R. Skinner, MBChB, MD, Green Lane Paediatric and Congenital Cardiac Services, Starship Children's Hospital, Private Bag 92024, Auckland 1142, New Zealand. E-mail jskinner@adhb.govt.nz

WHAT IS KNOWN

- Left cardiac sympathetic denervation reduces risk of cardiac events and sudden death in long QT syndrome and catecholaminergic polymorphic ventricular tachycardia
- Side effects have generally been reported as mild and uncommon but have not been reviewed systematically

WHAT THE STUDY ADDS

- Post-operative morbidity is common, most commonly due to dry skin on the left side of the body, a Harlequin-type (unilateral) facial flush with exercise, contralateral hyperhidrosis, differential hand temperatures, transient and permanent ptosis, thermoregulation difficulties, sensation of left arm paresthesia and loss of sympathetic flight/fright response.
- Post-operative satisfaction is generally high, despite the side effects, and patients feel safer following the procedure. Most patients recommend that a similarly affected person have the procedure.

to counsel our patients to help them make an informed choice, clinicians need to appreciate the experience of patients who have had the procedure previously for the same indications. To our knowledge, this is the first study to report the physical and psychological consequences of left cardiac sympathetic denervation (LCSD) and satisfaction among patients who had undergone video-assisted thoracoscopic LCSD for either LQTS or CPVT.

Methods

Study Population

Forty-seven patients who had undergone a minimally invasive, video-assisted LCSD for the treatment of LQTS or CPVT in New Zealand were included. All were enrolled in the New Zealand Cardiac Inherited Diseases Registry and consented to their data being used for research.[11] Procedures were performed between 2008 and 2014 by 1 of 2 surgeons; median age at the time of LCSD was 17 years (range, 2–64 years); 34 patients were women (72%), and 13 were men. Patients who had the same procedure for other indications, or who had open surgery, were excluded. Pretreatment counseling was performed by the senior author and the surgeon performing the procedure.

An experienced clinician made a clinical diagnosis of LQTS or CPVT, and genotyping was subsequently attempted in all but 1 patient.[11] Referral for LCSD was considered clinically appropriate.

Data Collection

Patient Information

Demographic and clinical data were obtained from medical records, most of which were stored prospectively as a part of the registry. Clinical diagnosis, genotype, mutation, most severe symptom pre-LCSD, medical therapy before and after the procedure, and indication for and details about procedure were recorded. Age at LCSD was recorded, and mean/median QTc is for LQTS patients only.

Physical and Psychological Consequences of LCSD

A single questionnaire was administered via telephone by the first author to patients aged >18 years (N=25) or to the parents if patients were younger at the time of the survey (N=18) (Data Supplement). One teenager responded to the questionnaire, but with parental consent. Questions were constructed to retrospectively assess baseline level of psychosocial stress, overall satisfaction, and physical and psychological sequelae from the procedure. Half of the questions provided scores out of 5. With regard to feelings of anxiety or depression, adult and pediatric patients and parents were asked to rate how often they felt anxious or depressed, where 1 = none of the time and 5 = all of the time. Answers were documented and were analyzed for common themes and notable side effects. Institutional ethical approval was obtained before survey.

ECG Analysis

Twelve-lead ECG analysis was performed by the first author blinded to patient identity, genotype, and clinical situation. The QT interval was measured from the beginning of the QRS complex to the end of the T wave (defined using the tangent technique, where the tangent of the steepest slope of the second limb of the T wave crosses the isoelectric line).[12] Bazett correction was used, and the longest measurement of lead II or V5 was taken from ECGs taken the day before and after LCSD or as near to this time as possible.

Statistical Analyses

Assumptions of the *t* test were tested, and all data were analyzed by unpaired parametric and nonparametric tests as appropriate, including 2-way ANOVA, unpaired *t* test, and column statistics. Statistical analyses were performed using GraphPad Prism version 6.0e for Mac (GraphPad Software, La Jolla, CA; www.graphpad.com) and using SAS version 9.4 (Cary, NC).

Surgical Technique

Surgeons performed the procedure using video-assisted thoracoscopic surgical approaches with double-lumen endotracheal intubation and selective deflation of the left lung. Resection of the sympathetic chain was performed using minimally invasive techniques via either 1 or 3 axillary ports. The proximal extent of sympathectomy was either aggressive, which included sacrificing the lower third to lower half of the stellate ganglion (n=13; 28%) or conservative, which involved sparing the majority of the lower third of the stellate ganglion (n=34; 72%). Patients' mean age was lower in the aggressive group than in the conservative group (16.5 versus 26 years; P=0.04). When comparing the aggressive and the conservative groups, there were no significant differences with reference to sex (with a preponderance of women in both groups; 8 [69%] versus 25 [74%]; P=0.3) or underlying disease (LQTS versus CPVT; P=1.0). Intraoperative intercostal drains were not used, and at the end of the procedure, air was evacuated. Patients were admitted to the intensive care unit postoperatively and discharged home after a median of 1 day (range, 0–13 days). One patient self-discharged on day 0, and the 13-day admission was because of complex management issues in a patient with Jervell and Lange-Nielsen syndrome, unrelated to LCSD. All other patients had 1 to 2 days of postoperative stay.

Results

Clinical Cohort

All patients had unequivocal phenotypic evidence of disease, 40 with LQTS and 7 with CPVT.[11] Additional details of the study cohort are shown in Table 1 and Figure 1.

The most common indications for LCSD related to medical therapy included inability to take β-blockers because of intolerance or contraindication such as asthma in 15 (32%) patients, and nonadherence to therapy in 10 (21%) patients.

