Orthostatic intolerance without postural tachycardia: how much dysautonomia?

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Abstract

Background—Chronic symptoms of orthostatic intolerance occur in postural tachycardia syndrome (POTS) and patients with orthostatic intolerance (OI) without tachycardia. We recently reported that deconditioning is almost universal in both patient groups. In this study, we focussed on the question of how much dysautonomia, besides orthostatic tachycardia, is there in POTS vs. OI, and how the two groups compare in regards to clinical, autonomic, laboratory, and exercise variables.

Methods—We retrospectively studied all patients referred for orthostatic intolerance at Mayo Clinic between January 2006 and June 2011, who underwent standardized autonomic and exercise testing.

Results—Eighty-four POTS and 100 OI fulfilled inclusion criteria, 89 % were females. The mean age was 25 and 32 years, respectively. Clinical presentation, autonomic parameters, laboratory findings, and degree of deconditioning were overall similar between the two groups, except for the excessive orthostatic heart rate (HR) rise and mild vasomotor findings observed in POTS but not in OI (slightly larger Valsalva ratio and incomplete blood pressure recovery during Valsalva). Both groups responded poorly to various medications. Severely deconditioned patients were similar to non-deconditioned patients, except for 24 h urine volume (1,555 vs. 2,417 ml), sweat loss on thermoregulatory sweat test (1.5 vs. 0.5 %), and few respiratory parameters during exercise, which are likely clinically insignificant.

Conclusion—Though similar in clinical presentation, POTS and OI are different entities with greater, albeit still mild, dysautonomia in POTS. The clinical and pathophysiological relevance of minimal dysautonomia in the absence of orthostatic tachycardia as seen in OI remain uncertain.

Keywords

Orthostatic intolerance; Postural tachycardia syndrome; Exercise capacity; Deconditioning

Background

We recently reported that deconditioning is an almost universal finding in patients with symptoms of orthostatic intolerance associated with orthostatic tachycardia (postural tachycardia syndrome, POTS) or without orthostatic tachycardia (orthostatic intolerance alone, OI) [1]. The focus of that report was on deconditioning. This part of the study is

focussed specifically on the role of dysautonomia in POTS and OI. Chronic orthostatic intolerance (OI) occurs in neurogenic orthostatic hypotension and symptoms are due to cerebral hypoperfusion [2]. In contrast, cerebral hypoperfusion is only sometimes present in POTS and when present, is thought to relate to hypocapnia-induced cerebral vasoconstriction [2]. Psychologic factors such as catastrophic cognitions, somatic hypervigilance, anxiety sensitivity, and neuroticism have been reported to occur in higher frequency in patients with orthostatic intolerance and likely add to functional limitations and symptoms [3, 4]. Autonomic testing has focussed on identifying reliable autonomic indices that characterize the dysautonomic components of the syndrome. Orthostatic tachycardia has been the most reliable index and has been demonstrated not to be due to anxiety [5]. Since this index is absent at the time of testing in OI, we sought to evaluate, retrospectively, if the severity and distribution of other autonomic indices would distinguish the two conditions.

We examined if the clinical presentation, autonomic and exercise parameters are similar in the two conditions, and also evaluated the relationship of these parameters to the degree of deconditioning. We have reported previously that most POTS patients have functional disability and limited activities of daily living [4]. However, patients with OI have not been studied for such functional limitations. We previously reported that deconditioning is similar between POTS and OI [1]; however, other exercise parameters have not been compared between the two groups nor have they been related to the degree of deconditioning. Our large cohort of patients with POTS and OI, who underwent standardized exercise, autonomic, and laboratory evaluations at Mayo Clinic, provides a unique data set that allows us to undertake this analysis.

We hypothesized that POTS and OI are phenotypically similar entities with subtle differences in the degree and pattern of dysautonomia. We furthermore hypothesized that deconditioned patients have a clinical presentation similar to patients with no or mild degrees of deconditioning and that autonomic and laboratory parameters do not vary with the degree of deconditioning.

