Practice Guidelines

Acute hemodynamics of cardiac sympathetic denervation

Kunal Sinkar, Avishek Bagchi*, Ankit Mahajan, Ramalingam Vadivelu, Meera Venkatraman, Reshma Motwani, Sanjeev Vichare, Suresh Joshi, Dinesh Parikh, Jude Vaz, Yash Lokhandwala

Holy Family Hospital, Bandra West, Mumbai, 400050, India

A R T I C L E  I N F O

Article history:
Received 18 April 2020
Received in revised form 2 June 2020
Accepted 11 June 2020
Available online 14 June 2020

Keywords:
ventricular tachycardia
Sympathectomy
Blood pressure

A B S T R A C T

Introduction: We aimed to study the immediate hemodynamic effects of thoracoscopic bilateral cardiac sympathetic denervation (CSD) for recurrent ventricular tachycardia (VT) or VT storm.

Method: We studied a group of 18 adults who underwent bilateral thoracoscopic CSD; the blood pressure (BP) and Heart Rate (HR) were continuously monitored during the surgery and up to 6 h post-operatively.

Results: Immediately on removal of the sympathetic ganglia, the patients had a drop in both the systolic (110 mm Hg to 95.8 mm Hg, p < 0.001) and diastolic BP (69.4 mm Hg to 65 mm Hg, p = 0.007) along with a drop in the HR (81.6 bpm to 61.2 bpm, p < 0.001). At 6 h after CSD, the systolic and diastolic BP did not recover significantly, while there was recovery in HR (61.2 bpm to 66 bpm, p = 0.02). There was no significant difference between those with and without left ventricular (LV) systolic dysfunction.

Conclusion: The acute hemodynamic changes during the perioperative period of CSD are significant but not serious. Awareness of this is useful for peri-operative management.

Copyright © 2020, Indian Heart Rhythm Society. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

The treatment of ventricular arrhythmias has been rapidly evolving over the past few decades. Starting with antiarrhythmic drugs, followed by defibrillation and implantable cardioverter-defibrillators (ICDs) and subsequent development of two dimensional and three-dimensional cardiac mapping and ablations, one can trace the encouraging journey we have had in the management of these complex patients.

A recent addition to the armamentarium against ventricular arrhythmias is thoracoscopic cardiac sympathetic denervation (CSD). Though CSD had traditionally been used as a treatment for refractory angina with good results [1–3], its antiarrhythmic potential has been explored only over the last few years. Beginning with a few isolated case reports [4,5], we now have several studies making a case to consider CSD for resistant ventricular arrhythmias [6–15].

Bilateral CSD from T1-T4 ganglia abolishes most of the sympathetic inputs to the heart. Since it compares with acute high dose complete beta blockade, there is a theoretical possibility of acute drop in blood pressure (BP) and heart rate (HR). These acute hemodynamic effects of bilateral CSD have been documented in few isolated case reports [16], but no substantial study has yet looked specifically for this effect in the intra-operative and immediate post-operative periods. This particular hemodynamic effect, though of smaller magnitude, has been observed in earlier studies where thoracic sympathectomy was performed for palmar hyperhidrosis and facial blushing [17–26]. This might have been mainly due to the fact that the stellate ganglion was not resected in these cases.

We aimed to study the acute hemodynamic effects of thoracoscopic bilateral CSD in a group of patients with recurrent refractory ventricular arrhythmias. We expected that the observations would help future perioperative management.

2. Method

All consecutive adult patients taken for CSD in Holy Family Hospital for recurrent ventricular tachycardia (VT) or VT storm between the time period of November 2018 to December 2019 were included in this study. VT storm was defined as ≥3 episodes of sustained VT, ventricular fibrillation (VF), or appropriate shocks from an ICD within 24 h [27]. Patients were taken up for CSD if they had pleomorphic VT (monomorphic VTs of different morphologies).
or if they had at least one failed attempt or recurrence after at least one attempt of radiofrequency ablation for monomorphic VT.

