

Published: October 31, 2022

Citation: Bruce B. K., Weiss K. E., et al., 2022. The Treatment of Postural Orthostatic Tachycardia Syndrome in Adolescents in an Interdisciplinary Treatment Program: Preliminary Outcomes, Medical Research Archives, [online] 10(10). <https://doi.org/10.18103/mra.v10i10.3227>

Copyright: © 2022 European Society of Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI:
<https://doi.org/10.18103/mra.v10i10.3227>

ISSN: 2375-1924

RESEARCH ARTICLE

The Treatment of Postural Orthostatic Tachycardia Syndrome in Adolescents in an Interdisciplinary Treatment Program: Preliminary Outcomes

*Barbara K. Bruce^a, Karen E. Weiss^b, Chelsea M. Ale^c, Madeleine E. Allman^d, Tracy E. Harrison^e, Philip R. Fischer^f

^aDepartment of Psychiatry and Psychology, Mayo Clinic, Jacksonville, Florida, USA

^bDepartment of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington, USA

^cDepartment of Psychiatry and Psychology, Mayo Clinic, La Crosse, Wisconsin, USA

^dDepartment of Psychology, University of Houston, Houston, Texas, USA

^eDepartment of Anesthesia, Division of Pediatric Anesthesia, Mayo Clinic, Rochester, Minnesota, USA

^fDepartment of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, USA

*bruce.barbara@mayo.edu

ABSTRACT

Importance: Estimates suggest that 1% of all teens struggle with Postural Orthostatic Tachycardia Syndrome. It can be a devastating condition for the adolescents who do not respond to the currently available pharmacologic and non-pharmacologic interventions. Preliminary data suggests that intensive interdisciplinary treatment may provide an effective intervention that can return these youth to normal functioning including full-time attendance at school, as well as reduce orthostatic symptoms, and psychological distress.

Objective: To determine the effectiveness and durability of a 3-week interdisciplinary treatment in adolescents with Postural Orthostatic Tachycardia Syndrome in improving orthostatic symptoms, functioning, and psychological distress.

Design: Patients diagnosed with Postural Tachycardia Syndrome admitted to an interdisciplinary treatment program were assessed at admission, discharge and 3-month follow-up to determine presence and severity of orthostatic symptoms, as well as functional status including return to school, and depression.

Setting: An intensive interdisciplinary treatment program in a tertiary hospital outpatient setting.

Participants: Forty-five adolescents ages 12-18 with confirmed diagnoses of Postural Tachycardia Syndrome referred to a tertiary medical center for interdisciplinary treatment.

Intervention: A 3-week intensive outpatient interdisciplinary rehabilitation program with significant parental involvement based on a cognitive-behavioral model.

Main Outcome and Measure(s): Self-reported orthostatic symptoms were assessed with the Compass 31; level of functioning was assessed with the Functional Disability Index, depressive symptoms were assessed with the Center for Epidemiological Studies-Depression for Children, and self-reported school attendance was assessed.

Results: Significant improvements were observed and maintained at the end of treatment and at 3-month follow-up on measures of orthostatic symptoms, physical functioning, and psychological distress. At admission, 32% of patients had completed high school or were attending school full-time. At 3-month follow-up, 90% were either attending school full-time or had completed their schooling.

Keywords: Postural Orthostatic Tachycardia Syndrome, POTS, interdisciplinary treatment, adolescents.

