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ORIGINAL ARTICLE

Thoracoscopic Sympathectomy for Long QT Syndrome. Literature Review and Case Study

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Background Multiple case studies have suggested that video-assisted thoracoscopic sympathectomy (VATS) reduces the occurrence and frequency of symptoms in long QT syndrome (LQTS) [1,2,3]. To date there has not been a literature review to report on the short-term and long-term outcomes of this procedure. Our primary aims are to review the literature findings on the clinical outcomes of VATS sympathectomy for long QT and present a local centre case report on the outcomes of T2-T5 sympathectomy.

Methods Relevant articles were identified by a systematic search of PubMed, Cochrane and Scopus databases, from November 1985 to October 2015. A total of 520 patients from 21 publications were included for analysis and discussion in three main areas: presenting symptoms and indication for surgery, perioperative complications, and patient quality of life following surgery. Our case study reviews a 49-year-old female with recently diagnosed long QT syndrome and intolerance to beta blocker therapy successfully managed with T2-T5 thoracic sympathectomy.

Results The most common presenting indication for operative management of long QT syndrome was syncope (208/520 patients) and tachyarrhythmia (207/520 patients). T1-T5 left sympathectomy was performed in 15/21 published reports (332/520 patients) with partial stellate removal or in its entirety. Follow-up of patients ranged from 1 month to 11 years. Four patients died in the postoperative period, from fatal arrhythmias. The most common postoperative findings were no symptoms (64/520 patients); tachyarrhythmia (55/520 patients), syncope (45/520 patients), and Horner's syndrome (13/520 patients with 27 patients reporting associated symptoms). Thirteen cases reported on the QTc changes post sympathectomy and 9/13 cases involving 220/520 patients showed marked QTc reduction following surgery. Mean preoperative QTc was 558 ms and median 559 ms. Mean postoperative QTc was 476 ms and median 466 ms. Our patient showed a marked reduction in QTc following surgery, with no evidence of arrhythmias and reduced beta blocker dependence.

Conclusions Surgical management of LQTS has historically involved a left cervicothoracic stellectomy removing stellate ganglia and typically part of the left thoracic sympathetic chain resulting in reduction in symptoms but increasing the risk of Horner's syndrome and intermittent temperature changes [4,5]. Surgical resection of the thoracic ganglia alone for management of LQTS is scarce in the literature. Short-term follow-up in our case study following a T2-T5 sympathectomy revealed reduction in symptoms, no requirement for beta blocker therapy and reduced QTc interval. Further follow-up using greater patient numbers will further support T2-T5 sympathectomy as an option for surgical management of LQTS.

Keywords Sympathectomy • Long QT syndrome

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Introduction

Long QT syndrome (LQTS) is a genetic or acquired condition characterised by a prolonged QT on the surface electrocardiogram (ECG) and is associated with a high risk of sudden cardiac death due to ventricular tachyarrhythmia. Mutations within 13 identified genes cause a variety of channelopathies affecting myocardial repolarisation, resulting in QT prolongation [3,7,8].

It is estimated that 1/2,500–1/7,000 people worldwide are affected with LQTS [8]. LQTS is more common in women potentially affected by the sex based differences in the upper limit for the QTc interval in post pubertal females compared to males [9]. Limited data is available to suggest worldwide racial or ethnic variation in prevalence, but this has not been widely studied. LQTS can be inherited or acquired. Acquired LQTS results from a variety of causative factors including: drugs that prolong QT or cause depletion of potassium and/or magnesium such as TCAs, amiodarone and sotalol; electrolyte imbalances such as hypokalaemia, hypomagnesaemia, hypocalcaemia; and bradyarrhythmias.

The treatment of patients with congenital and acquired LQTS differs to some extent because of pathophysiologic differences between the two forms. Traditionally, the major clinical indications for left cardiac sympathetic denervation (LCSD) are ß-blocker intolerance or refractoriness, high risk of sudden death with ß-blocker treatment (despite the patient being asymptomatic), frequent ICD shocks, or bridging to an ICD implantation in infants and small children. LCSD is especially effective in patients with poor ß-blocker compliance as it has good long-term outcomes. LCSD in patients with frequent ICD shocks significantly reduces the number of shocks, thus improving quality of life. Recently, LCSD via a video-assisted thoracoscopic surgery (VATS) approach has been used in patients with LQTS and catecholaminergic polymorphic ventricular tachycardia (CPVT), allowing for early ambulation and short hospital stays with minimal perioperative complications [3].

