Left Cardiac Sympathetic Denervation
Should We Sweat the Side Effects?

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Left Cardiac Sympathetic Denervation (LCSD) to prevent arrhythmia and sudden death in long QT syndrome (LQTS) nearly 45 years ago. In the past 15 years, there has been an increased focus on LCSD. The resurgence in interest is probably because of the presence of larger studies that demonstrate its potential use. Increased technical proficiency with thoracoscopic surgery, and additional focus on channelopathy research. The 2013 consensus statement for management of patients with primary arrhythmia syncope occurs despite optimal medical therapy, LCSD could be considered the next step rather than an ICD and could complement ICDs in patients with recurrent shocks.

LCSD is not first-line therapy for either LQTS or CPVT. β-adrenergic receptor blocker (β-blocker) therapy has remained the first option for LQTS and CPVT. β-blockers are effective in both diseases and the value of medication compliance has been dramatically illustrated in LQT1. Other medication regimens have been proposed, depending on clinical circumstances and genotype. However, no pharmacological treatment has eliminated mortality risk in either disease. In fact, the same studies that demonstrate the effectiveness of β-blockers caution that their protection is imperfect.

ICDs remain a backstop against lethal arrhythmias in these diseases. Although guidelines exist for ICD use in LQTS and CPVT, the clinical decision to implant one can be challenging. In children and young adults, the long-term complications of ICDs and the psychosocial drawbacks are concerning. Although ICDs may prevent sudden death in some cases, there are case reports of ICD discharges being proarrhythmic in CPVT and the high voltage function does nothing to prevent arrhythmia from occurring in the first place. For clinicians, LCSD is an appealing approach: its efficacy is independent of patient compliance and it avoids the pulmonary side effects of β-blockers.

In this issue of Circulation: Arrhythmia and Electrophysiology, Dr Waddell-Smith et al report the results of a telephone-based survey of 47 patients who received minimally invasive LCSD in New Zealand, with a median postsurgical follow-up of 29 months. The sympathetic chain was resected with some variation in technique, which they describe as “aggressive” or “conservative.” LCSD, based on their approach to the lower third of the stellate ganglion. For this article, they focused on 2 complementary aspects of the procedure. First, they asked about side effects, covering a broad range of complications that have previously been reported in the literature. Second, they asked about patient satisfaction. For both topics, they provided quantitative and qualitative data.

The authors report side effects in 95% of the patients, including 66% with left-sided dryness, 59% with unilateral facial flush, 55% with contralateral hyperhidrosis, 39% with differential hand temperatures, 11% with permanent ptosis, plus several complications occurring at <10% incidence. They report that 75% of subjects felt safer after the procedure and that 91% would recommend LCSD to others.

At first glance, the rate of side effects in this study seems to be an outlier in the literature. Several centers have reported their experience with LCSD for LQTS and CPVT. The rate of side effects in these studies is not as high as the current authors report. However, prevention of arrhythmia is not the only indication for sympathetic denervation. A review of the hyperhidrosis literature shows that the complication rates reported in this article may not be outliers. Hyperhidrosis is a pathological condition in which patients sweat in quantities greater than needed for physiological thermoregulation. Focal hyperhidrosis usually affects the palms, axillae, or the feet. Some patients have craniofacial hyperhidrosis that may cause severe emotional, occupational, and social distress. The Society of Thoracic Surgeons has published a consensus document on the surgical treatment of hyperhidrosis.17 The document is useful because it establishes a common nomenclature for sympathetic denervation and it emphasizes the large body of prospective randomized controlled surgical data for cardiac sympathetic denervation.

Table lists the results of a comparative literature analysis. In the top section of the table, the results of recent reports on LCSD for arrhythmia are summarized. In arrhythmia papers,
Compensatory hyperhidrosis is rarely mentioned and the immediate postsurgical complications and facial effects are the most prominent side effects. The rate of compensatory hyperhidrosis in this article is an outlier in the upper section of the table. However, when this study is compared with the results from the hyperhidrosis literature, the current report of 56% compensatory hyperhidrosis by Dr Waddell-Smith et al\textsuperscript{10} is in the middle of the pack. Randomized control trials are available in the hyperhidrosis literature, but absent in the arrhythmia literature. Both the article by Dr Waddell-Smith et al\textsuperscript{10} and the randomized controlled trials in Table followed patients over time. Patients were contacted again months to years after the surgery to inquire about side effects. It is especially interesting to note that in several of these studies, the rate of compensatory hyperhidrosis increases as follow-up passes the 1-year mark. Randomized controlled studies may be impractical in the small population of patients with inherited arrhythmia syndromes and refractory arrhythmias; however, we can learn from the established process of long-term side effect screening.

