



Original contribution

## Postural orthostatic tachycardia syndrome and general anesthesia: a series of 13 cases<sup>☆</sup>

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### Abstract

**Study Objective:** To investigate whether patients with postural orthostatic tachycardia syndrome (POTS) developed unexpected perioperative complications.

**Design:** Retrospective case series.

**Setting:** Academic medical center.

**Measurements:** The records of 13 patients with POTS, who underwent surgical procedures during general anesthesia, were studied. Details of disease management, anesthetic induction, hemodynamic response to induction and intubation, intraoperative course, and immediate postoperative management were analyzed.

**Main Results:** Three patients developed prolonged intraoperative hypotension, which was not associated with induction of anesthesia. All 13 patients were successfully treated and they recovered without complications. There were no unplanned hospital or intensive care admissions.

**Conclusions:** Intraoperative hypotension, but not tachycardia, was observed in three of 13 patients with POTS who received general anesthesia for a variety of surgical procedures using multiple medications and techniques.

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## 1. Introduction

Orthostatic intolerance defines a group of symptoms characterized by cerebral hypoperfusion and/or sympathetic

activation that appear on standing upright and remit in the supine position. Patients may complain of headache, nausea, abdominal pain, lightheadedness, diminished concentration, syncope, anxiety, weakness, fatigue, exercise intolerance, palpitations, dyspnea, and chest pain. Some patients also may have generalized complaints, including fatigue, sleep disturbance, and migraine headaches. Orthostatic intolerance may be diagnosed on the basis of these symptoms only and does not require any hemodynamic abnormalities. The postural orthostatic tachycardia syndrome (POTS) is

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characterized by symptoms of orthostatic intolerance associated with excessive tachycardia while in the upright position, without orthostatic hypotension. Diagnostic criteria include a) a sustained increase in heart rate (HR) of 30 beats per minute (bpm) or greater during 10 minutes of assuming an upright position, b) no associated hypotension, and c) symptoms of orthostatic intolerance, which must be present for at least three months [1]. In severe forms of the disease, HR may increase to more than 120 bpm on standing.

Little is known about the anesthetic implications of POTS. Anesthetic techniques have been described for other forms of autonomic dysfunction [2-6], but the optimal anesthetic management of a patient with POTS is uncertain. Few investigators have described the use of regional techniques for labor analgesia or cesarean delivery in obstetrical patients [7-9]. In one case of cesarean delivery [8], epidural anesthesia was converted to general anesthesia due to patient discomfort and tachycardia. The authors stated that "the patient was more cardiovascularly stable". A single case report described the management of general anesthesia in a patient with orthostatic intolerance syndrome associated with postural tachycardia and blood pressure (BP) lability. This case showed a possible intraoperative complication in patients with orthostatic intolerance, namely, wide swings in mean arterial blood pressure (MAP) and HR despite adequate preoperative intravenous (IV) hydration [10].

The aims of this study were to investigate the perioperative management of patients with POTS and to identify perioperative complications, including hemodynamic instability and unplanned admission to the intensive care unit (ICU). We hypothesized that patients with POTS would have an increased occurrence of hypotension and increased need for pressors (POTS pts have sympathetic denervation of the legs with loss of vasomotor tone), cardiovascular collapse (POTS pts have an unstable adrenergic system and baroreflex dysfunction), and arrhythmias (POTS pts have symptoms of sympathetic overactivity and elevated plasma norepinephrine levels).

## 2. Materials and methods

Following Mayo Clinic Institutional Review Board approval, the medical records of patients diagnosed with POTS at the Mayo Clinic between January 1, 1993 and December 31, 2003, who subsequently underwent general anesthesia for an elective procedure, were reviewed. Cases of POTS were previously defined and identified by Thielen et al. through a manual chart review of patients seen by two Mayo Clinic POTS specialists [1]. Briefly, POTS was diagnosed if patients met the following inclusion criteria: a) baseline sinus rhythm without arrhythmia or cardiac disease, b) sustained HR increment of 30 bpm or greater in response to 10 minutes of head-up tilt, c) symptoms of orthostatic intolerance (eg, lightheadedness, weakness, palpitations, blurred vision, breathing difficulties, nausea, or headache)