Schematic design of the study

Our study was approved by the Mayo Clinic Institutional Review Board. Electronic medical records of all patients, who presented with orthostatic symptoms at Mayo Clinic, Rochester, MN, between January 2006 and June 2011 and who underwent autonomic and exercise testing, were reviewed retrospectively. Patients who did not authorize the use of their medical records for research purpose, minors (<18 years), patients with medical conditions or on medications known to cause orthostatic tachycardia, and those with incomplete medical records were excluded from the study.

Definition of different variables

Orthostatic intolerance was defined as the development of previously defined symptoms of cerebral hypoperfusion or sympathetic activation upon standing along with a heart rate (HR) increment <30 bpm on head-up tilt (HUT) [6], while those with symptomatic increase in heart rate on HUT 30 bpm were defined as POTS. Patients with predicted VO_2 max of <85 % on exercise testing were considered deconditioned, <65 % severely deconditioned while those with 85 % were considered normal.

Exercise test parameters

Measured VO_2 max was defined as the maximum capacity of an individual's body to transport and use oxygen during incremental exercise, while predicted VO_2 max was calculated as $60 - (age \times 0.5)$ for males and $40 - (age \times 0.4)$ for females. Predicted VO_2

max % was calculated as measured VO_2 max/predicted VO_2 max multiplied by 100. HR recovery was calculated as peak HR – HR for 1 min during recovery period after the cessation of exercise. The following HR and BP variables were calculated: ΔHR_stage1: exercise stage1 HR – supine HR; ΔHR_peak: peak HR during – supine HR, ΔSBP_stage1: exercise stage 1 systolic blood pressure (SBP) – resting SBP, ΔDBP_stage1: exercise stage 1 diastolic blood pressure (DBP) – resting DBP; ΔSBP_peak: peak SBP during exercise – resting SBP, and ΔDBP_peak: peak DBP during exercise – resting DBP. Breathing reserve was defined as percentage of a subject's maximum voluntary ventilation that is not utilized at peak exercise [7]. Peak tidal volume (TV) was defined as the patient's highest value of TV sustained for at least 20 s and peak respiratory rate (RR) was defined as patient's highest RR during exercise testing. Respiratory effort was defined based on the peak respiratory exchange ratio (RER): RER < 1.05, inadequate effort; RER 1.05–1.15, near maximum; RER > 1.15, maximum effort.

Valsalva test parameters

The change (Δ) in SBP and DBP during early phase II (II_E), late phase II (II_L) and phase IV (IV) of the Valsalva maneuver (VM) were assessed compared to baseline average BP.

Head-up tilt parameters

Supine HR and BP were calculated as the average HR and BP during 5 min of resting in supine position. HUT was done routinely for 10 min. ΔSBP_H, ΔDBP_H, ΔHR and Δ pulse pressure were calculated as follows: ΔSBP_H: average SBP during second half of HUT – resting SBP; ΔDBP_H: average DBP during second half of HUT – resting ΔDBP; ΔHR: average HR during second half of HUT – resting HR; and Δpulse pressure: HUT pulse pressure – resting pulse pressure.

Exercise test

All subjects underwent symptom-limited graded treadmill exercise testing to maximum or near maximum level using metabolic cart (Medical Graphic CPX; Medical Graphic Corporation; St. Paul, MN). Initial workload was 2 mph at 0 % grade (equivalent to 2.5 METs), and the load was increased every 2 min by 2 METs until symptom-limited termination. This was followed by 3 min of active recovery at a speed of 1.7 mph with 0 % grade, then three or more additional minutes of seated recovery. Expired gases were monitored from rest throughout exercise and 1 min of active recovery. Simultaneous ECG recordings were obtained. BP was measured by left arm sphygmomanometer at 1.5 min of every stage, at peak exercise, and at 30 s and 2.5 min of seated recovery.

Autonomic tests

The quantitative sudomotor axon reflex test (QSART), heart rate response to deep breathing (HRDB), beat-to-beat BP responses to the VM, Valsalva ratio (VR), and thermoregulatory sweat test (TST) were performed in a routine fashion as previously described [8, 9]. The composite autonomic severity score (CASS) is an age- and sex-adjusted semiquantitative score ranging from 0 to 10 (normal to maximum dysfunction) which combines scores for the three tested autonomic domains (i.e., sudomotor 0–3, cardiovagal 0–3, adrenergic 0–4) [10].