Baseline Psychological Status

Self-reported retrospective scores of anxiety and depression were provided by adult patients, and by parents of the affected

Table 1. Baseline Characteristics of the Study Cohort

	LQTS (N=40)			CPVT (N=7)		
	Men	Women	Total	Men	Women	Total
Genotype and sex						
KCNQ1	6	17	23	…	…	…
KCNH2	3	8	11	…	…	…
SCN5A	0	1	1	…	…	…
Gene negative	3	2	5	…	…	…
RyR2	…	…	…	1	5	6
Untested	…	…	…	0	1	1
Preoperative symptoms						
Cardiac arrest	…	…	2	…	…	1
Near drowning	…	…	6	…	…	1
Syncope	…	…	12	…	…	4
Asymptomatic	…	…	20	…	…	1
Preoperative β-blockade						
Nadolol	…	…	14	…	…	3
Metoprolol controlled release	…	…	9	…	…	2
Atenolol	…	…	1	…	…	0
Indications for LCSD for the entire cohort (N=47)						
Medical therapy						
β-Blocker intolerance or contraindication	…	…	14	…	…	1
β-Blocker nonadherence	…	…	10	…	…	0
Disease-related factors						
Disease	…	…	1*	…	…	6†
Aggressive disease	…	…	3‡	…	…	0
Symptoms on medical therapy	…	…	2	…	…	0
QTc>550 ms	…	…	5	…	…	0
QTc>520 ms and near drowning	…	…	1	…	…	0
Patient choice						
Family history SCD	…	…	1	…	…	0
Desire to perform high level sports	…	…	2	…	…	0
For increased sense of safety	…	…	1	…	…	0
Indications for LCSD for the asymptomatic cohort (n=21)						
Medical therapy						
β-Blocker intolerance or contraindication, %	…	…	7	…	…	0
β-Blocker nonadherence	…	…	5	…	…	0
Disease-related factors			1*			2†
QTc≥560 ms	…	…	3	…	…	…
Patient choice, %	…	…	3	…	…	…

CPVT indicates catecholaminergic polymorphic ventricular tachycardia; LCSD, left cardiac sympathetic denervation; LQTS, long-QT syndrome; and SCD, sudden cardiac death.

*LQT3.

†CPVT.

‡3 pediatric patients presenting, respectively, with near drowning, syncope during running race, and syncope under water.

children for themselves and for their children if the patients were aged <18 years at the time of the survey.

Adult Patients (>18 Years)

Twenty-four of 25 adults answered the questions about preoperative anxiety and depression; median anxiety score was 2.5 (range, 1–4: ie, anxious none to most of the time, respectively), and baseline depression median score was 1 (range, 1–4). Seven adults (29%) reported feelings of anxiety related to LQTS/CPVT most of the time, and 6 (25%) reported feeling depressed most of the time.

Pediatric Patients

Nineteen of the 26 pediatric patients were still <18 years old at the time of the survey, and for this cohort, parents were asked about their own and their children's baseline scores. However, 1 child was too young (4 years old) at the time of surgery for the parents to assess psychological status, 1 parent was unable

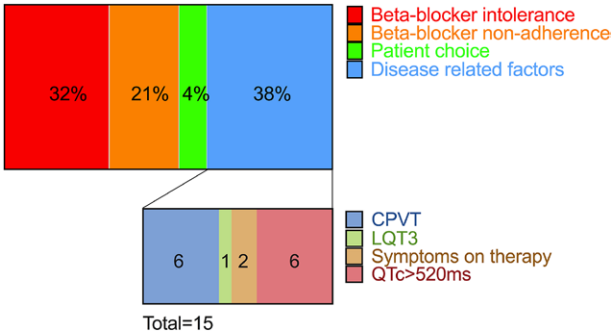

Figure 1. Major indication for each patient for left cardiac sympathetic denervation included β-blocker intolerance/contraindication, β-blocker nonadherence, disease-related factors, and patient choice. Disease-related factors include those with catecholaminergic polymorphic ventricular tachycardia (CPVT), long-QT syndrome 3 (LQT3), those who experienced symptoms while compliant with medical therapy, or those with a prolonged QTc (>550 ms or >520 ms with another indication). Patient choice includes those patients who had family history of sudden cardiac death, wished to perform high-level sport, or others.

to answer the questions on behalf of their child, and 1 teenager answered the questions herself (after parental consent). Retrospectively, parents' self-reported median anxiety and depression scores were 3 (range, 1–4). They rated their children's preoperative baseline anxiety and depression with median scores of 1 (range, 1–5). Five children were given a score of 4 or 5 of 5 for anxiety or depression by their parents. Of the 17 paired parent/child responses, baseline psychological scores were similar except in 5 cases where anxiety or depression was much higher in 3 parents than in their children and much higher in 2 children. Patient's depression and anxiety were highly correlated among the cohort (Spearman correlation, 0.84).

Postoperative Course

Follow-up by telephone survey and review of case notes were performed after a median follow-up of 29 months after LCSD (range, 1–67 months). Tables 2 and 3 show patient comments on side effects.

General Recovery

Majority of the patients (79%) were satisfied with their operation overall with regard to pain relief, side effects, physical and emotional recovery, and economic considerations (Table 4). There was no significant relationship between satisfaction and preoperative depression or anxiety (P=0.12 and P=0.08 respectively), length of postoperative follow-up (P=0.17), or severity of preoperative symptoms (P=0.61). Figure 2 and Table 4 show data on 44 patients who completed the survey, their side effects, and survey response scores.