developing after standing or head-up tilt and resolving with recumbency, and d) symptoms present for at least three months. A POTS diagnosis was excluded if patients experienced orthostatic hypotension [decline of 30 mmHg or more in systolic blood pressure (SBP) or 20 mmHg or more in MAP within three min of standing or head-up tilt], had failure of another organ system or systemic illness affecting autonomic function, or were pregnant or lactating. Patients had also undergone additional autonomic testing, including cardiovagal, adrenergic, and postganglionic sudomotor function tests as well as thermoregulatory sweat testing and measurement of ganglionic antibodies, plasma norepinephrine levels, and urinary sodium excretion. Sudomotor, cardiovagal, and adrenergic function tests were used to calculate the composite autonomic severity score [1].

The records of 152 patients were identified. An electronic search of the Mayo Clinic Anesthesia Database was conducted on the 152 patients to identify all surgical procedures performed during general anesthesia between January 1, 1993 and December 31, 2006 at Mayo Clinic, Rochester, Minnesota. Surgeries performed with cardiopulmonary bypass were excluded. The first anesthetic administered after the POTS diagnosis was included in the data for patients who underwent multiple surgeries. A total of 13 general anesthetics met our inclusion criteria. The complete medical records of these 13 patients were independently reviewed by two study physicians working together (JAR, CBG).

The following information was retrospectively collected for each study patient: gender, date of birth, and date of POTS diagnosis. For each anesthetic visit, the following information was collected: ASA physical status, surgical procedure, and current POTS therapy (medications, volume expansion, resistance exercise training, and compressive garments). Preoperative BP and HR were recorded from the preanesthetic evaluation form for comparison with induction response, intraoperative hemodynamic changes, complications, and Postanesthesia Care Unit (PACU) monitoring.

Details of each intraoperative course were collected, including the type of induction and maintenance anesthetic agents, use of invasive monitoring, hemodynamic response to induction, maintenance hemodynamics, total fluid input and output, use of neuromuscular blockade reversal, and the occurrence and management of intraoperative complications, including hemodynamic instability and arrhythmias. To assess hemodynamic response to induction, the minimum and maximum HR and corresponding SBP and diastolic blood pressure (DBP) recorded within 5 minutes of administration of induction medication, were collected. The minimum and maximum HR and corresponding SBP and DBP during the maintenance phase also were collected. Intraoperative hemodynamic complications were defined as follows: a) in accordance with the POTS definition, tachycardia was defined as a sustained HR increase of 30 bpm or to greater than 120 bpm from preoperative baseline levels, and b) hypotension and hypertension were defined as a decrease or increase of MAP of 30% or greater from baseline, sustained for more than

10 minutes and requiring IV vasopressor or beta-blocker therapy or additional fluid boluses.

In addition, the following information was collected from each PACU admission: minimum and maximum HR and corresponding SBP and DBP, development of POTS symptoms, development of postoperative nausea and/or vomiting (PONV), length of stay (LOS), and disposition. POTS symptoms occurring in the PACU were defined as lightheadedness, palpitations, presyncope, or syncope, as documented in the PACU record. If symptoms were not recorded, it was assumed none were present.

In cases where paper charting was used, vital signs were recorded every 5 minutes intraoperatively, and in cases where electronic charting was used they were recorded every three minutes. In cases where paper charting was used (1993 to 1999), HR and BP values were estimated to the nearest 5 units.

Statistics including means  $\pm$  standard deviation or medians (interquartile ranges) were used to describe parametric or nonparametric results, respectively.

### 3. Results

A total of 13 patients (12 women, one man) underwent surgical procedures following the POTS diagnosis. Demographic data are summarized in Table 1. Mean age at the time of POTS diagnosis was  $28 \pm 13$  years (range 15-55 yrs). The

median time from POTS diagnosis to surgery was one year (range 0-10 yrs). Procedures and anesthetic details are summarized in Table 2 and Table 3. The postoperative course is summarized in Table 4.