Data collection

Demographic, clinical symptoms, and other data were collected from electronic medical records, while exercise and autonomic parameters were collected from cardiophysiologic and autonomic databases, respectively. Laboratory test variables were obtained as per standard clinical laboratory protocols.

Statistical considerations

Continuous measures are reported as mean ± SD or median and range, while discrete variables are reported as counts and percentages. Comparisons between two groups were analyzed with Chi-square or Fisher exact test for categorical variables and with two-sample *t* test or Wilcoxon rank-sum test for continuous variables, as appropriate. Comparisons among three groups were performed using ANOVA for continuous variables and Chi-square test for categorical variables. ANOVA with $p < 0.05$ was followed by multiple comparisons between groups along with the Bonferroni correction for *p* value. Calculated *p* values were two-sided and *p* values <0.05 were considered statistically significant. All statistical analysis was performed using JMP 9 (SAS institute, Cary, NC).

Results

One-hundred and eighty-four patients fulfilled the study inclusion criteria. Eighty-four patients fulfilled the criteria for POTS, while the remaining 100 fulfilled those for OI. Median age at symptom onset was 27.5 (IQR 22–37) years, with the OI group being older (*p* < 0.0001) (Table 1). Patients were predominately female, 89 % (Table 1).

Table 1 describes the details of clinical presentation of both groups. For POTS patients, the onset of illness was acute (<1 month) in 5 (6 %), subacute (1–3 months) in 2 (2 %), gradual (>3 months) in 72 (86 %), and unknown in 5 (6 %) patients. For patients with OI, the onset was acute in 2 (2 %) patients, subacute in 2 (2 %), gradual in 83 (83 %), and unknown in 13 (13 %) patients. The work capacity was reduced in 98 % of POTS and OI both, while 1 % of POTS and 2 % of OI had near normal function.

Clinical symptoms were similar between POTS and OI, but the duration of symptoms was longer among patients with OI compared to POTS (*p* = 0.0094) (Table 1). Seventy- four (40 %) of the 184 patients had additional disorders, including psychiatric diagnoses (depression, anxiety, posttraumatic stress disorder, attention deficit disorder, somatoform disorder), autoimmune disorders (diabetes mellitus, Hashimoto thyroiditis, celiac disease, Sjögren syndrome), asthma, myalgia, arthralgia, hypertension, and chronic fatigue syndrome. The frequencies of these conditions were similar between the two groups. Response to different medications was poor in both groups.

ΔHR_H was markedly higher in patient with POTS as expected. Measures of cardiovagal sensitivity (VR and HRDB) were higher among POTS compared to OI (*p*   0.002), possibly reflecting the slightly younger age of this group. BP responses to the Valsalva maneuver showed a trend toward a greater decrease during phase II_E, and there was a less complete BP recovery during phase II_L in POTS compared to OI (ΔII_L DBP, *p* = 0.04), consistent with a suggestion of mild vascular adrenergic impairment limited to the POTS group (Fig. 1). The rest of the autonomic parameters was similar between the two groups (Table 2A).

Peak HR, ΔHR_stage1, ΔHR_peak, HR_cool down 1 min, peak HR and breathing reserve were significantly higher among POTS compared to OI patients; however, predicted VO_2 max % did not differ between the two groups (Table 2B).

Demographics and clinical presentation were similar between normal and deconditioned groups except for bloating and sleep disturbances, both of which were less frequent among deconditioned patients (*p* = 0.04 for both). Demographics and clinical presentation were also similar between mildly and severely deconditioned groups except for a history of vomiting (severely deconditioned 30 % vs. mildly deconditioned 15 %, *p* = 0.03).