Old myocardial infarction (MI), dilated cardiomyopathy (DCMP), catecholaminergic polymorphic ventricular tachycardia (CPVT), sarcoidosis, old myocarditis, hypertrophic cardiomyopathy (HCM), muscular dystrophy and arrhythmogenic right ventricular cardiomyopathy (ARVC) were the underlying substrates.

All patients underwent video assisted thoracoscopic surgery (VATS) guided bilateral upper thoracic sympathectomy. All procedures were performed under general anaesthesia. In patients with ICDs, therapies were turned off and the lower rate was set at 40/min. Three 1.5 cm incisions were made on each side at a time: fourth intercostal space in the mid-axillary line, second intercostal space in the mid-clavicular line and 2 cm further laterally. The sympathetic chain behind the parietal pleura was identified and the lower one-half to one-third of the stellate ganglion, as well as the thoracic ganglia at T2 to T4, were cauterized and excised. Specimens were sent for histological confirmation. After CSD, the presence of ganglionic tissue was confirmed by pathologist in all cases, using routine histopathology sections with H and E stain.

All the patients had arterial line put in one radial artery before the surgery and blood pressure and heart rate measured and noted invasively prior to shifting to the operation theatre. During the surgery, BP and HR were continuously monitored and the lowest values noted after removal of the ganglia intra-operatively were considered for analysis. After 6 h, intraarterial BP and HR were again noted and considered for analysis.

### 3. Statistics

Continuous variables were assessed as means with standard deviations (SDs) and categorical variables as percentages. Systolic BP (SBP), diastolic BP (DBP) and HR were compared both between preoperative state and intra-operative state and between intra-operative state and post-operative state by means of multiple paired t-tests. To compare the acute changes in BP and HR across various groups based on presence or absence of severe left ventricular (LV) dysfunction, we used independent student’s t-test. The significance level adopted in the statistical analyses was 0.05. All statistical analyses were performed with the SPSS software, version 23.0 (SPSS Inc. Chicago, IL, USA).

### 4. Results

The study involved a group of 18 patients. Patient data are summarized in Table 1. The age varied from 21 year to 78 years with a mean of 48.7 ± 15.5 years. The baseline parameters are described in Table 1. The group was very heterogenous as regards the underlying substrate, with old myocardial infarction, dilated cardiomyopathy and myocarditis being the major categories.

As regards the VT characteristics, most (17/18, 94%) patients had

| Table 1 | Baseline characteristics (n = 18). |
|---|---|
| Characteristics | Percent |
| Age (years ± SD) | 48.67 ± 15.51 |
| Gender | Male 15 83.3 |
| | Female 3 16.7 |
| Hypertension | Yes 3 16.7 |
| | No 15 83.3 |
| Diabetes | Yes 3 16.7 |
| | No 15 83.3 |
| Hyperlipidemia | Yes 16 88.9 |
| Primary Diagnosis | Old MI 6 33.3 |
| | DCMP 5 27.8 |
| | CPVT 1 5.6 |
| | Myocarditis 2 11.1 |
| | Sarcoïdosis 1 5.6 |
| | HCM 1 5.6 |
| | ARVC 1 5.6 |
| | Muscular dystrophy 1 5.6 |
| Left ventricular ejection fraction (LVEF) | Mild dysfunction (LVEF 0.45–0.54) 1 5.6 |
| | Moderate dysfunction (LVEF 0.3–0.44) 6 33.3 |
| | Severe dysfunction (LVEF < 0.3) 11 61.1 |
| NYHA (New York Heart Association) Class | I 3 16.7 |
| | II 6 33.3 |
| | III 6 33.3 |
| | IV 3 16.7 |
| Ventricular Tachycardia (VT) Morphologies | 1 1 5.6 |
| | 2 2 11.1 |
| | ≥3 15 83.3 |