The composite autonomic severity score was equal to or less than 3 for all patients, indicating mild adrenergic dysfunction [1]. All patients were evaluated within one month of anesthesia. Four patients were asymptomatic at the time they received general anesthesia, while 9 had symptoms consistent with a POTS diagnosis. As part of the definition of POTS for the Mayo POTS database, none of the patients had lability of BP while in the standing position. Patients were treated with medications in 12 of 13 (92%) cases, volume expansion (increased oral fluid intake) in three of 13 (23%) cases, and resistance exercise training in one case. Preoperative POTS medications included beta-receptor antagonist in 8 of 13 (62%) cases, the alpha-1 receptor agonist, midodrine, in three of 13 (23%) cases, selective serotonin reuptake inhibitor (SSRI) in one case, alpha-2 receptor agonist in two of 13 (15%) cases, and fludrocortisone in two cases. The response rate in the form of partial symptom relief to treatment in the Mayo POTS database varied between 40% and 60% for each treatment [1].

At the time of anesthesia, the patient was classified as ASA physical status 2 or 3 in 12 of 13 (92%) cases. In one case, the patient was classified as ASA physical status 1. The underlying cardiac, pulmonary, renal, and endocrine comorbidities were as follows: one patient had underlying cardiac disease (aortic

**Table 1** Demographics and preoperative data in 13 patients with postural orthostatic tachycardia syndrome (POTS)

| Patient | Gender | Age at diagnosis (yrs) | Age at anesthetic (yrs) | POTS symptoms                          | Treatment                     | ASA physical status | Comorbid conditions | Weight (kg) |
|---------|--------|------------------------|-------------------------|--|-------------------------------|---------------------|---------------------|-------------|
| 1       | F      | 35                     | 37                      | Fatigue, exercise intolerance, syncope | Beta blocker, Clonidine       | 2                   | None                | 100         |
| 2       | M      | 55                     | 63                      | None                                   | Beta blocker                  | 3                   | s/p CABG, AVR; OSA  | 120         |
| 3       | F      | 15                     | 15                      | Tremulousness, syncope                 | Midodrine                     | 2                   | None                | 47          |
| 4       | F      | 32                     | 42                      | Syncope                                | Beta blocker                  | 3                   | OSA, hypothyroidism | 108         |
| 5       | F      | 17                     | 20                      | None                                   | Midodrine, beta blocker       | 2                   | None                | 89          |
| 6       | F      | 32                     | 33                      | Lightheadedness, fatigue, presyncope   | Beta blocker                  | 2                   | None                | 82          |
| 7       | F      | 19                     | 19                      | None                                   | Beta blocker, fludrocortisone | 2                   | None                | 71          |
| 8       | F      | 30                     | 31                      | Fatigue, diaphoresis                   | Fludrocortisone               | 2                   | None                | 51          |
| 9       | F      | 19                     | 20                      | Unknown                                | None                          | 1                   | None                | Unknown     |
| 10      | F      | 23                     | 23                      | Fatigue, diaphoresis                   | SSRI                          | 2                   | None                | 50          |
| 11      | F      | 20                     | 23                      | None                                   | Beta blocker                  | 3                   | None                | 57          |
| 12      | F      | 51                     | 51                      | Fatigue, tremulousness, diaphoresis    | Beta blocker, clonidine       | 3                   | None                | 70          |
| 13      | F      | 19                     | 19                      | Lightheadedness, weakness, syncope     | Midodrine                     | 3                   | None                | 52          |

F = female, M = male, CABG = coronary artery bypass graft, AVR = aortic valve replacement, OSA = obstructive sleep apnea, SSRI = selective serotonin reuptake inhibitor.

**Table 2** Procedures and intraoperative details of general anesthetics in 13 patients with postural orthostatic tachycardia syndrome