Follow-up occurred over a median of 29 months postoperatively (range, 1 month to 5 years and 7 months). There was no perioperative mortality or major complications requiring surgical reintervention. One death occurred 47 months after LCSD, but this was noncardiac and unrelated to the procedure.

Cardiac Events

During 116 patient-years of follow-up, 1 patient with LQTS, 1 with Jervell and Lange-Nielsen LQTS, and 3 with CPVT experienced cardiac events (ie, 1+1/40 patients with LQTS, 5%; 3/7 patients with CPVT, 43%). This did not vary with the degree of sympathetic resection (LQTS, P=0.45; CPVT, P=0.43). The patient with single-mutation LQTS was 17 years old at LCSD and carried the KCNQ1 c.797T>C missense mutation, and her longest preoperative QTc was 522 ms. QTc before the procedure was 483 ms, and 431 ms after 2 years. She adhered to controlled-release metoprolol both pre- and postoperatively, and her worst symptom (in both time periods) was classic arrhythmic syncope, which resulted in implantable cardioverter defibrillator insertion after the postoperative event. Five of the 7 patients with CPVT had their procedure performed before flecainide was known to be therapeutic.[13] Of the 3 patients with CPVT who experienced postoperative cardiac events, 1 refused medical therapy, 1 was on low-dose β-blockade without uptitration because of failure to attend follow-up appointments, and the third was on both nadolol and flecainide at the time of her arrest. There was no relationship between degree of sympathetic resection and occurrence of postoperative symptoms.

Table 2. Patient and Caregiver Comments Describing Side Effects Occurring After Left Cardiac Sympathetic Denervation for Long-QT Syndrome or Catecholaminergic Polymorphic Ventricular Tachycardia

Dry skin	Old lady skin on the left side
	My left hand doesn't crinkle, even in the pool
Harlequin-type facial split	Jekyll and Hyde
	Embarrassing
Compensatory hyperhidrosis	It's really bizarre. I'm a freak, a smelly freak on the right hand side
	Embarrassing! I'd get the other side done, but then where would all the sweat go?
Differential hand temperatures	Ice cold left hand
Difficulties in temperature regulation	One hot side and one cold side make it difficult in bed
Emotional and psychological sequelae	Now I get butterflies in my stomach instead of fast heart beats and faints/seizures. I feel more detached, and don't feel embarrassed, sad, angry, or disappointed anymore. Not getting angry is a bonus with a 15-year-old daughter. At times I know that I'm angry, but I don't have a fright/flight response, I have no startle response, and have a dull thud feeling instead. I don't actually feel sad when I hear sad/bad news. I recognize that the situation is a sad one, so cognitively adjust my behavior and response accordingly
	I don't get really anxious anymore, no more sudden adrenaline surges
	I used to hate getting a fright, but now there is much less of a jolt, and I'm much calmer with frights

Table 3. Patient and Caregiver Comments Describing Satisfaction Having Had Left Cardiac Sympathetic Denervation for Long-QT Syndrome or Catecholaminergic Polymorphic Ventricular Tachycardia

I see sympathectomy as a passage back to normal life
Peace of mind for parents. Do it the "sooner the better." Extra insurance
Made my life better. I wish it was done earlier. Ends suffering
Reduces risk of sudden death, its lifesaving, and the benefits far outweigh the side effects
Might as well have it done, because no difference afterward (back to normal). I'm safe; it's an extra thing to be safe
Eliminates worry, and if something happens in the future, I don't have to think "what if?"
Helps keep you alive, wouldn't want to be left wondering
It's given me confidence; I've done something to make me safer

Electrocardiographic Changes

Median QTc among patients with LQTS was 461±60 ms preoperatively and was 476±54 ms postoperatively (P=0.49).

Physical Sequelae

Dry Skin

The most common effect reported from the procedure was dry skin on the left side of the body (67%). Twenty-nine patients reported a dry left hand, including 3 who also reported a dry face (on left side), and 3 reported dry left foot. Seven patients used extra (or stronger) moisturizer on the left side.

Harlequin-Type Facial Flush

The second most common effect was having a marked Harlequin-type demarcation in color on, at least, the face (63%): 17 reported this on the face only, 3 on the hand only, and 5 on the whole body, and 8 patients reported worsening of this effect after exertion (Figure 3A).

Compensatory Hyperhidrosis

Fifty-five percent of patients reported problems with excessive sweating on the right side (Figure 3B). Lifestyle adjustments included using heavy-duty antiperspirant (including the lumbar back), carrying a towel always, and using grip aids to play sport (with the dry left hand losing grip). One patient used grip aids because of sweaty right hand, one slipped because of dry left hand, and a third used sticky stuff on the hands while playing netball (parent unsure of side).

Pain

Five patients reported severe pain in hospital, necessitating extra analgesia (11%). Three patients (7%) experienced a shooting type of pain down the left side, which resolved after 1 to 8 months. No patients had chronic pain, and 1 patient reported resolution of pre-existing chronic upper back pain.

Hand Temperature

Eleven patients (25%) reported significant differences in the temperature of their hands; however, they were not all able to state which hand was warm or cold.

Thermoregulation Difficulties

Five patients (11%) reported a definite hot and cold side of the body (right:left, 50:50). They commented that it was difficult to regulate their body temperature, particularly in bed or in cold weather.