(MI : Myocardial Infarction; DCMP: Dilated cardiomyopathy; CPVT : catecholaminergic polymorphic VT; HCM: Hypertrophic Cardiomyopathy; ARVC: Arrhythmogenic right ventricular dysplasia)

| Table 2 | Treatment modalities used prior to surgery (n = 18). |
|---|---|
| Characteristics | N % |
| Anti-Arrhythmics | Amiodarone 1 5.6 |
| | Beta-blockers 1 5.6 |
| | Amiodarone and beta-blockers 8 44.4 |
| | Amiodarone, phenytoin and beta blockers 4 22.2 |
| | Amiodarone, beta blockers and mexiletine 1 5.6 |
| | Amiodarone and sotalol 1 5.6 |
| | Amiodarone, sotalol and phenytoin 1 5.6 |
| | Sotalol and phenytoin 1 5.6 |
| ICD | No ICD 2 11.1 |
| | Single chamber ICD 11 61.1 |
| | Dual chamber ICD 5 27.8 |
| VT Ablations | 0 13 72.2 |
| | 1 4 22.2 |
| | 2 1 5.6 |
| Revascularization | None 15 83.3 |
| | Old Angioplasty 1 5.6 |
| | Old Bypass Surgery 2 11.1 |
pleomorphic VTs. Also, they were on maximum tolerated dosage of anti-arrhythmic drugs, with 16/18 (88.9) % of patients on two or more drugs. Furthermore, 16/18 (88.9%) of patients had ICDs and were receiving appropriate therapies. A few (5/18) patients had undergone radiofrequency (RF) ablation. The details of the anti-arrhythmic drugs and therapies are shown in Table 2. The patients with LV dysfunction were on optimal guideline directed medical therapy including beta blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, diuretics and spironolactone; these therapies were continued perioperatively with last dose being given 8 h prior to the surgery.

The patients had significant hemodynamic alterations in the intra-operative period (Figs. 1–3). Immediately on removal of the ganglia, the patients had a significant drop in both the systolic BP and diastolic BP along with a significant drop in the HR (shown in Table 3). No patient needed pacing. Patients mostly had sinus bradycardia, with some patients having intermittent junctional rhythm initially after removing the stellate ganglia which subsequently recovered to sinus rhythm in all cases.

We did not find significant difference in acute BP and HR responses intra-operatively between patients with and without severe LV dysfunction (LV Ejection Fraction <0.3 and ≥ 0.3 respectively) as displayed in Table 4.

When the post-operative hemodynamic parameters were compared with those intra-operatively, we found that there was increase in the HR but no significant increase in the systolic BP or diastolic BP (Table 5).

5. Discussion

This study had two objectives: i) To see the BP and HR changes, for which BP and heart rate (HR) were continuously monitored, and the lowest values noted after removal of the ganglia intra-operatively were considered for analysis. ii) From a management
perspective, in our initial CSD procedures we sometimes had sudden drop in HR and BP and the surgical team would be taken unawares. CSD is undertaken by very few centres even now. Hence, in this study we mentioned the lowest values to help guide other emerging groups performing CSD about the problems that can occur.

In our study, the patients were predominantly middle-aged and there was a marked (15/18) male preponderance. The substrates were heterogeneous and except for 1 patient with CPVT, all had structural heart disease. They were refractory to several modalities of treatment, with most having been tried on at least a combination of 2 anti-arrhythmic drugs. Only 1 patient had a single VT morphology, while of the remaining 17 patients, 15 had at least 3 different VTs. A clear underlying infarct scar was present in only 6 patients. Thus, it was not surprising that only 5 patients had undergone RF ablation attempts prior to CSD.

The cardiac autonomic nervous system (NS) has both sympathetic and parasympathetic arms. The sympathetic cardiac NS comprises of the brain stem, the spinal cord, the dorsal root ganglia, the paravertebral sympathetic ganglia and the mediastinal cardiac plexus. Sympathetic preganglionic neurons destined for heart have their cell-bodies in the intermediolateral column of spinal cord and they synapse with the postganglionic neurons located in the lower cervical and upper thoracic paravertebral ganglia. The lowest cervical ganglion (C8) and the highest thoracic ganglion (T1) are generally fused bilaterally to constitute the left and the right stellate ganglia. The stellate ganglia convey a large amount of cardiac sympathetic postganglionic fibres. The remaining are provided by T2-4 paravertebral ganglia [26]. These ganglia receive inputs from multiple spinal levels, process those and finally deliver output to the heart via the post-ganglionic neurons. Nor-epinephrine is the final neurotransmitter of these post-ganglionic neurons. The cardiac feedback to the autonomic NS is carried via these post-ganglionic neurons to the spinal cord and brainstem [28].