| Patient and procedure (positioning)                                 | Anesthetic  |        |       | Induction |        |     | Maintenance                        |        |     | Intraoperative complications |                        |   |
|---|-------------|--------|-------|-----------|--------|-----|------------------------------------|--------|-----|------------------------------|------------------------|---|
|   | Monitors    | Airway | Agent | Dose (mg) | Opioid | NMB | Anesthetic (%)                     | Opioid | NMB | Complication                 | Management             | Drug, doses                             |
|   | ASA         | ETT    | Prop  | 200       | Fent   | Sux | Iso 1.5-1.7                        | No     | No  | No                           | No                     | No                                      |
| Patient 1 Lipoma excision (supine)                                  | ASA         | ETT    | Prop  | 200       | Fent   | Sux | Iso 1.5-1.7                        | No     | No  | No                           | No                     | No                                      |
| Patient 2 Decompressive lumbar laminectomy (prone)                  | ASA         | A-line | ETT   | Prop      | 200    | Sux | Iso 0.5-0.8 N <sub>2</sub> O 45-50 | Oxy-M  | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 3 Right thoracic sympathectomy (left lateral)               | ASA         | ETT    | Thio  | 300       | Fent   | Vec | Iso 0.8 N <sub>2</sub> O 30        | Fent   | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 4 Exploratory laparotomy (Trendelenburg)                    | ASA         | A-line | ETT   | Prop      | 90     | Cis | Sevo 1.8-2.4                       | Hyd-M  | Cis | Cis                          | Cis                    | Cis                                     |
| Patient 5 Cystoscopy (lithotomy)                                    | ASA         | LMA    | Prop  | 200       | Fent   | No  | Propofol TIVA                      | No     | No  | No                           | No                     | No                                      |
| Patient 6 Hysteroscopy, D&C, cystoscopy, laparoscopy (lithotomy)    | ASA         | ETT    | Sevo  | NA        | Fent   | Cis | Sevo 0.5-1.0 N <sub>2</sub> O 50   | Fent   | Cis | Cis                          | Hypotension for 20 min | Ephedrine, 10 mg/10 mg                  |
| Patient 7 Resection cervical rib (supine)                           | ASA         | ETT    | Thio  | 175       | Fent   | Vec | Sevo 1.1-1.4 N <sub>2</sub> O 50   | No     | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 8 Left thyroid lobectomy (reverse Trendelenburg)            | ASA         | ETT    | Thio  | 225       | Fent   | Sux | Iso 0.5 N <sub>2</sub> O 50        | Fent   | Vec | Vec                          | Hypotension for 30 min | Ephedrine, 5 mg/10 mg                   |
| Patient 9 ORIF frontal sinus fracture (supine)                      | ASA         | ETT    | Prop  | 100       | Fent   | Vec | Iso 0.6-0.7 N <sub>2</sub> O 62-68 | Morph  | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 10 Laparoscopy & hysteroscopy (Trendelenburg)               | ASA         | ETT    | Prop  | 100       | Fent   | Vec | Des 5.3-6.0 N <sub>2</sub> O 60    | Fent   | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 11 Atrial pacemaker lead extraction (supine)                | ASA, A-line | ETT    | Thio  | 250       | Fent   | Sux | Iso 0.9-1.2                        | No     | Vec | Vec                          | Vec                    | Vec                                     |
| Patient 12 Removal spinal cord stimulator and cable (right lateral) | ASA         | ETT    | Prop  | 100       | Fent   | Roc | Sev 1.2-1.9 N <sub>2</sub> O 62-72 | Fent   | No  | No                           | No                     | No                                      |
| Patient 13 Excision perimandibular lymph node (supine)              | ASA         | ETT    | Prop  | 50        | Fent   | Vec | Sev 1.0-2.8 N <sub>2</sub> O 20-50 | No     | Vec | Vec                          | Hypotension for 30 min | Phenylephrine, 50/50/100/100/100/200 µg |

NMB = neuromuscular blocker, ASA = standard ASA monitors, ETT = endotracheal tube, Prop = propofol, Fent = fentanyl, Sux = succinylcholine, Iso = isoflurane, A-line = arterial catheter, N<sub>2</sub>O = nitrous oxide, Oxy-M = oxymorphone, Vec = vecuronium, Thio = thiopental, Cis = cisatracurium, Sevo = sevoflurane, Hyd-M = hydromorphone, LMA = Laryngeal Mask Airway, TIVA = total intravenous anesthesia, D&C = dilatation and curettage, ORIF = open reduction internal fixation, morph = morphine, Des = desflurane, Roc = rocuronium.

requiring intervention with additional fluid boluses and vasopressor medications. The first patient developed hypotension after being placed in the lithotomy position for cystoscopy. Hypotension lasted 20 minutes and was adequately controlled with ephedrine boluses; no additional fluid was needed and no other intraoperative or postoperative complications were observed. The second of the three patients was placed in the reverse Trendelenburg position for thyroid lobectomy and soon developed hypotension lasting 30 minutes; interestingly, the hypotension was not associated with tachycardia. Treatment consisted of ephedrine boluses only and there were no additional complications. The third patient to develop hypotension had excision of a perimandibular lymph node in the supine position and was treated with multiple boluses of phenylephrine over a 30-minute period. The patient suffered no additional complications.