Ptosis

Nine patients reported ptosis on the left side. In 4 individuals, this was transient lasting between 3 days and ≈6 months. Five patients (11%) had permanent ptosis (at median follow-up of 26 months; range, 9–55 months), all reported as very mild, and none reported disappointment (Figure 4). One patient reported that the ptosis worsened with fatigue.

Paresthesia

Two women (5%) reported a sensation of reduced feeling and tingling in the left fingers and arm up to the elbow.

Emotional/Psychological Sequelae

Loss of Sympathetic Flight/Fright Response

Three women (7%) reported that they were much calmer in situations that previously would have been alarming or frightening. One also felt detached in sad or angry circumstances.

Satisfaction

The majority of patients were satisfied postoperatively and they felt positive, felt safer, and were happy to recommend the procedure to others (Figure 2; Table 3 for patient comments).

Table 4. Postoperative Physical and Psychological Consequences of LCSD, Postoperative Satisfaction

	N (%)
Postoperative physical and psychological sequelae of LCSD	
Dry skin	29 (67)
Harlequin-type flush	27 (63)
Hyperhidrosis	24 (56)
Pain	8 (19)
Difference in hand temperature	11 (26)
Thermoregulation difficulties	5 (12)
Ptosis (permanent plus transient)	9 (21)
Ptosis (permanent)	5 (12)
Ptosis (transient)	4 (9)
Paresthesia	2 (5)
Loss of sympathetic flight/fright response	3 (7)
Postoperative satisfaction	34/43 (79)
Feel happy with their surgical scar appearance (score 1, 2, or 3 of 5)	41/44 (93)
Feel positive after procedure (positive vs negative)	35/41 (85)
Feel safer after procedure (score 1 or 2 of 5; the remainder felt the same as preoperatively, score 3/5)	33/44 (75)
Feel happy the procedure happened (score 1 or 2 of 5)	38/44 (86)
Feel no regret that the procedure happened (score 4 or 5 of 5)	40/44 (91)
Would recommend the procedure to someone like you/your child (yes vs no, unsure)	40/44 (91)

LCSD indicates left cardiac sympathetic denervation.

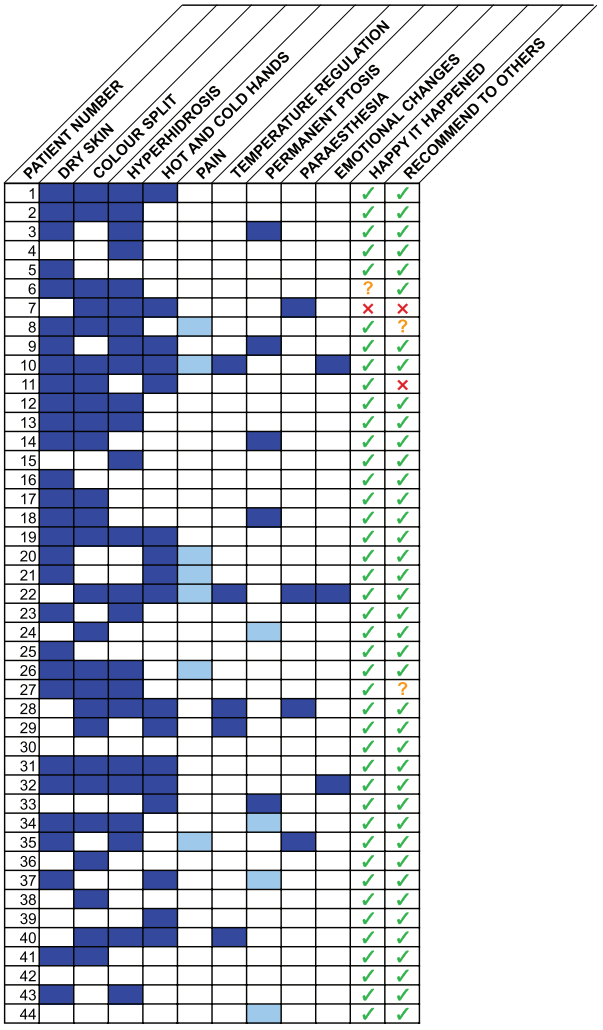

Figure 2. Results from 44 patients who completed the telephone follow-up survey. Dark blue boxes represent symptoms, and light blue boxes indicate transient symptoms. Green ticks represent that patients are happy with the procedure (score 4–5 of 5) and would recommend the procedure to a similarly affected person. Orange question marks represent that the patients feel neutral toward the procedure or recommending it to others. Red crosses represent the patient was unhappy that the sympathectomy was carried out (score 2 of 5) or that they would not recommend the procedure to others.

Symptom Duration

Three patients reported that their symptoms were worst in the first year (or second), and then improved.

Comparison of Side Effects According to Degree of Resection

When comparing the aggressive versus conservative resection groups, there were no significant differences in dry skin (P=0.14), Harlequin-type facial flush (P=0.72), compensatory hyperhidrosis (P=1.0), hand temperature (P=0.47), pain (P=0.32), thermoregulation difficulties (P=1.0), paresthesia (P=0.56), or loss of sympathetic drive (P=0.55). When both transient and permanent ptosis were included, then there was a significant difference between aggressive (n=5/10) and conservative (n=3/31; P=0.009) groups.

Discussion

The left cardiac sympathectomy, first described in 1971,[14] has recently re-emerged as an important therapeutic option for both LQTS and CPVT and can now be performed thoracoscopically. The procedure is both safe[10] and efficacious.[5] For some patients, it is first-line therapy when β-blockers are contraindicated or cannot be tolerated. In our New Zealand population, poor long-term adherence to therapy, a major hazard in those severely affected,[15] remains a significant problem. The fact that 3 of our patients who underwent LCSD for nonadherence can no longer be traced underscores the potential value of this procedure in patients who only intermittently engage with health services. Nevertheless, this is a procedure with side effects, most of which are permanent, so accurate counseling before the procedure is essential.