Baseline DBP and TST anhydrosis were slightly different across the three groups (normal, mildly, and severely deconditioned), both slightly higher among severely deconditioned patients (Table 3). VR, ΔIV SBP, and 24 h urine volume also varied across the three groups (Table 3). VR was mildly but significantly higher for the mildly deconditioned compared to the severely deconditioned group ($p = 0.03$ after Bonferroni correction). Urine volume did not differ between mildly and severely deconditioned groups ($p = 0.16$) but was lower among both groups compared to normal (normal vs. mild, $p = 0.02$, normal vs. severe $p = 0.016$ after Bonferroni correction). Using multiple comparisons, ΔIV SBP was not significant between the different groups after Bonferroni correction. Looking only at POTS patients, only 24 h urine volume and upright plasma NE were different between the degree of deconditioning, lower among severely deconditioned patients compared to normal (p 0.03). Peak RER (indicator of respiratory efforts) was almost identical among normal (1.19 ± 0.1), mildly deconditioned (1.22 ± 0.1) and severely deconditioned patients (1.18 ± 0.13) ($p = 0.05$).

Discussion

Even though many autonomic researchers have focused on POTS, OI has remained a nondescript entity. Some have regarded these patients as having a functional or psychiatric disorder. Others have considered OI to be a POTS variant (or in the POTS spectrum). Our findings support the hypothesis that POTS as a group is associated with greater dysautonomia (with a greater orthostatic heart rate increment, by definition) than OI, which is further supported by mild differences in the blood pressure responses during phase II between the two groups. Otherwise, autonomic deficits are similar, but not illuminating here, since they are minimal (at least in the majority of patients). As the wide spectrum of clinical complaints is generally disproportionate to the degree of abnormality found on testing, it cannot be completely explained by the autonomic abnormalities, suggesting that the two disorders may share a psychologic substrate or overlay. However, the abnormal autonomic responses are undeniably present, albeit mild. Their etiology remains still incompletely understood and is likely heterogeneous.

A prospective study similar to our previous one on POTS would be required to assess and compare this notion satisfactorily [4].

The exercise abnormalities in both conditions indicate a high prevalence of deconditioning in POTS and OI alike. We found that deconditioned patients had a clinical presentation and symptom aggravating factors similar to those with normal predicted VO_2 max %. Subtle statistical differences between different degrees of deconditioning observed in certain autonomic and laboratory variables are unlikely to be of clinical significance. Some patients with POTS show evidence of a limited autonomic neuropathy [9], and our sudomotor findings would indicate that such findings are most prominent among severely deconditioned patients. Beside cardiovascular compromise, deconditioned patients also had lower peak TV, peak RR and higher breathing reserve. Peak RR was not different between normal and mildly deconditioned patients; however, it was lower in the severely deconditioned group. These findings suggest mechanical respiratory impairment in the deconditioned groups, especially the severely deconditioned patients given that peak RER (measure of respiratory effort) was similar between deconditioned and normal groups. Significant correlation between peak TV and vital capacity ($r = 0.827$, $p < 0.000l$) described by Gowda et al. [11] supports our findings of mechanical respiratory impairment in deconditioned patients but requires further evidence to make definitive conclusions.

Symptom onset was mostly gradual in both groups with few patients having subacute and acute onset. About one-third of the patients had an antecedent trigger with viral illness being

the most common in both groups; yet, this finding was less frequent than reported previously [9, 12]. However, a direct association between different risk factors and onset of orthostatic intolerance is difficult because most patients are not able to precisely identify the date and nature of those potential factors. Prolonged immobilization during a recovery phase after a major illness or surgery can lead to deconditioning, thus exaggerating the symptoms. Other triggers could also elicit orthostatic symptoms and affect autonomic nervous system function, and this aspect clearly requires further study.

In OI patients, the duration of illness was longer and OI patients were generally older than POTS patients. That may explain lower vagal sensitivity in OI patients as suggested by VR and HRBD, but the reason for the age difference remains elusive.

What interim conclusions can we draw and what management recommendations can we make? First, we should continue to use autonomic function testing to identify patients with orthostatic tachycardia and identify those with an autonomic neuropathy or hyperadrenergic state, since they need specific treatment. Second, both POTS and OI have underlying deconditioning, which requires treatment. Even though promising short-term response to different medications has been reported previously [13, 14], we found evidence of poor long-term responses to all medications in both groups. Furthermore, many side effects related to different medications have been described [15]. Hence, POTS and OI should be managed with a combination of exercise and other measures including suitable medications, as well as behavioral therapy in selected patients that present with a somatic hypervigilance component.