The majority of patients (77%) received two liters (L) or less of IV crystalloid fluids intraoperatively, and in three of 13 (23%) cases the patient received more than two L. No patients received a blood transfusion. The positions in which surgery was performed are listed in Table 2.

### 3.2. Postoperative course

In the PACU, the average minimum and maximum HR values were  $74 \pm 18$  bpm and  $99 \pm 18$  bpm, respectively. In two (25%) cases, patients had HR values greater than

110 bpm. No patients experienced hypotension during their PACU stay. Two patients had documented PONV (one after a gynecologic procedure, one after atrial lead extraction). No patients had documented POTS symptoms.

The average PACU length of stay was 95 minutes (range 43-285 min). In three of 13 (23%) cases, the patient was discharged home, 8 of 13 (62%) cases were admitted to an unmonitored floor, and two of 13 (15%) cases were admitted to a monitored care setting. There were no unplanned hospital or ICU admissions. The average hospital LOS for those admitted was three days (range 1-10 days). No patients had documented POTS symptoms during the remainder of the hospital stay.

## 4. Discussion

### 4.1. Discussion of results

We report a series of 13 surgical procedures during general anesthesia in patients with POTS. The major findings of this case series include the observation that three patients had prolonged intraoperative hypotension requiring vasopressor medications and additional fluid boluses during a variety of procedures that differed in stress level. Of note, all patients recovered without additional complications or long-standing effects from hypotension. PACU LOS was not excessive and there were no unplanned ICU admissions.

**Table 4** Postoperative details of general anesthesia in 13 patients with postural orthostatic tachycardia syndrome

| Patient and Procedure   | Postoperative anesthesia care unit |           |              |           |                             | Hospital admission |                                |
|---|------------------------------------|-----------|--------------|-----------|-----------------------------|--------------------|--------------------------------|
|   | Min HR (bpm)                       | BP (mmHg) | Max HR (bpm) | BP (mmHg) | Postoperative complications | Level of care      | Hospital length of stay (days) |
| Patient 1 Lipoma excision                                     | 105                                | 150/90    | 135          | 150/85    | None                        | General floor      | 1                              |
| Patient 2 Decompressive lumbar laminectomy                    | 73                                 | 116/52    | 98           | 101/55    | None                        | General floor      | 10                             |
| Patient 3 Right thoracic sympathectomy                        | 85                                 | 115/75    | 100          | 140/90    | None                        | ICU                | 4                              |
| Patient 4 Exploratory laparotomy                              | 84                                 | 115/67    | 98           | 101/55    | None                        | General floor      | 3                              |
| Patient 5 Cystoscopy  | 86                                 | 130/99    | 100          | 143/93    | None                        | Outpatient         | NA                             |
| Patient 6 Hysteroscopy, Cystoscopy D&C, laparoscopy           | 50                                 | 120/80    | 75           | 145/75    | PONV                        | General floor      | 1                              |
| Patient 7 Resection cervical rib                              | 65                                 | 120/50    | 70           | 120/65    | None                        | General floor      | 4                              |
| Patient 8 Left thyroid lobectomy                              | NA                                 | NA        | NA           | NA        | None                        | General floor      | 2                              |
| Patient 9 ORIF frontal sinus fracture                         | 66                                 | 102/45    | 94           | 111/45    | None                        | General floor      | 2                              |
| Patient 10 Laparoscopy & hysteroscopy                         | 95                                 | 118/64    | 121          | 134/59    | None                        | Outpatient         | NA                             |
| Patient 11 Atrial pacemaker lead extraction                   | 57                                 | 141/77    | 110          | 124/91    | PONV                        | ICA                | 2                              |
| Patient 12 Removal spinal cord stimulator and extension cable | 47                                 | 148/51    | 83           | 112/50    | None                        | General floor      | 2                              |
| Patient 13 Excision perimandibular lymph node                 | 85                                 | 115/63    | 103          | 126/79    | None                        | Outpatient         | NA                             |

Hemodynamics given as minimum heart rate (HR) with corresponding blood pressure (BP) and maximum HR with corresponding BP. ICU = monitored intensive care, NA = not applicable, D&C = dilatation and curettage, PONV = postoperative nausea and vomiting, ICA = monitored floor.