The present study documents high rates of morbidity related to side effects, sometimes associated with significant levels of embarrassment and distress. The side effects described by our cohort are consistent with those when the sympathectomy is done for other reasons,[2,8–10,16] and may be more severe because of the ablation of the second thoracic ganglion, which is associated with more pronounced compensatory hyperhidrosis.[10,17] However, most other indications, such as hyperhidrosis, involve bilateral sympathectomy, so the harlequin effect does not occur. Furthermore, patients with LQTS and CPVT tend to have underlying anxiety[18] and sometimes depression[19] related indirectly to their condition and also to the sacrifices and lifestyle changes they must make. They often also have a traumatic personal or family history. This background, confirmed by the baseline psychological profile in this study, may explain the overall satisfaction among patients with LQTS and CPVT who have undergone LCSD. The sympathectomy gives them a sense of safety and a sense that they can lead a relatively normal life, which is evident from a patient's comment: "I see sympathectomy as a passage back to normal life."

Before this investigation, we and others have counseled our patients that permanent ptosis was the most significant (but uncommon) side effect.[20] However, in this study, patients often recalled their side effects with some distress. They described embarrassment, inconvenience, and annoyance. We are now able to give a more thorough and honest account of life after an LCSD. The findings of this review have resulted in a change of emphasis in our counseling practice; we highlight the compensatory hyperhidrosis, Harlequin-type facial flush, and the less common and very mild ptosis. Advising the patients about overwhelming patient satisfaction is as important as warning them of the side effects. Regarding the occurrence of Horner syndrome, we found no difference between aggressive and conservative surgical technique, but given the low prevalence, a larger series may be needed to clarify this.

This study adds a new perspective to the side effects of sympathectomy. Studies on LQTS and CPVT populations suggest that the side effects of LCSD are mild and limited.[21] Previous reports of side effects from the larger cohorts where sympathectomy is performed for hyperhidrosis or facial flushing were based on physician-only assessments[8,9]; patient commentary was excluded and may anyway be different since the procedure was largely for cosmetic reasons.[10] The majority

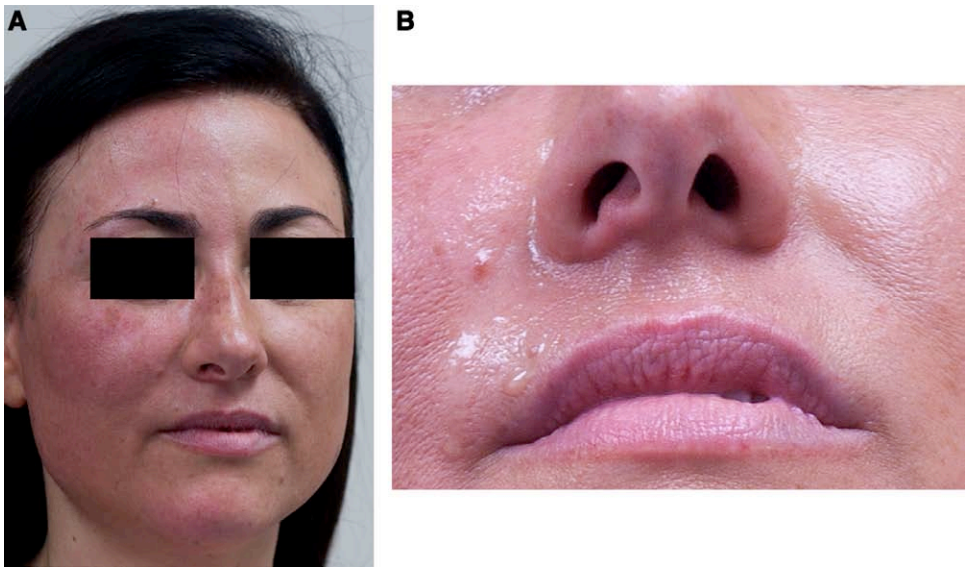

Figure 3. Patient 10 after 10.1 metabolic equivalents of exercise demonstrating (**A**) the Harlequin-type facial flush, with flushed right side of face and normal/pale left side, and (**B**) the differences in sweating, with sweaty right side of face and dry left side.

of patients in our cohort would strongly disagree that side effects are minimal, but agree that they are outweighed by the benefits.[21]

This study was not designed to assess the efficacy of reducing cardiac events; nevertheless, there are still important findings. In case reports and small series, LCSD has been reported to have significantly reduced the occurrence of cardiac events in patients with CPVT.[2,7,22–27] In the largest and most recent series published, 54 symptomatic patients with CPVT underwent LCSD. Although the number of patients who had an incomplete LCSD was small, the authors reported that those who had a complete LCSD were much less likely to have postoperative cardiac events compared with those who had an incomplete denervation (8/47 [17%] versus 5/7 [71%]; $P<0.01$).[27] Six patients (86%) were preoperatively symptomatic, and 3 of 7 (43%) were postoperatively symptomatic (postoperative median follow-up of 45 months; range, 6–67 months; 24 patient-years). Therefore, it should be emphasized that long-term adherence to medical therapy, importantly flecainide therapy, is paramount in the care of individuals with CPVT.