Left cardiac sympathetic denervation (LCSD) involves surgical resection of the left thoracic sympathetic chain from T2 to T4 and the lower pole of the left stellate ganglion (T1), thereby diminishing the noradrenergic input to the heart [11]. There are several approaches to this procedure, including the cervical approach, thoracotomy and more recently VATS [1–3]. This procedure reduces the occurrence and frequency of symptoms in LQTS and CPVT, even in very high risk populations. An early review of the literature reported that early results of LCSD to treat LQTS had disappointing results in patients who underwent sympathectomy and concluded that medical therapy, extension of the procedure to lower thoracic segments, or cardiac pacing is often required for a successful result [9]. Adverse effects associated with sympathectomy have been well documented and include Horner's syndrome [4,5], ventricular arrhythmia, pneumothorax, facial flushing and asymmetrical facial sweating [3]. The aim of this study was to review all reported cases in the literature, to document the complications and clinical outcomes and to discuss a local centre case report.

Materials and Methods

PubMed, Embase and Scopus databases were searched for original articles and case reports using MESH search terms;

1. Long QT syndrome AND sympathectomy AND/OR Surgery
2. Long QT AND sympathectomy AND/OR surgery

The literature search was performed by one independent author. Abstracts and original articles were screened and reviewed if considered relevant. Articles were included if the following criteria were met: 1. Procedural and patient details were provided; 2. Patient outcomes were reported. Articles published in English were included, and abstracts presented at conferences were excluded. Selection details on the articles included/excluded are shown in the table below. Article publication dates ranged from 1971 to 2016 (Table 1).

Results

Using the defined search terms, 89 articles were returned in PubMed, 142 articles using EMBASE, and 182 articles using Scopus. After screening, 40 full text articles were identified for further evaluation and 21 articles were identified for inclusion (see Figure 1). Of the 21 cases reviewed, 8 were case reports; 11 were retrospective and 2 were systematic reviews. Total patient numbers in Table 2 are reduced because those studies did not specify patient numbers associated with treatment indication, perioperative symptom or QTc value. Total patient numbers across the 21 studies totals 520.

Preoperative symptoms were reported in 294/520 patients (57%). The most common preoperative symptom was tachyarrhythmia (208 patients) and syncope (207 patients). Postoperative symptoms were reported in 181/520 patients (35%). Immediate postoperative complications were reported in 68/520 patients (13%) and persistent symptoms reported during follow-up occurred in 147/520 patients (28%). The most common postoperative symptoms were no symptoms (64 patients); followed by tachyarrhythmia (55 patients), syncope (45 patients), and Horner's syndrome (13 patients). Note that 27/520 patients reported some but not all of the symptoms of Horner's syndrome including ptosis and anhydrosis. Death was reported in one patient in the immediate postoperative period and three patients in the long-term follow-up period.

Thirteen of the 21 studies reported perioperative QTc values (264/520 patients). Nine of these studies (220/520 patients or 42%) showed a marked reduction in QTc postoperatively. The remaining four studies (44/520 patients) did not show reduced QTc following surgery. The range of QTc preoperatively was 401–732 ms, and the range postoperatively was 370–694 ms

Table 1 Study indications, complications and long-term outcomes.