Our study has certain limitations which include its retrospective nature, the fact that the magnitude of HR increment during tilt may fluctuate during the day, being maximal usually in the morning. Thus, some OI patients may have fulfilled POTS criteria if tested at different time. Other limitations include the bias of a tertiary referral center, a small number of patients with normal predicted VO_2 max %, and inadequate effort during exercise testing in some patients. However, patients referred for exercise testing comprised >80 % of the patients with orthostatic intolerance seen at Mayo Clinic during the timeframe of the study, and therefore, we are confident they are representative of this population seen at Mayo Clinic, Rochester, Minnesota. A key unanswered question is whether a postulated psychologic contribution to the clinical syndrome is different in OI and POTS. A prospective evaluation similar to what we have undertaken in POTS previously is needed to address this important question [3, 4].

Acknowledgments

Abbreviations

POTS	Postural tachycardia syndrome
OI	Orthostatic intolerance without excessive tachycardia
HR	Heart rate

BP	Blood pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
HUT	Head-up tilt
ΔHR	Change/difference in heart rate
ΔSBP	Change/difference in systolic blood pressure
ΔDBP	Change/difference in diastolic blood pressure
MET	Metabolic equivalent of task
TV	Tidal volume
RER	Respiratory exchange ratio
RR	Respiratory rate
II_E	Early phase II of Valsalva maneuver
II_L	Late phase II of Valsalva maneuver
IV	Phase IV of Valsalva maneuver
ΔHR_H, ΔSBP/DBP_H	Change in heart rate and blood pressures during head-up tilt
QSART	Quantitative sudomotor axon reflex test
HRDB	Heart rate response to deep breathing
VM	Valsalva maneuver
VR	Valsalva ratio
TST	Thermoregulatory sweat test
CASS	Composite autonomic severity score