A limitation of this study is the reliance on patient reporting and lack of objective measures. This may result in a higher incidence of reported side effects compared with other series. Nonconfidential responses may introduce bias, but given the high morbidity reported, we feel that the impact of this would be minimal. Furthermore, no validated questionnaire was suitable for this study cohort. Although there are inherent challenges in interviewing children and there may be a discordance between responses of parents and children, we performed an ordinal logistic regression excluding parental data to minimize this issue. Follow-up is variable and <1 year in 23% of the cohort, a time when side effects are more pronounced (both in our series and in others).[8]

Figure 4. Patient 3 has permanent left eyelid ptosis and miosis.

Conclusions

This study documents, for the first time, side effects and patient satisfaction associated with minimally invasive video-assisted thoracoscopic LCSD in LQTS and CPVT populations. Although morbidity was high (most commonly because of dry skin, compensatory hyperhidrosis, and Harlequin-type facial flush), so too was patient satisfaction, with 91% of patients recommending the procedure to other affected patients. Extent of surgical resection influenced risk of ptosis, but not of other outcomes. This study enables us to counsel patients better before they undergo this treatment.

Acknowledgments

This article is presented on behalf of the Cardiac Inherited Diseases Group, which was generously supported by Cure Kids. We gratefully acknowledge the statistical advice from Avinesh Pillai and Ying Huang from the Department of Statistics, the University of Auckland; Iris Fontanilla and Liz Painter, the Clinical Cardiac Psychologists from the Department of Cardiovascular Services, Green Lane Cardiovascular Services, Auckland City Hospital, Auckland, New Zealand, who assisted with the preparation of the patient questionnaire; Cardiac Inherited Diseases Group cardiologists who referred patients for left cardiac sympathetic denervation; Charlene Nell from the Department of Cardiovascular Services, Green Lane Cardiovascular Services, Auckland City Hospital, Auckland, New Zealand, who assisted with article preparation and, of course, thank patients, without whom this research would not be possible.

Sources of Funding

Dr Skinner receives salary support from Cure Kids, Dr Waddell-Smith is supported by the National Heart Foundation of New Zealand.

Disclosures

None.