Author	Study type	Patient numbers included within study cohort	Mean study follow-up (range)	Presenting symptoms	Perioperative complications	Outcome and follow-up	T1 (stellate) ganglion resection (partial or total)
Ouriel 1995 [13]	Retrospective	10	1.3 (0.3) years (mean)	Syncope, ventricular tachyarrhythmia's, VF arrest	Horner's syndrome	Single patient death, reduction in syncopal episodes	yes
Epstein 1996 [14]	Retrospective	5	18+/−12 months	Transient syncope	Nil reported	Non sustained ventricular torsades	
Wong 1996 [15]	Case report	1	10 months (not clearly stated)	Paroxysmal palpitations, shortness of breath, syncope	Intercostal neuralgia, pleural effusion, transient Horner's syndrome	Symptom free over a 10-month period	yes
Chen 1997 [16]	Case report	1	4 months (not clearly stated)	Transient syncopal episodes	Horner's syndrome	Persistent Horner's syndrome, antiarrhythmic medication free	
Reardon 2000 [17]	Case report	1	9 months	Failed initial resection of sympathetic chain	Nil reported	Asymptomatic after 9 months	yes
Weng 2000 [18]	Case report	1	3 months	Palpitations and syncope	Nil reported	Transient palpitations 1-year follow-up	
Wang 2003 [19]	Systematic review	123	7 months	Transient syncopal episodes and shortness of breath	Transient left sided ptosis	Symptom free after 7-month follow-up and shortening of QTc	yes
Schwartz 2004 [20]	Systematic review	147	7.8 years	Syncope and tachyarrhythmia	Syncope, cardiac arrest and death	Cumulative free survival was 45% for any event over 5 years	
Li 2005 [21]	Retrospective	5	21 months	Syncope	Nil reported	Multiple syncopal episodes over a 21-month period	
Li 2008 [22]	Retrospective	11	37+/−26.3 months	Refractory to beta blocker therapy	Ptosis, decreased sweating on left face	Syncopal events, and one death in the 2nd postoperative year of cardiac arrest	yes
Collura 2009 [23]	Retrospective	20	16.6+/−9.5 months	Syncope, tachyarrhythmia, and refractory to beta blocker therapy	Ptosis, arrhythmias, and decreased sweating on the left side	Symptom free over a 37-month period	yes
Murphy 2008 [24]	Case report	1	4 months	Tachyarrhythmia	Horner's syndrome	Nil in a 4-month follow-up	yes
Atallah 2008 [25]	Retrospective	4	1 month	Tachyarrhythmia, refractory medical therapy	Facial flushing and sharp shoulder pain		yes

Table 1. (continued).

Author	Study type	Patient numbers included within study cohort	Mean study follow-up (range)	Presenting symptoms	Perioperative complications	Outcome and follow-up	T1 (stellate) ganglion resection (partial or total)
						Marked arrhythmia reduction over a 30-month follow-up period	
Miller 2011 [26]	Case report	1	3 months	Polymorphic VT episodes and AICD discharge	Nil reported	No syncopal episodes and a shortened QTc at 3-months follow-up	yes
Bos 2013 [27]	Retrospective	54	3.6+/−1.3 years	Tachyarrhythmia, intolerance to beta blocker therapy	Left-sided ptosis, pneumothoraces	Increased prevalence of cardiac event at >5 years follow-up	yes
Nagels 2014 [28]	Case report	1	35 months	Multiple episodes of torsades	Horner's syndrome	Improvement in Horner's at 35-month follow-up	yes
Waddell Smith 2015 [29]	Retrospective	40	1-67 months	Near drowning, syncope, cardiac arrest, asymptomatic ECG changes	Symptoms of Horner's syndrome and loss of flight-fight response	No reported morbidity or mortality related to the procedure over a mean follow-up period of 29 months	yes
Hofferberth 2014 [30]	Retrospective	14	4-131 months	Tachyarrhythmia and failed medical therapy	Pneumothoraces, facial flushing	Two patients suffered ICD shocks, but reduced antiarrhythmic burden was reported over 28-month period	yes
Antiel 2016 [10]	Retrospective	62	2.7+/−4.1 years (adults)	Cardiac arrest, ICD shocks, seizures, syncope	Symptoms of Horner's syndrome, temperature variation, shoulder blade pain and chest pain	Nil in treated patients. 6 patients who didn't respond to therapy had persisting symptoms at follow-up	yes
Jang 2016 [31]	Retrospective	15	927+/−350 days	Syncope, torsades, seizures	Minor transient chest pain	Increased and decreased sweating episodes and one episode of cardiac arrest on 17-58-month follow-up	yes
Upadya 2016 [4]	Case reports	3	Not stated	Palpitations, syncope, seizures and strong family history	Ventricular tachyarrhythmias	Asymptomatic at 9-months follow-up	
		520					