Introduction

Postural Orthostatic Tachycardia Syndrome (POTS) is a clinical disorder diagnosed primarily in women of childbearing age and adolescents. The prevalence of POTS in adolescents is estimated to be 1% of all teens world-wide.¹ However, the lack of comprehensive epidemiological data prevents accurate determination of the true prevalence of POTS.² Further, an increase in POTS cases have been reported following COVID-19 infection likely amplifying previous estimate.³⁻⁵

POTS is a disorder of the autonomic nervous system whose cardinal manifestation is symptomatic orthostatic tachycardia. The symptoms include syncope, tachycardia, palpitations, dizziness, light-headedness, nausea, tremulousness, and fatigue generally upon assuming an upright posture.⁶ Adolescent patients are diagnosed with POTS when typical chronic symptoms (such as fatigue, postural dizziness, nausea, and pain) are associated with postural heart rate increments in excess of 40 beats per minute on head up tilt testing.⁷⁻⁸ POTS is incompletely understood and has been misdiagnosed as panic attacks, anxiety, vaso-vagal syncope, inappropriate sinus tachycardia or chronic fatigue syndrome.⁹

For patients with severe symptoms, the effects can be significant debilitation and distress.¹⁰⁻¹² As a result of orthostatic intolerance, patients can become wheelchair users or bed-bound and are often unable to continue in education or employment. Up to

a quarter of adults with POTS are on disability and unable to work due to their symptoms.¹³ The disability associated with POTS has been considered equivalent to that found in patients with chronic obstructive pulmonary disease or congestive heart failure.¹⁴ For adolescents, the inability to attend school or participate in age-appropriate social and recreational activities is a consequence that is of significant concern.¹¹ Recent research has found that patients with POTS reported more suicidal ideation and suicide attempts than control subjects.¹⁵

Treatment of POTS includes both non-pharmacologic and pharmacologic strategies. Non-pharmacologic strategies include increasing fluid and salt intake as means of expanding the blood volume, engaging in daily exercise training for reconditioning and to increase blood volume and total hemoglobin mass, enhancing sleep hygiene, wearing compression stockings to improve circulation by increasing blood return to the heart from superficial veins in the legs, and using cognitive behavioral therapy to improve symptom management and address anxiety and avoidance that have developed as a result of these symptoms.¹⁶⁻¹⁸ The commonly used pharmacologic agents such as beta blockers and midodrine facilitate blood flow, and fludrocortisone helps build blood volume. Less frequently, other agents such as selective serotonin reuptake inhibitors, pyridostigmine, and ivabradine are used.^{6,16}

When patients do not employ or respond to these interventions, functional

ability and psychological balance can be significantly impaired.^{11,19,20} Patients describe fear associated with unclear diagnoses and prognoses, frustration with not getting clear answers or trying so many treatments without benefit, sadness of quitting sports, pulling away from school, and significant worries about their future including attendance at college or entering the work world.

Researchers have noted the lack of evidence-based treatment for POTS despite the high levels of disability and associated comorbidity observed in these patients.²¹ An interdisciplinary approach to treatment has been suggested and initial efforts to improve functioning and distress in these patients with an interdisciplinary intervention appears promising.^{22,23} An interdisciplinary setting can bring multiple and concurrent treatments for adolescents with POTS together with the goal of returning adolescents to full functioning including return to school. When patients remain debilitated despite first line interventions such as medications and non-pharmacologic strategies, focusing on increasing functioning despite symptoms seems warranted. Similar programs for adolescents with chronic pain also target somatization, fear avoidance, catastrophizing and resulting disability leading to improvement in functional status and psychological distress.^{24,25}

First in a single case study and then in an initial short-term study, we found that adolescents with POTS did benefit from participating in an intensive interdisciplinary

program, with large improvements in functioning and psychological distress.^{20,22} However, our group study was limited in that we did not measure orthostatic symptoms and we did not have follow-up data to assess the maintenance of gains. The current study was designed to examine the efficacy and durability of an intensive interdisciplinary treatment program in reducing the orthostatic symptoms of POTS, as well as the associated functional impairment and psychological distress observed in adolescents with debilitating POTS that had been refractory to initial pharmacologic and non-pharmacologic treatment.