References

1. Hashmonai M, Kopelman D. History of sympathetic surgery. *Clin Auton Res*. 2003;13(suppl 1):I6–I9. doi: 10.1007/s10286-003-1103-5.
2. Hofferberth SC, Cecchin F, Loberman D, Fynn-Thompson F. Left thoracoscopic sympathectomy for cardiac denervation in patients with life-threatening ventricular arrhythmias. *J Thorac Cardiovasc Surg*. 2014;147:404–409. doi: 10.1016/j.jtcvs.2013.07.064.
3. Collura CA, Johnson JN, Moir C, Ackerman MJ. Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery. *Heart Rhythm*. 2009;6:752–759. doi: 10.1016/j.hrthm.2009.03.024.
4. Bos JM, Bos KM, Johnson JN, Moir C, Ackerman MJ. Left cardiac sympathetic denervation in long QT syndrome: analysis of therapeutic nonresponders. *Circ Arrhythm Electrophysiol*. 2013;6:705–711. doi: 10.1161/CIRCEP.113.000102.
5. Schwartz PJ, Priori SG, Cerrone M, Spazzolini C, Odero A, Napolitano C, Bloise R, De Ferrari GM, Klersy C, Moss AJ, Zareba W, Robinson JL, Hall WJ, Brink PA, Toivonen L, Epstein AE, Li C, Hu D. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. *Circulation*. 2004;109:1826–1833. doi: 10.1161/01.CIR.0000125523.14403.1E.
6. Li J, Liu Y, Yang F, Jiang G, Li C, Hu D, Wang J. Video-assisted thoracoscopic left cardiac sympathetic denervation: a reliable minimally invasive approach for congenital long-QT syndrome. *Ann Thorac Surg*. 2008;86:1955–1958. doi: 10.1016/j.athoracsur.2008.07.100.
7. Schneider HE, Steinmetz M, Krause U, Kriebel T, Ruschewski W, Paul T. Left cardiac sympathetic denervation for the management of life-threatening ventricular tachyarrhythmias in young patients with catecholaminergic polymorphic ventricular tachycardia and long QT syndrome. *Clin Res Cardiol*. 2013;102:33–42. doi: 10.1007/s00392-012-0492-7.
8. Bryant AS, Cerfolio RJ. Satisfaction and compensatory hyperhidrosis rates 5 years and longer after video-assisted thoracoscopic sympathotomy for hyperhidrosis. *J Thorac Cardiovasc Surg*. 2014;147:1160–1163.e1. doi: 10.1016/j.jtcvs.2013.12.016.
9. Kapetanos AT, Furlan AD, Mailis-Gagnon A. Characteristics and associated features of persistent post-sympathectomy pain. *Clin J Pain*. 2003;19:192–199.
10. de Andrade Filho LO, Kuzniec S, Wolosker N, Yazbek G, Kauffman P, Milanez de Campos JR. Technical difficulties and complications of sympathectomy in the treatment of hyperhidrosis: an analysis of 1731 cases. *Ann Vasc Surg*. 2013;27:447–453. doi: 10.1016/j.avsg.2012.05.026.
11. Earle N, Crawford J, Smith W, Hayes I, Shelling A, Hood M, Stiles M, Maxwell F, Heaven D, Love DR, Skinner JR. Community detection of long QT syndrome with a clinical registry: an alternative to ECG screening programs? *Heart Rhythm*. 2013;10:233–238. doi: 10.1016/j.hrthm.2012.10.043.
12. Postema PG, De Jong JS, Van der Bilt IA, Wilde AA. Accurate electrocardiographic assessment of the QT interval: teach the tangent. *Heart Rhythm*. 2008;5:1015–1018. doi: 10.1016/j.hrthm.2008.03.037.
13. van der Werf C, Kannankeril PJ, Sacher F, Krahn AD, Viskin S, Leenhardt A, Shimizu W, Sumitomo N, Fish FA, Bhuiyan ZA, Willems AR, van der Veen MJ, Watanabe H, Laborderie J, Haïssaguerre M, Knollmann BC, Wilde AA. Flecainide therapy reduces exercise-induced ventricular arrhythmias in patients with catecholaminergic polymorphic ventricular tachycardia. *J Am Coll Cardiol*. 2011;57:2244–2254. doi: 10.1016/j.jacc.2011.01.026.
14. Moss AJ, McDonald J. Unilateral cervicothoracic sympathetic ganglionectomy for the treatment of long QT interval syndrome. *N Engl J Med*. 1971;285:903–904. doi: 10.1056/NEJM197110142851607.
15. Vincent GM, Schwartz PJ, Denjoy I, Swan H, Bithell C, Spazzolini C, Crotti L, Piippo K, Lupoglazoff JM, Villain E, Priori SG, Napolitano C, Zhang L. High efficacy of beta-blockers in long-QT syndrome type 1: contribution of noncompliance and QT-prolonging drugs to the occurrence of beta-blocker treatment "failures". *Circulation*. 2009;119:215–221. doi: 10.1161/CIRCULATIONAHA.108.772533.
16. Atallah J, Fynn-Thompson F, Cecchin F, DiBardino DJ, Walsh EP, Berul CI. Video-assisted thoracoscopic cardiac denervation: a potential novel therapeutic option for children with intractable ventricular arrhythmias. *Ann Thorac Surg*. 2008;86:1620–1625. doi: 10.1016/j.athoracsur.2008.07.006.
17. Alvarez MA, Ruano J, Gómez FJ, Casas E, Baamonde C, Salvatierra A, Moreno JC. Differences between objective efficacy and perceived efficacy in patients with palmar hyperhidrosis treated with either botulinum toxin or endoscopic thoracic sympathectomy. *J Eur Acad Dermatol Venereol*. 2013;27:e282–e288. doi: 10.1111/j.1468-3083.2012.04630.x.
18. Hamang A, Eide GE, Rokne B, Nordin K, Bjorvatn C, Øyen N. Predictors of heart-focused anxiety in patients undergoing genetic investigation and counseling of long QT syndrome or hypertrophic cardiomyopathy: a one year follow-up. *J Genet Couns*. 2012;21:72–84. doi: 10.1007/s10897-011-9393-6.
19. Hintsa T, Keltikangas-Järvinen L, Puttonen S, Ravaja N, Toivonen L, Kontula K, Swan H. Depressive symptoms in the congenital long QT syndrome. *Ann Med*. 2009;41:516–521. doi: 10.1080/07853890903037254.
20. Schwartz PJ. Efficacy of left cardiac sympathetic denervation has an unforeseen side effect: medicolegal complications. *Heart Rhythm*. 2010;7:1330–1332. doi: 10.1016/j.hrthm.2010.04.038.
21. Odero A, Bozzani A, De Ferrari GM, Schwartz PJ. Left cardiac sympathetic denervation for the prevention of life-threatening arrhythmias: the surgical supraclavicular approach to cervicothoracic sympathectomy. *Heart Rhythm*. 2010;7:1161–1165. doi: 10.1016/j.hrthm.2010.03.046.
22. Wilde AA, Bhuiyan ZA, Crotti L, Facchini M, De Ferrari GM, Paul T, Ferrandi C, Koolbergen DR, Odero A, Schwartz PJ. Left cardiac sympathetic denervation for catecholaminergic polymorphic ventricular tachycardia. *N Engl J Med*. 2008;358:2024–2029. doi: 10.1056/NEJMoa0708006.
23. Salvi V, Karnad DR, Panicker GK, Natekar M, Hingorani P, Kerkar V, Ramasamy A, de Vries M, Zumbrunnen T, Kothari S, Narula D. Comparison of 5 methods of QT interval measurements on electrocardiograms from a thorough QT/QTc study: effect on assay sensitivity and categorical outliers. *J Electrocardiol*. 2011;44:96–104. doi: 10.1016/j.jelectrocard.2010.11.010.
24. Makanjee B, Gollob MH, Klein GJ, Krahn AD. Ten-year follow-up of cardiac sympathectomy in a young woman with catecholaminergic polymorphic ventricular tachycardia and an implantable cardioverter defibrillator. *J Cardiovasc Electrophysiol*. 2009;20:1167–1169. doi: 10.1111/j.1540-8167.2009.01441.x.
25. Scott PA, Sandilands AJ, Morris GE, Morgan JM. Successful treatment of catecholaminergic polymorphic ventricular tachycardia with bilateral thoracoscopic sympathectomy. *Heart Rhythm*. 2008;5:1461–1463. doi: 10.1016/j.hrthm.2008.07.007.
26. Gopinathannair R, Olshansky B, Iannettoni M, Mazur A. Delayed maximal response to left cardiac sympathectomy for catecholaminergic polymorphic ventricular tachycardia. *Europace*. 2010;12:1035–1039. doi: 10.1093/europace/euq058.
27. De Ferrari GM, Dusi V, Spazzolini C, Bos JM, Abrams DJ, Berul CI, Crotti L, Davis AM, Eldar M, Kharlap M, Khoury A, Krahn AD, Leenhardt A, Moir CR, Odero A, Olde Nordkamp L, Paul T, Rosés I Noguer F, Shkolnikova M, Till J, Wilde AA, Ackerman MJ, Schwartz PJ. Clinical management of catecholaminergic polymorphic ventricular tachycardia: the role of left cardiac sympathetic denervation. *Circulation*. 2015;131:2185–2193. doi: 10.1161/CIRCULATIONAHA.115.015731.