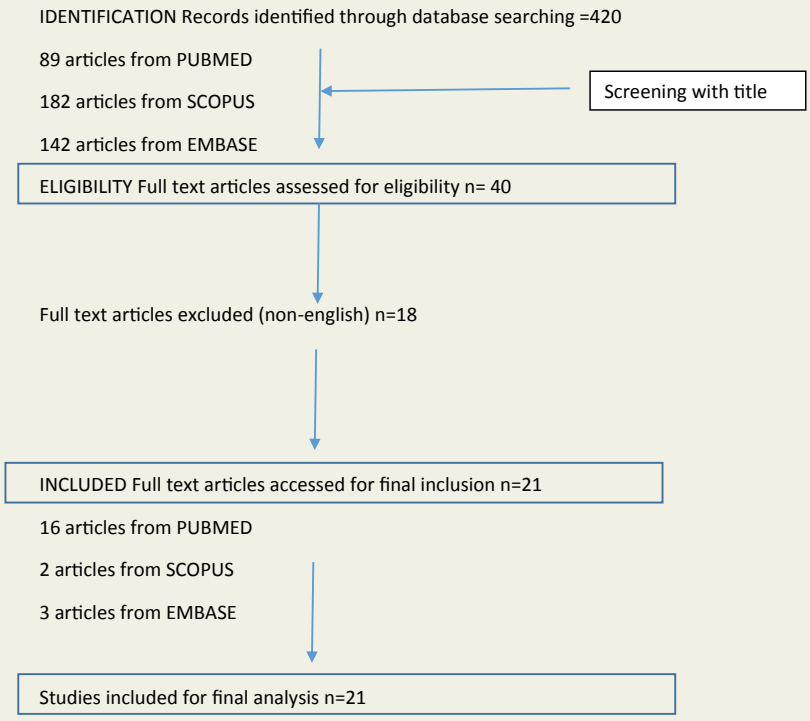

Figure 1 Selection details of articles included/excluded.

Table 2 **Preoperative and postoperative clinical findings in discussed studies.**

Author	Preoperative QTc (ms)	Postoperative QTc (ms)	Reporting symptoms preoperatively	Reporting symptoms postoperatively	Immediate complications	Long-term complications
Ouriel 1995 [13]	460-600 (530)	440-540 (490)	9/10 patients	4/10 patients	9/10 patients	1/10 patients
Epstein 1996 [14]	562-710 (635)	480- 643 (562)	5/5 patients	0/5 patients	0/5 patients	3/5 patients
Wong 1996 [15]	600-690 (645)	400-490 (445)	1/1 patients	1/1 patients	1/1 patients	0/1 patients
Chen 1997 [16]	620 (620)	370 (370)	1/1 patients	1/1 patients	1/1 patients	1/1 patients
Reardon 2000 [17]	not stated	not stated	1/1 patients	0/1 patients	0/1 patients	0/1 patients
Weng 2000 [18]	600 (600)	430 (430)	1/1 patients	1/1 patients	0/1 patients	0/1 patients
Wang 2003 [19]	not stated	not stated	not stated	41/123	0/123	not stated
Schwartz 2004 [20]	478-608 (543)	424-439 (432)	145/147 patients	80/147 patients	10/147 patients	77/147 patients
Li 2005 [21]	557-563 (560)	473-451 (462)	5/5 patients	0/5 patients	0/5 patients	1/5 patients
Li 2008 [22]	not stated	not stated	11/11 patients	1/11 patients	0/11 patients	4/11 patients
Collura 2009 [23]	430-687 (559)	434-645 (540)	8/20 patients	3/20 patients	0/20 patients	5/20 patients
Murphy 2008 [24]	not stated	not stated	1/1 patients	1/1 patients	1/1 patients	0/1 patients
Atallah 2008 [25]	470-500 (485)	480-500 (490)	1/4 patients	1/4 patients	0/4 patients	1/4 patients
Miller 2011 [26]	584 (584)	439 (439)	1/1 patients	0/1 patients	0/1 patients	0/1 patients
Bos 2013 [27]	454-602 (528)	not stated	52/52 patients	7/52 patients	3/52 patients	12/52 patients
Nagels 2014 [28]	516 (516)	not stated	1/1 patients	1/1 patients	1/1 patients	0/1 patients
Waddell Smith 2015 [29]	401- 522 (462)	422-530 (476)	25/40 patients	29/40 patients	4/40 patients	29/40 patients
Hofferberth 2014 [30]	360-630 (495)	372-560 (466)	14/14 patients	7/14 patients	1/14 patients	7/14 patients
Antiel 2016 [10]	not stated	not stated	not stated	10 of 34	not stated	not stated
Jang 2016 [31]	490-732 (611)	472- 694 (583)	9/15 patients	6/15 patients	0/15 patients	6/15 patients
Upadya 2016 [4]	not stated	not stated	3/3 patients	0/3 patients	1/3 patients	0/3 patients
Mean	558.2 (range)	476				
Median	559 (range)	466				