Methods

Participants

Patients aged 12 to 18 years who were diagnosed with POTS and attended the Mayo Clinic Pediatric Pain Rehabilitation Center program were eligible for this study. POTS patients often have chronic pain complaints in addition to their orthostatic symptoms, but pain was not a requirement for entry into the program. The interdisciplinary structure of the program provided an ideal intervention for adolescents with POTS, because of the program's focus on restoring function and improving psychological distress. The adolescent POTS patients and their parents were asked to complete several questionnaires upon admission and discharge from the program. All 45 patients who were recruited and their parents agreed to be in the study. Participants received follow-up questionnaires one week prior to the three-month follow-up date. A reminder letter was

sent if questionnaires were not received within one week. Only data that was sent back within two weeks of the three-month follow-up date were used. The Mayo Clinic Institutional Review Board approved the study.

Procedure

Adolescents completed questionnaires that measured level of self-perceived orthostatic symptoms, disability, depressive symptoms, and school attendance, at admission and discharge via a web-based survey tool. They were also mailed the same survey at three months following discharge. Medical chart reviews and parental input provided validation of the information.

Dependent Variables

Orthostatic Symptoms. The COMPASS-31 is a questionnaire that assesses the severity and distribution of autonomic symptoms.²⁶ It is based on a well-established measure, the Autonomic Symptoms Profile, and its 84-question scoring instrument, The Composite Autonomic Symptom Score (COMPASS).²⁷ The COMPASS-31 is an abbreviated measure that produces a global autonomic severity score as well as domain scores. Reliability and validity have been established.²⁸ We utilized the Orthostatic Symptom subscale for this study, and also reported the composite score, realizing that many non-orthostatic symptoms are potentially representative of general disability rather than to a primary autonomic disorder.²⁹

Disability. The Functional Disability Inventory (FDI) is a validated 15-item scale

developed to assess the impact of illness on a child's ability to function in physical and psychosocial activities of everyday life.³⁰⁻³² Each item is scored from "0=no trouble" to "4=impossible" across areas of functioning. Three ranges of disability have been defined and include scores of 0-12 reflecting no/minimal disability, 13-29 reflecting moderate disability, and scores ≥ 30 reflecting severe disability.

School attendance is thought to reflect an essential indicator of functioning in children and was assessed in this study through adolescent self-report. The type of schooling was identified by patients as "full-time," "part-time," "home-schooled," "home tutored" (e.g., homebound services), "no schooling/no longer attending school," or "completed high school or received graduation equivalency diploma". School attendance was measured for the month prior to enrolling in the program and at 3-month follow-up. It was not assessed immediately post-treatment, as all adolescents had missed the past 3 weeks of school to be enrolled in the program. Each child left the program with a structured return to school plan in place as a routine part of the program.

Depressive symptoms. Symptoms of depression were assessed with the Center for Epidemiological Studies-Depression-Children scale (CES-DC).^{33,34} Acceptable reliability and validity have been demonstrated for this measure.³⁵ The scale is composed of 20 items that result in scores from 0 to 60 with higher scores reflecting

higher frequency and severity of depressive symptoms. Scores above 14 on this measure are suggestive of depression while a score of 21 and above has been used to diagnose major depression.

Medication use. Medications focused on the management of POTS were not altered during the program.

Treatment Program

The Mayo Clinic Pediatric Pain Rehabilitation Center is primarily an interdisciplinary pain treatment program. However, adolescents with POTS have been treated in this setting with the same cognitive-behavioral strategies used for the management of chronic pain since its inception. In a recent study of the first one-thousand patients treated in this program, 20.2% of the patients had a diagnosis of POTS.³⁶ Patients without POTS who have debilitating fatigue, nausea, and vomiting have been treated in this program as well.