All patients were part of the POTS database and therefore had POTS treatment managed by physicians specializing in this disease. In addition, all patients in this group underwent elective, nonemergent procedures. The fact that one of the patients was categorized as ASA physical status 1 may indicate insufficient awareness of POTS amongst anesthesiologists. During induction, one patient developed a single episode of hypotension (70/28 mmHg) during induction with propofol that lasted less than 5 minutes, and another patient developed isolated tachycardia on induction with propofol and initiation of desflurane. It is possible that these hemodynamic changes, although commonly seen in healthy patients, represented an interaction between the anesthetic agent and POTS. The only IV induction agents used in this case series were propofol and thiopental. Both of these drugs cause central and peripheral cardiovascular depression and decreased baroreflex-mediated responses to changes in BP [11]. With propofol, this leads to a decrease in BP and HR, and with thiopental it leads to hypotension and tachycardia. Thus, one may be concerned that thiopental may exacerbate tachycardia in POTS patients, and both propofol and thiopental may cause disproportionate hypotension during induction in POTS patients.

Based on the relative absence of anesthesia literature on the intraoperative course and management of POTS, we did not know which complications to expect. The factors that predisposed three patients to developing prolonged intraoperative hypotension are unknown. All were hemodynamically stable during the induction phase; however, two of the three patients developed hypotension after positional changes, one from supine to lithotomy and one from supine to reverse Trendelenburg. Position change from supine to reverse Trendelenburg does elicit orthostatic intolerance in POTS patients, and this finding was not surprising. On the other hand, a change to the lithotomy position should improve symptoms of orthostatic intolerance secondary to improved venous return to the right heart; therefore, we have no explanation for this event, as a different patient tolerated this position without hypotension.

One patient in this series underwent right thoracic sympathectomy. It is possible that once the surgery had been performed, and for subsequent surgeries, this patient would not have altered responses of POTS.

#### 4.2. Review of POTS

POTS findings typically present in patients 15 to 50 years of age, of whom 80% are female. The prevalence of POTS is unknown, particularly as it is often undiagnosed. It is probably about 5 to 10 times as common as orthostatic hypotension and one estimate is that prevalence is at least 170/100,000 [12]. At the time of diagnosis, most patients will have been symptomatic for several years. The etiology of primary POTS is unknown; however, up to 50% of patients may experience a viral prodrome prior to developing symptoms; these patients may slowly improve after the

initial episode only to relapse during subsequent infections or periods of stress. POTS also may be secondary to autonomic neuropathies seen with other diseases, including diabetes, amyloid neuropathy, multiple system atrophy (Shy-Drager syndrome), and primary autonomic failure. Symptoms may be cyclical in nature, especially during certain times of the menstrual cycle, and may be associated with fluid retention and weight gain. However, a hormonal basis for the disease has not been established. Exercise, heat, and the postprandial state also may worsen POTS symptoms. It is unknown whether symptoms may worsen or remain stable during the perioperative process. POTS presents postoperatively in about 10% cases.

Based on physical and biochemical characteristics, POTS may be distinguished as either neuropathic or hyperadrenergic, or associated with deconditioning; however, etiology and pathophysiologic mechanisms are heterogeneous and not mutually exclusive between the groups [1,12-16].

A common underlying finding is venous pooling of the lower extremities and mesenteric vessels in the standing position, causing decreased venous return to the right heart resulting in decreased stroke volume (SV) and ultimately causing cerebral hypoperfusion. In response, central sympathetic activation results in tachycardia and other hyperadrenergic symptoms. A subset of patients has decreased plasma volume and red cell mass, thereby contributing to symptoms. Almost all have reduced exercise tolerance.