Table 3 Preoperative and postoperative symptoms reported.

	syncope		tachyarrhythmia		discharge of defibrillator		cardiac arrest		Horner's syndrome		asymptomatic
	preoperative	postoperative	preoperative	postoperative	preoperative	postoperative	preoperative	postoperative	preoperative	postoperative	preoperative
	9		8				3			9	
Ouriel 1995 [13]	5		4								
Epstein 1996 [14]	1		1							1	
Wong 1996 [15]	1									1	
Chen 1997 [16]											
Reardon 2000 [17]	1		1								
Weng 2000 [18]	not stated	not stated	not stated	not stated	not stated	not stated	not stated	not stated	not stated	not stated	not stated
Wang 2003 [19]	145	41	145	32							2
Schwartz 2004 [20]	5										
Li 2005 [21]	11	3									
Li 2008 [22]	5				11						
Collura 2009 [23]	1		1	1	1					1	
Murphy 2008 [24]				1	1		2				
Atallah 2008 [25]			1								
Miller 2011 [26]			35	12					29		
Bos 2013 [27]	1									1	
Nagels 2014 [28]	12						2		6	not stated (9/21) with miosis	20
Waddell Smith 2015 [29]	3		6	7	3	3	2				
Hofferberth 2014 [30]	not stated		not stated		not stated		not stated		not stated	not stated (10/36 with ptosis) and 8/35 with miosis	not stated
Antiel 2016 [10]	7	1	3	1			1	1			6
Jang 2016 [31]	1		2	1					3	not stated	
Upadya 2016 [4]	208	45	207	55	16	3	10	1	48	13 (27 with related features)	28

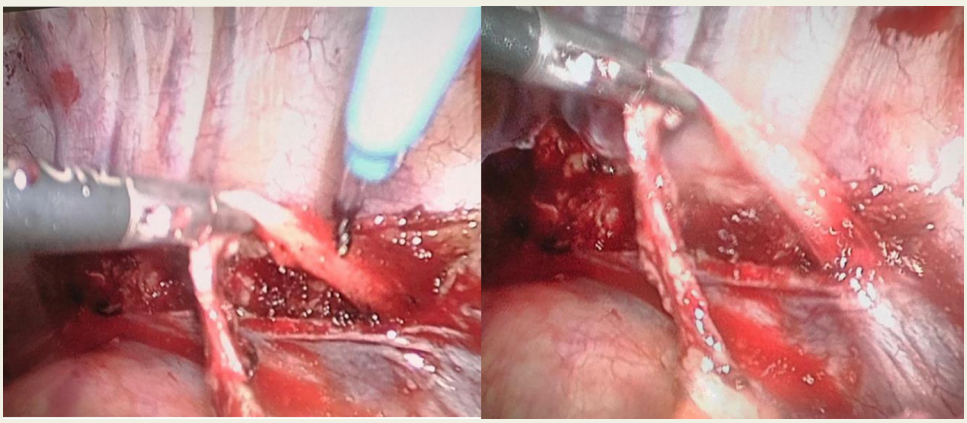

Figure 2 Intraoperative photograph showing sympathectomy of the thoracic ganglia.