Physical and Psychological Consequences of Left Cardiac Sympathetic Denervation in Long-QT Syndrome and Catecholaminergic Polymorphic Ventricular Tachycardia

Kathryn E. Waddell-Smith, Kjetil N. Ertresvaag, Jian Li, Krish Chaudhuri, Jackie R. Crawford, James K. Hamill, David Haydock and Jonathan R. Skinner
on behalf of the Cardiac Inherited Disease Group New Zealand*

Circ Arrhythm Electrophysiol. 2015;8:1151-1158; originally published online July 29, 2015;
doi: 10.1161/CIRCEP.115.003159
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3149. Online ISSN: 1941-3084

SUPPLEMENTAL MATERIAL

CIDG (the Cardiac Inherited Disease Group)

CIDG (the Cardiac Inherited Disease Group) is a national network of clinicians and scientists in New Zealand. In particular regarding the present work we would like to acknowledge the following clinicians for contributing patients to the study and assisting with referral planning.

Dr Margaret Hood
Consultant Electrophysiologist
Green Lane Cardiovascular Services/Cardiology Department
Auckland City Hospital
Auckland

Dr David Heaven
Consultant Cardiologist
Cardiology Department
Middlemore Hospital
Auckland

Dr Iain Melton
Consultant Electrophysiologist
Cardiology Department
Christchurch Hospital
Christchurch

Dr Warren Smith
Consultant Cardiologist
Green Lane Cardiovascular Services/Cardiology Department
Auckland City Hospital
Auckland

Dr Martin Stiles
Consultant Cardiologist
Cardiology Department
Waikato District Hospital
Hamilton

Tom Donoghue
Cardiac Disease Regional Nurse
Cardiology Department
Wellington Hospital
Wellington

Mandy Graham
Cardiac Nurse
Cardiology Department
Waikato District Hospital
Hamilton

Questionnaire

TO BE COMPLETED PRIOR TO TELEPHONE CONTACT

PATIENT DETAILS **STICKY LABEL**	
Treating cardiologist	
Date of procedure	
Surgeon / Anaesthetist	
Surgical technique -number of ports -patient position	
Anaesthetic/Intubating technique -CO2 insufflation -apnoea	
Age, height, weight at op, ethnicity	
Date of follow up: clinical	
Date of follow up: phone	
Medications pre op	
Medications post op	
Other medical problems/PMH	
Type of LQTS/ gene result	
Significant LQTS history (ICD/arrest etc)	
Indication: Primary/Secondary	
Family history	
Pre-operative QT and QTc	
Pre-operative T wave morphology	
Post-operative QT & QTc in hospital	
Post-operative QT & QTc follow up (date)	
T wave morphology post operative	

COLLECT AT TIME OF TELEPHONE CONTACT

Name of person completing questionnaire	

Name of person completing questionnaire	
Age/Sex/Clinically affected	
Relationship to person having LCSD	

How did you (adult) feel BEFORE the procedure:	1= none of the time, 2= a little of the time, 3 = some of the time, 4 = most of the time, 5= all of the time Not anxious 1 2 3 4 5 Anxious all the time Not sad/Depressed 1 2 3 4 5 Sad/depressed all the time
How did your child feel BEFORE the procedure:	1= none of the time, 2= a little of the time, 3 = some of the time, 4 = most of the time, 5= all of the time Not scared 1 2 3 4 5 Scared all the time Not flat/down 1 2 3 4 5 Flat/down all the time
Was it a difficult decision to have the procedure? Why? If prompting needed, eg:	Not hard 1 2 3 4 5 Hard Risks and worry about side effects of sympathectomy? Worry about operation/anaesthetic Worry about what your child would think later in life? Other…….
Why did your child have the procedure? If prompting needed, eg:	Because they/I wanted it Because the doctor recommended it Couldn't take beta blockers Needed more protection Other…….
Any effects from the procedure?	Overall recovery: Considering pain relief, side effects, physical and emotional recovery and economic considerations, how satisfied are you with the operation? Not satisfied 1 2 3 4 5 Very satisfied Scars: Very unhappy 1 2 3 4 5 Very happy Droopy eye lid: Immediate post op Yes / No Now: Yes / No How long before it resolved?..... Sweating: Left hand: Dry / Normal Left arm pit: Dry / Normal Right hand…… Excessive sweating post op…… Change in colour…… Any others……..

Are any effects negative? From a mood or body image or physical perspective?	Mood is different: Embarrassed/Sad/Angry/Disappointed Feel different about body image: Feel different physically: Other
How do you/your child feel overall after the procedure?	Positive/Negative Safer 1 2 3 4 5 Less safe Happy it happened 1 2 3 4 5 Not happy it happened Regret it happened 1 2 3 4 5 No regret Any faints or cardiac arrest since sympathectomy? Other

Having gone through the sympathectomy, would you recommend someone like you/your child have the procedure Why?	Yes/No
Could we do anything to make it easier for your and your child?	
Do you have any concerns or issues regarding your LCSD or LQTS Tx you would like us to contact your treating cardiologist about?	