Fig. 3. Peri-operative alteration of HR (n – 18).

Table 3
Intra-operative hemodynamic alterations (n – 18).

| Parameter         | Time          | Values  | p Value (paired t-test) |
|-------------------|---------------|---------|------------------------|
| Systolic BP (mm Hg) | Pre-operative | 110 ± 12.8 | <0.001 |
| Diastolic BP (mm Hg) | Pre-operative | 69.4 ± 8 | 0.007 |
| HR (bpm)          | Pre-operative | 81.2 ± 8.1 | <0.001 |
|                   | Intra-operative | 95.8 ± 12.2 |      |
|                   | Intra-operative | 65 ± 7.9 |      |
|                   | Intra-operative | 61.2 ± 9.9 |      |

Table 4
Intra-operative hemodynamic alteration according to LVEF (n – 18).

| Parameter         | LVEF | n | Mean ± SD | p value ( paired t-test) |
|-------------------|------|---|-----------|------------------------|
| Pre-operative systolic BP | <0.3 | 11 | 105.5 ± 8.2 | 0.06 |
|                   | ≥0.3 | 7 | 117.1 ± 16 |           |
| Drop in systolic BP     | <0.3 | 11 | 11.5 ± 9 | 0.25 |
|                   | ≥0.3 | 7 | 18.6 ± 13.5 |          |
| Pre-operative Diastolic BP | <0.3 | 11 | 67.3 ± 4.7 | 0.25 |
|                   | ≥0.3 | 7 | 72.9 ± 11.1 |           |
| Drop in Diastolic BP     | <0.3 | 11 | 2.7 ± 4.7 | 0.20 |
|                   | ≥0.3 | 7 | 7.1 ± 7.6 |           |
| Pre-operative HR         | <0.3 | 11 | 80.8 ± 8.7 | 0.61 |
|                   | ≥0.3 | 7 | 82.9 ± 7.6 |           |
| Drop in HR               | <0.3 | 11 | 18.4 ± 11 | 0.30 |
|                   | ≥0.3 | 7 | 23.6 ± 9.5 |           |

Kingma et al. [19] studied the hemodynamic response on removal of the upper thoracic ganglia for the treatment of palmar hyperhidrosis. They showed a drop in mean HR in sitting position and a decrease in total peripheral resistance and BP in both sitting and standing positions. However, this study compared the pre-operative readings with those at four weeks after the surgery. Similar response has been documented by Papa et al. [17], who
found an acute drop in HR immediately after sectioning of T2 and T3 ganglia of either side in a group of 10 patients. In a patient population of 29 patients they have demonstrated a significant drop in systolic BP, diastolic BP and HR both at rest and on exercise after a period of one month after the surgery. There are also a few older animal and human studies analysing the hemodynamic response of unilateral and bilateral upper thoracic sympathetic denervation [32–37]. They demonstrated that right and left thoracic sympathetic denervation may produce opposite effects on cardiac arrhythmias in experimental animals and in humans, with left sided sympathectomy producing more drop in BP, shortening of QTC and decrease in HR. However, none of these studies had removal of the stellate ganglion done and hence they were incomplete CSD. Song et al. [38] have shown no significant effect on heart rate or blood pressure immediately on bilateral stellate ganglia block; in fact, a subgroup of their patients has shown vagal blockade and increase in heart rate and blood pressure acutely. However, their study was a study of percutaneous stellate ganglia block with lignocaine and there is no study available till date looking at the immediate hemodynamic response of the surgical complete bilateral CSD.

In our ‘learning curve’ of CSD (prior to this study), there were instances of sudden marked drop in heart rate and BP, needing chronotropic drugs/increase in pacing rate and inotropes/vaso-pressors. However, now our anaesthesiologists and surgeons have learnt to anticipate and avoid these situations. In the present study, there was a significant acute hemodynamic alteration across the study population. Mostly patients were in sinus bradycardia, with few minutes of junctional rhythm seen intermittently. These acute hemodynamic changes were similar in patients with and without LV dysfunction. This finding is interesting and needs to be further evaluated in a large group of patients.