(Table 2). Mean preoperative QTc was 558 ms and median 559 ms. Mean postoperative mean was 476 ms and median 466 ms. In the 11 cases that reported Horner's syndrome or symptoms of Horner's syndrome, all had undergone a T1 or stellate ganglionectomy (Table 3).

Case Report

This case report presents a 49-year-old woman with the problem of long QT syndrome diagnosed in February 2016 when she had a cardiac arrest at home. She was subsequently treated with beta blockers and implant of a defibrillator device.

Significant condition progression included: syncope with torsades de pointe and documented QTc > 600 ms, implantable cardiac defibrillator (ICD) pocket infection and defibrillator removal later in 2016, ICD re-implantation the following month, and worsening depression on beta blocker therapy.

The indication for sympathectomy was beta blocker intolerance. The patient was on metoprolol 75 mg BD and reported symptoms of severe depression. This culminated in a drug overdose. She also reported night terrors. Propranolol was trialled as an alternative, however, she did not tolerate this medication due to excessive fluid retention. Her depressive symptoms resolved significantly upon cessation of beta blockers. Unfortunately symptoms of major depression returned upon restarting of her beta blocker medication. Anti-depressants were contraindicated due to the risk of further QTc prolongation.

The patient underwent VATS sympathectomy of T2-T5 under general anaesthesia in a right lateral decubitus position. Four port VATS were introduced into the 3–5th intercostal spaces (Figure 3) Conservative resection of the T2-T5 sympathetic chain was performed (Figure 2) The patient decided against aggressive resection of the stellate ganglion due to the risk of Horner's syndrome. The patient recovered uneventfully with no evidence of postoperative Horner's syndrome, tachyarrhythmia or other complications in the immediate postoperative period. The patient was discharged day 1 postoperatively.

At 7-week phone follow-up with the patient, the following adverse effects were noted: left sided hair loss, facial flushing and reduced sweating on the left side. She reported no syncopal events or pain. She had reduced her beta blocker dependence from 150 mg of to 50 mg of metoprolol. She reported no postoperative ICD discharge. Postoperative ECG demonstrates a reduced QTc interval (Figure 4).

On subsequent follow-up with her cardiologist 10 weeks following her operation, symptoms had further improved. She remained arrhythmia free, QTc had further reduced to 440 ms, metoprolol dose was now 25 mg BD and with

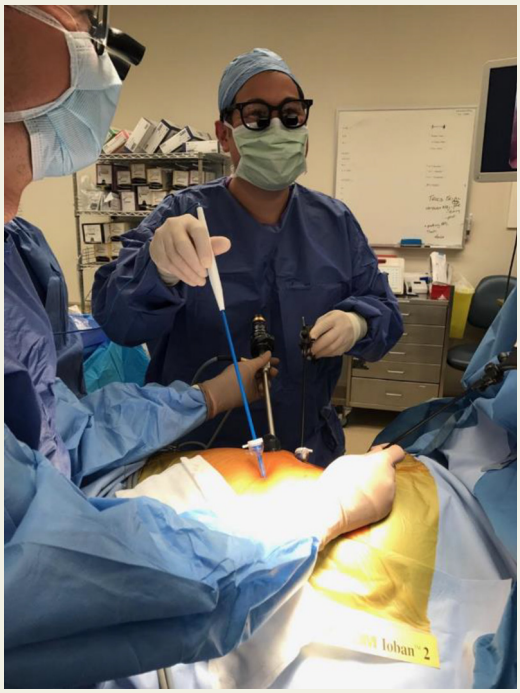

Figure 3 Intraoperative photograph showing the video-assisted thoracoscopic (VATS) approach to the thoracic ganglia.