The program is an intensive, 3-week, hospital-based outpatient interdisciplinary rehabilitation program designed to assist adolescents in improving their ability to manage and reduce chronic symptoms. Multiple disciplines are represented in the care team and include pain physicians, psychologists, child psychiatrists, nurses, physical therapists, and occupational therapists.³⁷ It is a group-based program in which typically 12-16 patients work together to focus on goals related to functional restoration and self-management skills. An

essential goal of the program for patients with POTS is to learn to self-manage orthostatic symptoms so that fainting, falling or becoming so dizzy that a patient is incapacitated are resolved. These symptoms are the ones that appear to interfere with school attendance, driving, participation in sports or social activities and that cause the patient and family the most distress.

The program consists of 8 hours per day of therapeutic programming for 15 consecutive working days. Orthostatic feelings of lightheadedness, dizziness or feeling faint are not addressed in the program as an emergency. Rather, patients are encouraged to use the strategies they have been taught of relaxed diaphragmatic breathing, increased fluid intake, and tensing leg muscles to address increases in such symptoms, and other stress management skills aimed at reducing autonomic reactivity. The multi-modal treatment program integrates various components including physical therapy and exercise, exposure-based therapy, and education to reduce parent anxiety, stress management strategies including relaxation therapies and biofeedback, as well as recreational therapy and wellness instruction that includes sleep hygiene and healthy diet; all of which are thought to decrease autonomic symptoms and improve functioning of patients. The program requires extensive parent involvement with parents directly involved in treatment up to 20 hours a week. The parent portion of the program focuses upon cognitive-behavioral parenting skills for parents with a chronically

ill child with a goal of assisting the child out of the sick role and reducing the anxiety of the parents in coping with autonomic symptoms in their child. Parents of adolescents with POTS have been shown to demonstrate high levels of catastrophizing, and this aspect of parenting appears related to their children's mood and functioning³⁸.

Data analysis

Numeric variables are presented as either median (range) or mean (SD) while categorical variables are presented as N (%). Changes in orthostatic symptoms (Compass-31), functioning (Functional Disability Index), and affective distress (CES-DC) from admission to program discharge (3 weeks after admission) and from admission to 3-month follow-up were estimated along with 95% confidence intervals (CI) using mixed effects regression models with random effects for subject and fixed effects for time (admission, discharge, and 3-month follow-up). Paired t-tests were also used to compare changes from admission to discharge and from admission to 3-month follow-up, limited to those subjects with data at both time points being compared. All analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC).

Missing data

Completion rate was 91% (41/45) for post-treatment evaluation and 53% (24/45) for 3-month follow-up evaluations. Comparisons of demographic and clinical characteristics between subjects lost at post-treatment or at 3 month follow up and subjects successfully

contacted revealed no significant differences between groups (Table 1). There were no significant differences in pre-treatment clinical measures/outcomes, therefore we assume the missing data is missing at random (MAR) and unlikely to introduce systematic bias to the outcomes and our conclusions, especially for pre- and post-treatment comparisons, when all available data are included in the analysis.

Table 1. Baseline characteristics of 45 participants

Characteristic	Non-completer (N=21)	Completer (N=24)	All (N=45)
Median age (range), years	16 (12-18)	15 (12-17)	16 (12-18)
Female sex, n (%)	14 (66.7%)	19 (79.2%)	33 (73.3%)
White/Caucasian race, n (%)	19 (90.5%)	24 (100.0%)	43 (95.6%)
Median change in beats per minute pre-tilt to post-tilt (range)	48 (42-72)	51 (40-93)	48 (40-93)
Current schooling, n (%)			
Attend school full-time	6 (28.6%)	5 (21.7%)	11 (25.0%)
Attend school part-time	4 (19.0%)	6 (26.1%)	10 (22.7%)
Home-schooled	5 (23.8%)	6 (26.1%)	11 (25.0%)
Receive tutoring	2 (9.5%)	3 (13.0%)	5 (11.4%)
Receive no schooling/ no longer attend school	2 (9.5%)	2 (8.7%)	4 (9.1%)
Completed high school / GED	2 (9.5%)	1 (4.3%)	3 (6.8%)
Medication(s)			
Blood volume regulators, n (%)	2 (10.0%)	2 (8.3%)	4 (9.1%)
Vasoconstrictors, n (%)	1 (5.0%)	6 (25.0%)	7 (15.9%)
Cardiac control, n (%)	7 (35.0%)	10 (41.7%)	17 (38.6%)
SSRIs/SNRIs, n (%)	12 (60.0%)	11 (45.8%)	23 (52.3%)
Pyridostigmine, n (%)	0 (0.0%)	1 (4.2%)	1 (2.3%)