Subsequently, systolic and diastolic BP gradually started to increase, but did not show significant change in the immediate post-op period. However, the HR showed significant recovery in the immediate post-op period. Overall, our study adds to the currently available literature on CSD. It helps care givers to anticipate and deal with such issues during the peri-operative period.

6. Conclusion

Ours is the first study specifically aimed at assessing immediate and early post-operative hemodynamic response of bilateral complete CSD. We validated each sympathectomy with histopathology. Immediately after CSD, there was a drop in systolic BP, diastolic BP and HR. At 6 h after CSD, there was some recovery in HR. There was no significant difference between those with and without LV systolic dysfunction.

Declaration of competing interest

None.

Table 5

Comparison of intra-operative and post-operative (at 6 h) hemodynamic parameters (n = 18).

| Parameter          | Time          | Values               | p Value |
|--------------------|---------------|----------------------|---------|
| Systolic BP (mm Hg) | Intra-operative | 95.8 ± 12.2          | 0.354   |
|                    | Post-operative | 98.8 ± 5.8           |         |
| Diastolic BP (mm Hg) | Intra-operative | 65 ± 7.9             | 0.495   |
|                    | Post-operative | 66.1 ± 9.2           |         |
| HR (bpm)           | Intra-operative | 61.2 ± 9.9           | 0.020   |
|                    | Post-operative | 66 ± 7.5             |         |

References

[1] François-Franck C. Signification physiologique de la resection du sympathique dans la maladie de Basedow, l'epilepsie, l'idiotie et de glaucome. Bull Acad Med 1899;41:565.

[2] Jonnesco T. Traitement chirurgical de l'angi'se de poitrine par la resection du sympathique cervico-theraco. Presse Med 1921;20:221–30.

[3] Biondi Zoccai G, Fontaine R. The surgical treatment of angina pectoris: what it is and what it should be. Am Heart J 1928;3:649–71.

[4] Estes Jr EH, Ijalr Jr HL. Recurrent ventricular tachycardia. A case successfully treated by bilateral cardiac sympathectomy. Am J Med 1961;31:493–7.

[5] Zipes DP, Festoff B, Schaaf SP, Cox C, Soaly WC, Wallace AG. Treatment of ventricular arrhythmia by permanent atrial pacemaker and cardiac sympathectomy. Ann Intern Med 1968;68:591–7.

[6] Schwartz PJ, Priori SG, Cerrone M, et al. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long QT syndrome. Circulation 2004;109:1826–33.

[7] Wilde AAM, Bhuiyan ZA, Crotti L, et al. Left cardiac sympathetic denervation for catecholaminergic polymorphic ventricular tachycardia. N Engl J Med 2008;358:2024–9.

[8] Ajjola AO, Vasgehi M, Mahajan A, Shikumkar K. Bilateral cardiac sympathetic denervation: why, who and when. Expert Rev Cardiovasc Ther 2012;10(8):947–9.

[9] 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(1):404–11.

[10] Te Reue AS, Ajjola OA, Shikumkar K, Tandi R. Role of bilateral sympathetic denervation in the treatment of refractory ventricular arrhythmias or electrical storms: intermediate-long term follow-up. Heart Rhythm 2014;11(3):360–6.

[11] Vasgehi M, Barwad P, Corrales FJ, Tandir H, Mathuria N, Shah R, Sorg JM, Gunja J, Mandal K, Morales LC, Lohandwala Y. Cardiac sympathetic denervation for refractory ventricular arrhythmias. J Am Coll Cardiol 2017;69(25):3070–80.

[12] Richardson T, Lugo R, Savaedra P, Crossley G, Clair W, Shen S, Estrada JC, Montgomery J, Shoemaker MB, Ellis C, Michaud GF. Cardiac sympathectomy for the management of ventricular arrhythmias refractory to catheter ablation. Heart Rhythm 2018;15(1):56–62.