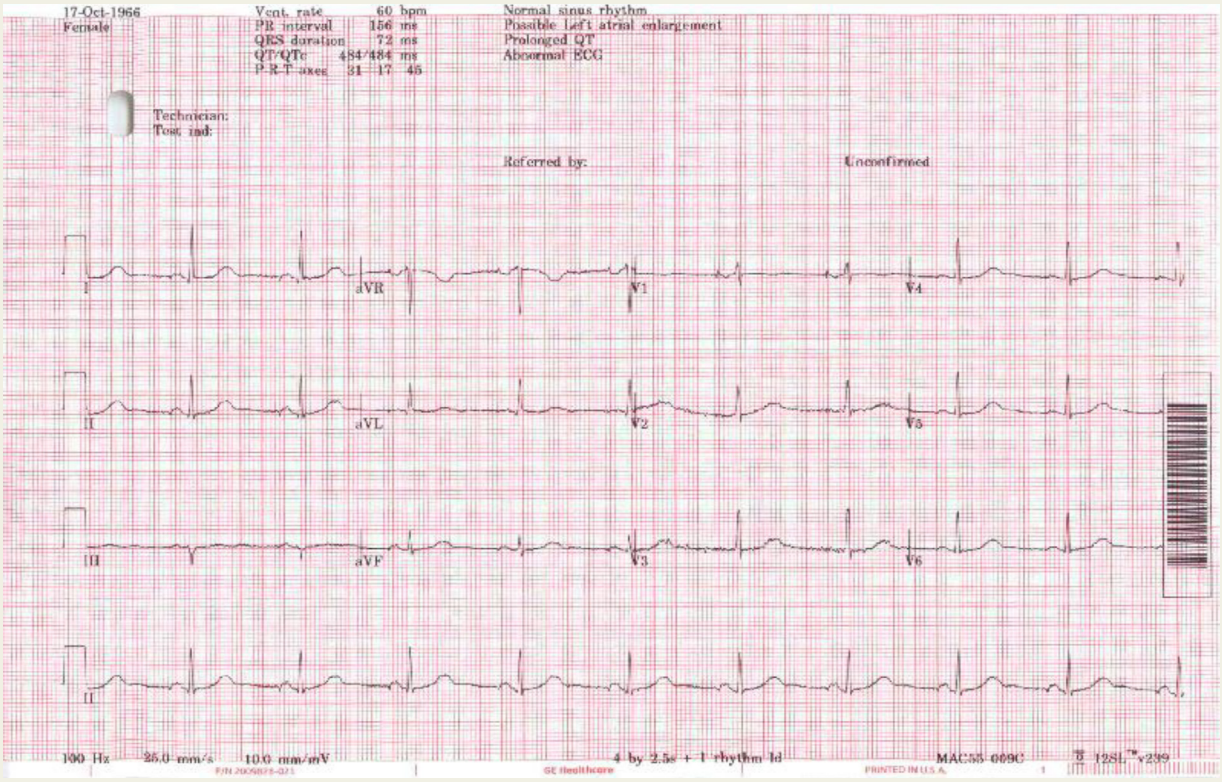

Figure 4 12 Lead electrocardiograph (ECG) 7 weeks' postoperative showing QTc interval of 484 ms.

planned cessation in subsequent weeks; and she reports improvement in mood. Defibrillator interrogation showed normal functioning, with no ventricular arrhythmia logged on the device. Planned follow-up is in 6 months time.

This systematic review identifies a reduction in symptoms that patients presented with preoperatively including ventricular tachyarrhythmias and syncope or AICD discharge events; and the most commonly reported outcome was no symptoms. The most common early complication following VATS sympathectomy is Horner's syndrome and associated symptoms including ptosis. Horner's syndrome and symptoms were reported in a total of 27/520 patients. All patients who reported symptoms associated with Horner's syndrome were amongst the T1 sympathectomy group. Given that 220/264 patients (83%) of patients reported QTc reduction at follow-up, this suggests that VATS sympathectomy is effective in reducing arrhythmia burden in LQTS patient. If all publications provided data on their QTc findings, this would allow for more definitive conclusions to be made.

Conclusions

Our short-term follow-up study suggests that T2-T5 sympathectomy in the management of refractory long QT syndrome is successful at reducing long QT burden and risk of sudden cardiac death with resulting mild to moderate clinical sequelae. Long-term follow-up and use of quality of life questionnaires will assist clinicians in interpreting whether the adverse effects of a T1-T5 sympathectomy is desirable for individuals involved or if taking a less invasive approach to sympathetic ganglia resection will improve patient's quality of life.

Disclosures

Nil.

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