Non-completers (N=21) included 4 participants who did not have either post-program or 3-month follow-up evaluations and 17 participants who completed the post-program evaluation but did not complete the 3-month follow-up evaluation. Information was not reported for current schooling (N=1 completer) and medications (N=1 non-completer).

Results

Baseline demographic and clinical characteristics as well as school status are provided in Table 1. Participants were on average age 16 (range=12-18). The sample was predominantly Caucasian (95.6%) and female (73.3%). The median degree of postural tachycardia prior to entry into the study was 48 with a range of 40-86 beats. Patients continued POTS-related medications as per the prescribing physicians separate from participation in the rehabilitation program.

School attendance had been significantly impacted by orthostatic symptoms in this study. At baseline, education type was reported for 44 of the 45 patients. Of these 44 patients, 3 (6.8%) had completed HS, 11 (25.0%) were attending school full-time, and 30 (68.2%) were not attending full-time (10 part-time, 11 home-schooled, 5 received tutoring, and 4 reported no schooling).

Descriptive summaries of outcome scores for the sample at admission to the program, at discharge from the program three weeks later, and at 3-month follow-up are contained in Table 2.

Changes in Orthostatic Symptoms. Patients endorsed significant orthostatic symptoms on the Compass-31 at admission to the interdisciplinary program with average scores of 24.18 (Table 2). Significant improvements were observed at the end of the 3-week program (mean change from admission: -6.2;

95% CI: -9.1, -3.2) and were maintained at 3-month follow-up (mean change from admission: -7.9; 95% CI: -11.4, -4.3).

Changes in Functioning. Table 2 contains the baseline, post-treatment and 3-month follow-up data on the Functional Disability Index. Significant levels of functional impairment were observed at admission to the program with average scores of 27.69 (Table 2) that significantly improved at the end of the program (mean change from admission: -17.9; 95% CI: -20.5, -15.3). These improvements were maintained at 3-month follow-up (mean change from admission: -20.5; 95% CI: -23.7, -17.3). A score of 0-12, indicating no-to-minimal disability, was observed in 4.4% (2/45) of participants at admission, 68.3% (28/41) at the end of the program, and 82.6% (19/23) at follow-up.

Table 2. Outcome measures at program admission, discharge, and 3-month follow-up.

Outcome	Admission Mean (SD), n	Discharge Mean (SD), n	Effect Size ^a	P- Value ^a	Follow-		
					Up Mean (SD), n	Effect Size ^b	P- value ^b
Orthostatic Intolerance Subscale	24.18 (10.58), n=45	17.56 (9.29), n=41	0.600 3	<0.00 1	15.67 (7.91), n=24	0.222 8	0.30
COMPASS 31 Total Score	41.01 (15.49), n=45	32.09 (14.64), n=40	0.744 0	<0.00 1	29.91 (12.98), n=19	0.517 0	0.037
FDI Total Score	27.69 (9.59), n=45	9.44 (6.80), n=41	2.021 0	<0.00 1	6.57 (7.57), n=23	2.040 7	<0.00 1
CES-D Total Score	25.76 (11.52), n=45	14.46 (9.84), n=41	1.083 7	<0.00 1	12.63 (9.49), n=24	1.036 2	<0.00 1

Abbreviations:

SD - Standard Deviation; FDI - Functional Disability Index; CES-DC - Center for Epidemiologic Assessment of Depression for Children.