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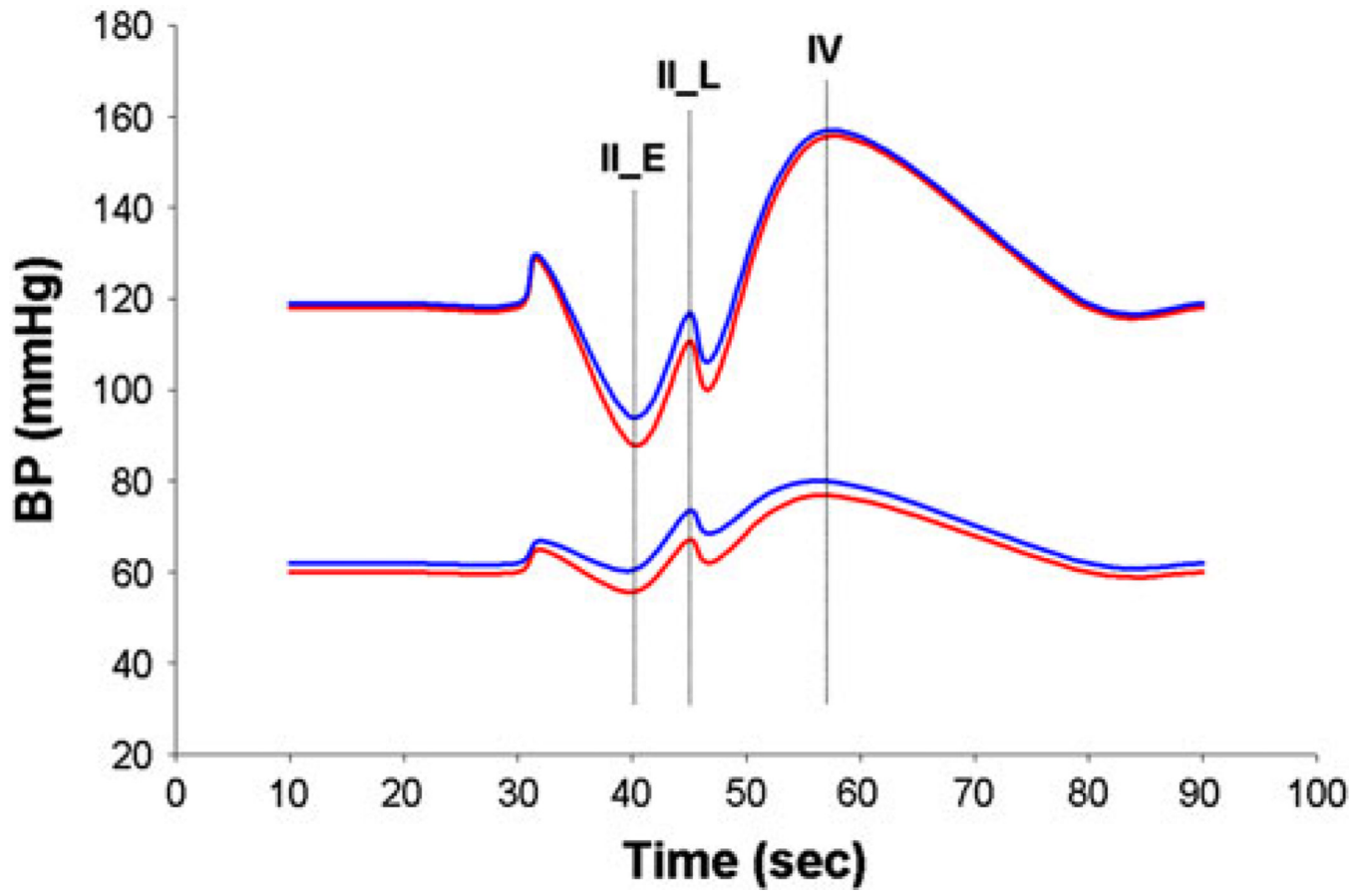
Fig. 1.
Blood pressure (systolic and diastolic) profile comparison between POTS (*red*) and OI
(*blue*) during the Valsalva maneuver

Table 1

Baseline demographic and clinical presentation of POTS and OI

	POTS (84)	OI (100)	*p* value
Age at onset of symptoms	25 (IQR 0–32)	32 (IQR 4–40)	**<0.0001**
Females	73 (87 %)	91 (91 %)	0.37
Duration of illness (years)	3 (IQR 1.1–6)	5 (IQR 2–8)	**0.0094**
Lightheadedness	82 (98 %)	95 (93 %)	0.18
Weakness	34 (41 %)	49 (49 %)	0.25
Presyncope/syncope	58 (69 %)	68 (68 %)	0.87
Head pressure/headache	55 (66 %)	59 (59 %)	0.37
Palpitation	68 (81 %)	83 (83 %)	0.72
Tremulousness	14 (17 %)	14 (14 %)	0.62
Dyspnea	31 (37 %)	31 (31 %)	0.40
Chest pain	27 (32 %)	32 (32 %)	0.98
Decreased sweating	3 (4 %)	2 (2 %)	0.51
Increased sweating	15 (18 %)	15 (15 %)	0.60
Heat intolerance	20 (24 %)	21 (21 %)	0.65
Exercise intolerance	84 (100 %)	97 (97 %)	0.25
Post prandial intolerance	2 (2 %)	7 (7 %)	0.18
Bloating	20 (24 %)	20 (20 %)	0.53
Nausea	48 (57 %)	61 (61 %)	0.60
Vomiting	15 (18 %)	27 (27 %)	0.14
Abdominal pain	19 (23 %)	25 (25 %)	0.71
Constipation	24 (29 %)	41 (41 %)	0.08
Diarrhea	25 (30 %)	34 (34 %)	0.54
Visual abnormality (blurring, diplopia, etc.)	14 (17 %)	22 (22 %)	0.36
Bladder symptoms	16 (19 %)	16 (16 %)	0.59
Sleep disturbances	45 (54 %)	56 (56 %)	0.42
Fatigue	62 (74 %)	69 (69 %)	0.47
Migraine	35 (42 %)	47 (47 %)	0.47
Myofascial pain	14 (17 %)	16 (16 %)	0.90
Neuropathic pain	3 (4 %)	4 (4 %)	1.00
Orthostatic intolerance related to menstruation	3 (4 %)	4 (4 %)	1.00
Cognitive decline/mental clouding	21 (25 %)	19 (19 %)	0.33
Past history of orthostatic intolerance	3 (4 %)	7 (7 %)	0.35
Family history of orthostatic intolerance	4 (5 %)	1 (1 %)	0.18
Mitral valve regurgitation	6 (7 %)	11 (11 %)	0.37
Mitral valve prolapse	1 (1 %)	2 (2 %)	1.00
Panic attack	6 (7 %)	5 (5 %)	0.54
Bud Chiari syndrome	2 (2 %)	1 (1 %)	0.59
Motor examination[a]	84 (100 %)	99 (99 %)	1.00
Sensory examination[a]	79 (94 %)	95 (95 %)	1.00