[13] Télices LJ, Garzon JC, Vinck EE, Castellanos JD. Video-assisted thoracoscopic cardiac denervation of refractory ventricular arrhythmias and electrical storms: a single-center series. J Cardiothorac Surg 2019;14:17.

[14] Lee LS, Lin CC, Ng SM, Au CF. The haemodynamic effect of thoracoscopic electrocautery of the upper thoracic sympathetic chain. Eur J Surg 1994;160:70.

[15] Kingma R, Ten Voorde BJ, Scheffer GJ, Karemaker JM, Mackaay AJ, Wesseling KH, de Lange JJ. Thoracic sympathectomy: effects on hemodynamics and baroreflex control. Clin Auton Res 2002 Feb;12(1):35–42.

[16] Schwartz PJ. The rationale and role of left stellotomy for the prevention of malignant arrhythmias. Ann NY Acad Sci 1984;427:199–221.

[17] Hillman A, Schwartz PJ, Zanchetti A. Neural mechanisms in life threatening arrhythmias. Am Heart J 1980;100:705–15.

[18] Schwartz PJ, Stone HL. Effects of unilateral stellotomy upon cardiac performance during exercise in dogs. Can J Res 1979;44:637–45.

[19] Drott C, Claes G, Thamby-Jayasundera S. Cardiac effects of endoscopic electrocautery of the upper thoracic sympathetic chain. Eur J Surg 1994;160:65–70.

[20] Kingma R, Ten Voorde BJ, Scheffer GJ, Karemaker JM, Mackaay AJ, Wesseling KH, de Lange JJ. Thoracic sympathectomy: effects on hemodynamics and baroreflex control. Clin Auton Res 2002 Feb;12(1):35–42.

[21] Battipaglia I, Lanza GA. The autonomic nervous system of the heart. In: Slatr R, Tio R, Elings P, Schwager M, editors. Autonomic innervation of the heart.
Berlin, Heidelberg: Springer; 2015.

[30] Irie T, Yamakawa K, Hamon D, Nakamura K, Shivkumar K, Vaseghi M. Cardiac sympathetic innervation via the middle cervical and stellate ganglia and anti-arrhythmic mechanism of bilateral stellectomy. Am J Physiol Heart Circ Physiol 2017;312:H392–405.

[31] Khalsa SS, Shahabi L, Ajijola OA, Bystritsky A, Naiboff BD, Shivkumar K. Synergistic application of cardiac sympathetic decentralization and comprehensive psychiatric treatment in the management of anxiety and electrical storm. Front Integr Neurosci 2014;7:98.

[32] Malliani A, Lombardi F, Pagani M, Recordati G, Schwartz PJ. Spinal sympathetic reflexes in the cat and the pathogenesis of arterial hypertension. Clin Sci Mol Med Suppl 1975;2. 259s–60s.

[33] Malliani A, Recordati G, Schwartz PJ. Nervous activity of afferent cardiac sympathetic fibres with atrial and ventricular endings. J Physiol 1973;229:457–69.

[34] Schwartz PJ, Foreman RD, Stone HL, Brown AM. Effect of dorsal root section on the arrhythmias associated with coronary occlusion. Am J Physiol 1976;231:923–8.

[35] Masood SA, Kazmouz S, Heydemann P, Li H, Kenny D. Under-recognition of low blood pressure readings in patients with duchenne muscular dystrophy. Pediatr Cardiol 2015;36(7):1489–94.

[36] Marui Fabiane RRH, Bianco HT, Bombig MTN, et al. Behavior of blood pressure variables in children and adolescents with duchenne muscular dystrophy. Arq Bras Cardiol 2018 June;110(6):551–7.

[37] Johnson JN, Harris KM, Moir C, et al. Left cardiac sympathetic denervation in a pediatric patient with hypertrophic cardiomyopathy and recurrent ventricular fibrillation. Heart Rhythm 2011 Oct;8(10):1591–4.

[38] Song JC, Hwang CS, Lee EH, et al. Effects of bilateral stellate ganglion block on autonomic cardiovascular regulation. Circ J 2009;73(10):1909–13.