Compensatory hyperhidrosis is not the only side effect that appears in the literature; however, it is the most widely reported and so it is useful as a comparison. The point of making the comparison is not to presume that arrhythmia outcomes and hyperhidrosis outcomes should be identical. They are not. The pathophysiology of these diseases is different and the underlying causes of hyperhidrosis may exacerbate postoperative compensatory hyperhidrosis. The consensus lesions for hyperhidrosis recommend a narrower excision than the lesions for arrhythmia. The point of the comparison is that long-term, patient-centered interventions for atrial fibrillation. These include a minimum follow-up duration of 1 year, with serial evaluations at 3 months and every 6 months for 2 years.

There is one more similarity between the study by Dr Waddell-Smith et al\textsuperscript{10} and the hyperhidrosis literature: patients report high levels of satisfaction with the operation. In particular, this article notes that patients feel safer and that they would recommend LCSD to others. This is a valuable outcome for patients, but safer remains a more appropriate word than safe: short-term follow-up after LCSD demonstrates a decrease in clinical events, but not an extinction of events.\textsuperscript{3,13,14} We are beginning to understand the short-term consequences of LCSD. The surgery seems to reduce rates of cardiac events in highly selected patients. We can offer some short-term predictions on pneumothorax and ptosis or Horner syndrome after the surgery may have imperfect recollection about their results. In addition, transient and permanent side effects were considered with equal weight in Table (because the reporting was not uniform in the literature). In clinical care, they are not equivalent: temporary is preferable to permanent.

This article is important because it suggests that we may not yet fully understand the long-term side effects of LCSD for arrhythmia. In clinical practice, if patients do not complain of side effects after an operation, it is easy to presume that none exist. Patient-centered outcomes studies help us expand the scope of the questions that we ask during follow-up visits. This study is a bridge to assess quality of life outcomes for patients. As our field gains comfort with disease-specific measures for quality of life reporting, we can make direct comparisons of the impact that various interventions have on quality of life.\textsuperscript{3,27} Our field can adopt standardized intervals for research follow-up. For example, the Heart Rhythm Society published consensus guidelines for reporting outcomes of interventions for atrial fibrillation. These include a minimum follow-up duration of 1 year, with serial evaluations at 3 months and every 6 months for 2 years.

Cells with a 0 indicate that the article reports a zero rate of complication. Cells with a dash indicate that the article does not explicitly report a complication rate.

\*Randomized controlled trial of sympathetic denervation.

\begin{table}
\centering
\caption{Comparison of Left Cardiac Sympathetic Denervation in Arrhythmia and Hyperhidrosis Literature}
\begin{tabular}{llccc}
\hline
\textbf{First Author} & \textbf{Yr of Publication} & \textbf{n} & \textbf{Any Complication, \%} & \textbf{Compensatory Hyperhidrosis, \%} & \textbf{P/HS Syndrome, \%} & \textbf{Pneumothorax, \%} \\
\hline
Arrhythmia literature & & & & & & \\
Bos et al\textsuperscript{11} & 2013 & 52 & 13 & - & 8 & - \\
Hofferberth et al\textsuperscript{13} & 2014 & 24 & 13 & - & - & 8 \\
Roston et al\textsuperscript{15} & 2015 & 18 & 16 & - & 11 & 3 \\
Olde Nordekamp et al\textsuperscript{14} & 2014 & 17 & 23 & - & 6 & 18 \\
Coleman et al\textsuperscript{12} & 2012 & 27 & 26 & - & 11 & 15 \\
Vaseghi et al\textsuperscript{16} & 2014 & 41 & 37 & 10 & 7 & 10 \\
Schneider et al\textsuperscript{18} & 2013 & 10 & 70 & - & 70 & 6 \\
Waddell-Smith et al\textsuperscript{10} & 2015 & 47 & 95 & 56 & 21 & 11 \\

Hyperhidrosis literature & & & & & & \\
Li et al\textsuperscript{19} & 2008* & 232 & 31 & 21–29 & 0 & 6 \\
Munia et al\textsuperscript{20} & 2008* & 64 & 87 & 48–87 & - & - \\
Bryant et al\textsuperscript{21} & 2014 & 193 & 77 & 52–77 & 0 & 0.5 \\
Liu et al\textsuperscript{22} & 2009* & 141 & 77 & 56–77 & 0 & 0 \\
Yazbek et al\textsuperscript{23} & 2009* & 60 & 90 & 67–90 & 2 & - \\
Katara et al\textsuperscript{24} & 2007* & 25 & 80 & 80 & - & 0 \\
de Andrade Filho et al\textsuperscript{25} & 2013 & 1731 & 89 & 89 & 1 & 4 \\
Yazbek et al\textsuperscript{26} & 2005* & 60 & 90 & 87–90 & 2 & - \\
\hline
\end{tabular}
\end{table}
as periprocedural complications. This is only the first step. We need define what clinical role LCSD should play and counsel families accurately about the risks and benefits. Studies like the current one serve to illustrate why we are obligated to also sweat the details of long-term side effects of LCSD.

Disclosures

None.

References


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