	POTS (84)	OI (100)	*p* value
Pupillary examination[a]	84 (100 %)	96 (96 %)	0.13

Bold values indicate statistical significance

[a] Normal neuroexamination

Table 2

Autonomic and laboratory (A) and exercise (B) parameters between POTS and OI

	POTS ($n = 4$)	OI ($n = 00$)	p value
A			
Baseline SBP	118 ± 17	119 ± 16	0.46
ΔSBP_H	−4.4 ± 15.2	−2.1 ± 12.2	0.26
Baseline DBP	60 ± 14	62 ± 10	0.12
ΔDBP_H	8.6 ± 9.5	6.6 ± 7.1	0.11
Baseline HR	74 ± 12	74 ± 12	0.99
ΔHR_H	40.19 ± 8.6	19.9 ± 7.3	**<0.0001**
% Anhydrosis on TST	1(IQR 0–4.3)	1 (IQR 0–3)	0.16
ΔII$_E$ SBP	−30.1 ± 19.3	−25.0 ± 21.6	0.09
ΔII$_E$ DBP	−4.4 ± 10.4	−1.6 ± 10.6	0.07
ΔII$_L$ SBP	−7.4 ± 22.5	−2.2 ± 22.0	0.11
ΔII$_L$ DBP	7.1 ± 14.2	11.4 ± 13.7	**0.04**
ΔIV SBP	37.6 ± 19.1	38.0 ± 20.6	0.91
ΔIV DBP	16.8 ± 9.7	18.0 ± 9.5	0.40
Valsalva ratio	2.32 ± 0.68	2.07 ± 0.48	**0.0024**
HRDB	24.25 ± 9.21	20.09 ± 8.81	**0.0021**
Hemoglobin	13.6 ± 1.2	13.6 ± 1.1	0.75
24 h Urine volume	1,649.1 ± 836.6	1,667.9 ± 1025.5	0.90
24 h Urine sodium	131.8 ± 6.9	119.6 ± 60.6	0.19
Plasma norepinephrine supine	252.9 ± 127.0	295.6 ± 241.9	0.18
Plasma norepinephrine upright	562.9 ± 349.8	573.1 ± 334.4	0.9
B			
Supine HR	82.5 ± 13.6	85.3 ± 14.8	0.20
Sitting HR	87.6 ± 15.6	85.9 ± 14.1	0.44
Standing HR	95.6 ± 18	91.7 ± 16.4	0.11
Stage 1 HR	109 ± 16	106.2 ± 16.4	0.24
Peak HR	174.2 ± 17.9	166 ± 19.9	**0.004**
ΔHR_stage1	26.5 ± 13.2	20.9 ± 10.6	**0.002**
ΔHR_peak	91.6 ± 21.6	80.7 ± 20.8	**0.0006**
HR_cool down 1 min	151.9 ± 19.8	144.2 ± 20.6	**0.01**
HR Recovery (1 min)	22.3 ± 9.2	21.9 ± 9.8	0.76
Peak HR	171.7 ± 9	164 ± 9.9	**<0.0001**
Resting SBP	108.5 ± 12.4	110.1 ± 14.1	0.42
Resting DBP	75 ± 9.1	73.6 ± 13.8	0.42
ΔSBP_stage1	7.2 ± 10.2	8.2 ± 12.7	0.55
ΔDBP_stage1	−3.1 ± 8.1	−1.6 ± 11.8	0.33
ΔSBP_peak	38.6 ± 20.8	36.5 ± 20.6	0.50
ΔDBP_peak	−10.8 ± 19.6	−6.5 ± 19.8	0.15
Peak RR	34 ± 8.1	33 ± 0.8	0.39