Patients with neuropathic POTS have a neuropathy involving the postganglionic sympathetic fibers of the lower extremities, of which an autoimmune etiology is postulated. The resultant sympathetic denervation is associated with loss of vasomotor tone and pooling of blood in the legs on standing, leading to symptoms of cerebral hypoperfusion. Antibodies to ganglionic alpha 3 acetylcholine receptors are found in 14% of patients [17,18]. Autonomic studies testing postganglionic sympathetic function, including the quantitative sudomotor axon test (QSART) and thermoregulatory sweat test (TST), show peripheral sudomotor (sweat gland) denervation in up to 54% of patients [1].

Hyperadrenergic POTS is characterized by excessive symptoms of sympathetic activation, including palpitations, anxiety, tremulousness, and, in some, an increase in SBP on assuming the upright position. In addition, elevated norepinephrine levels on standing ( $> 600$  pg/mL) is typical. An exaggerated BP response to phenylephrine and isoproterenol may be observed; however, sympathetic activation in this subgroup of patients is related to increased norepinephrine release and decreased clearance whereas the systemic sensitivity of postsynaptic alpha- and beta-adrenoreceptors may be unaltered [19,20]. These patients' symptoms may significantly respond to beta-blocker therapy.

Fatigue and exercise intolerance are prominent symptoms in all POTS patients and almost all patients are deconditioned at presentation. Exercise is associated with a greater tachycardia response versus controls and may be related to reduced SV secondary to venous pooling [15]. This finding

is very similar to that seen in severe deconditioning and prolonged bed rest [16]. The theory is that in some patients an inciting event, for example, a viral illness, leads to POTS, which is associated with ever decreasing physical activity and worsening deconditioning; patients then find themselves in a downward spiral that is hard to break without appropriate therapy, including exercise training.

Absolute or relative hypovolemia has been noted in a number of patients with POTS [21] and postulated mechanisms include capillary leakage secondary to venous pooling [22], low renin activity [23], or an intrinsic renal defect [24] leading to plasma and red blood cell volume deficits. Saline infusion may acutely improve orthostatic tachycardia [25]; however, overnight hydration with IV crystalloid did not improve orthostatic intolerance in a study conducted at our institution [16].

Management of POTS is challenging, as no single management plan controls symptoms in all patients. Efforts are directed at improving fitness and general conditioning combined with increased intake of salt and fluids to increase intravascular volume. Compressive support hose may assist in decreasing venous pooling [12]. Medication use should be individualized based on underlying symptoms and the type of POTS suspected. Fludrocortisone is used in neuropathic POTS to expand the intravascular fluid compartment and to sensitize peripheral alpha-adrenergic receptors to endogenous catecholamines. Midodrine, an alpha-1-receptor agonist that causes vasoconstriction of peripheral vasculature, is used successfully in various forms of orthostatic intolerance. It may be associated with excessive supine hypertension, nausea, and urinary retention. Other medications used include methylphenidate, also an alpha-agonist, and yohimbine, an alpha-2-antagonist. Desmopressin (DDAVP) and erythropoietin may increase intravascular volume and red cell mass [17]. Patients with the hyperadrenergic form of the disease are medically treated with beta blockers to attenuate sympathetic activation. Propranolol and labetalol seem to be most effective. In addition clonidine, an alpha-2-agonist with central sympatholytic effects, also may be very useful in this group [10]. Studies have suggested a central disturbance in serotonin production in some patients, and SSRIs have been used successfully [17].

#### 4.3. Limitations

This study had several limitations in addition to those inherent to any retrospective study. There was variable information available on several important parameters, including volume status and ventilatory parameters. Intraoperative HR and BP were recorded only every three minutes (electronic charting) or 5 minutes (paper charting), and postoperative hemodynamic data were recorded every 15 minutes. The values collected may not have represented the true maximum or minimum readings, nor could we perform calculations of hemodynamic variance.

The variation in patient demographics, procedures, and procedure-related stress, anesthetic technique, and medications, as well as the lack of control data, meant that we had to base our recommendations on review of the POTS literature. While all of our cases were uncomplicated, the limited number of anesthetics administered may not represent the true spectrum of reactions that POTS patients may experience during general anesthesia.

#### 4.4. Conclusion

Autonomic dysfunction associated with POTS may present unusual physiologic challenges in the perioperative period. This case series observed patients with POTS who were anesthetized for a variety of procedures, with three patients experiencing sustained intraoperative hemodynamic instability. No patients developed complications in the immediate postoperative period or during the rest of their hospital stay.

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