	POTS ($n = 4$)	OI ($n = 00$)	p value
Peak TV	$1,714 \pm 491.6$	$1,756.3 \pm 517.8$	0.57
Peak O_2 saturation	97.4 ± 1.6	97.5 ± 2	0.55
VO_2 max % (predicted)	64.1 ± 15.8	65.2 ± 14.6	0.61
Breathing reserve	58.9 ± 11.5	55.4 ± 10.6	**0.03**

Bold values indicate statistical significance

Table 3

Autonomic characteristics of normal and deconditioned patients

	Normal (13)	Mildly deconditioned (78)	Severely deconditioned (93)	*p* value
Baseline SBP	117.3 ± 12.8	115 ± 16.2	120.8 ± 16.7	0.13
Baseline DBP	56.8 ± 6.2	58.9 ± 11.8	63.3 ± 12.2	**0.02**
Baseline HR	69.2 ± 10.8	73.2 ± 12.1	75.3 ± 12.2	0.18
ΔSBP_H	−5.7 ± 11.5	−4.1 ± 12.8	−2.0 ± 14.6	0.48
ΔDBP_H	8.8 ± 4.9	8.0 ± 7.8	6.9 ± 9.1	0.58
ΔHR_H	30.1 ± 14.4	30.9 ± 11.7	27.5 ± 13.4	0.22
ΔPulse pressure	−14.5 ± 8.4	−12.1 ± 9.4	−8.9 ± 13	0.08
Valsalva ratio	2.1 ± 0.5	2.3 ± 0.7	2.1 ± 0.5	**0.04**
HRDB	17.5 ± 7.5	23.4 ± 9.0	21.4 ± 9.4	0.07
TST %	0.5 (IQR 0–6.25)	0 (IQR 0–2)	1.5 (IQR 0–6)	**0.017**
Valsalva baseline HR	78.5 ± 11.9	79.1 ± 12.2	79.3 ± 12.1	1.0
Valsalva baseline SBP	117 ± 21.9	120.8 ± 16.5	125.3 ± 17.7	0.12
Valsalva baseline DBP	59.6 ± 9.6	64.5 ± 11.7	66.6 ± 11.4	0.09
ΔII_E SBP	−31.8 ± 29.1	−27.6 ± 18.8	−26.4 ± 21.1	0.68
ΔII_E DBP	−2.4 ± 14.2	−2.7 ± 10.3	−3.2 ± 10.4	0.94
ΔII_L SBP	−10.5 ± 24.9	−3.8 ± 21.7	−4.3 ± 22.6	0.61
ΔII_L DBP	8.7 ± 14.4	9.8 ± 13.6	9.2 ± 14.4	0.94
ΔIV SBP	42.8 ± 20.0	41.4 ± 21.0	34.2 ± 18.4	**0.04**
ΔIV DBP	15.8 ± 8.4	17.6 ± 9.4	17.6 ± 10.0	0.81
24 h urine volume	2,416.5 ± 1,045.2	1,661.4 ± 842.2	1,554.7 ± 971.8	**0.012**
24 h urine sodium	130.3 ± 52.4	130.9 ± 64.2	119.5 ± 57.2	0.48
Plasma NE supine	220.2 ± 91.1	261.7 ± 163.9	299.8 ± 238.3	0.31
Plasma NE upright	610.1 ± 202.8	562.3 ± 274.3	567.8 ± 409	0.90
Hemoglobin	14.0 ± 1.1	13.6 ± 1.1	13.5 ± 1.2	0.44

Bold values indicate statistical significance