Effect size was calculated as the absolute value of the mean difference divided by the standard deviation of the difference. Paired T-Tests were used to compare changes from admission to discharge and admission to 3-month follow-up.

^aAdmission vs. Discharge.

Changes in School Attendance. Upon admission, educational status was reported for 44 of the 45 patients in the study. Of these patients, 3 (6.8%) had graduated from high school and 11 (25%) were attending school full-time. Thirty (68.2%) patients were not attending school full-time and included 10 students attending part-time, 11 were home-schooled, 5 were receiving tutoring in lieu of school, and 4 were not engaged in any type of school.

At 3-month follow-up, educational status was only reported for 24 of the 45 patients in the study. Among the 24 patients with follow-up data, 1 (4.2%) had then completed high school, 22 (91.7%) were attending school full-time, and only 1 (4.2%) was not attending school full-time and reported no schooling.

Changes in Affective Distress. Patients scored on average 25.76 (Table 2) on the Center for Epidemiologic Assessment of Depression for Children on admission which suggests high level of depressive symptoms. At discharge from the program 3 weeks later, scores fell showing significant improvement (mean change from admission: -11.2; 95% CI: -14.4, -8.0). This improvement was maintained at 3-month follow-up (mean change from admission: -12.6; 95% CI: -16.6, -8.6).

Discussion

POTS is a chronic disorder of the autonomic nervous system that is complex and challenging to treat. It is characterized by orthostatic tachycardia without hypotension

and orthostatic intolerance. The orthostatic symptoms experienced by adolescents with POTS often significantly interfere with functioning including attendance at school, plans for college, and ability to participate in age-appropriate social and recreational activities. Parents may view their children as “in danger” due to these symptoms and may curtail their driving or traveling.

Treatment options are few and cases appear to be increasing as post-viral POTS cases are being identified in recent years. Few interdisciplinary programs are available for the treatment of POTS despite data to support the effectiveness of intensive interdisciplinary care.

The current study provides the first documented evidence of a significant and sustained decrement in orthostatic intolerance in adolescents with POTS following interdisciplinary treatment. The program specifically targets orthostatic symptoms of dizziness and strategies are provided to manage these symptoms. Symptomatic improvements were reported following treatment, and these improvements were maintained for at least three months

This study also provides the first 3-month follow-up data on measures of functioning, and psychological distress in adolescents with POTS following interdisciplinary treatment. The present study confirms previous findings of improved functioning and psychological distress

following intensive treatment and now shows the maintenance of these gains at three months.²²

The interdisciplinary program targeted return to school as a critical outcome variable. If an adolescent with POTS can return to school full-time, it can be viewed as an important marker for health. The current study showed that the majority of patients were able to successfully return to school following treatment.

Limitations and Further Considerations

These findings may not be generalizable to the larger population of adolescents with POTS. The interdisciplinary program had stringent requirements for participation including that the patient had to be significantly debilitated (typically missing at least 30 days of school during the previous academic year) and one parent had to be present and participate in the program for the entire three weeks. The findings of this study can not necessarily be generalized to less severely debilitated adolescents or to adolescents with less-involved parents. Further follow-up study is needed to determine the longer-term effects of this intensive intervention. The current data of 3-month follow-up is positive and promising. Ongoing research has been designed to examine 6-month and one-year follow-up to

assess the maintenance of gains in orthostatic symptoms as well as in functional and psychological status.

Future research aimed at determining the relative value of various treatment components of our intensive program is needed in order to appropriately focus and structure future programs. Does the program structure enhance compliance with standard non-pharmacologic approaches to the treatment of POTS? Is it the supervised physical therapy that is conducted in the interdisciplinary program in a small group setting that leads to a decrease in autonomic symptoms and improved functioning? Is exercise the key, but patients are unable to perform this level of conditioning alone or outside of a structured program due to anxiety or lack of support? Are the behavioral exposure-based therapies the key to decreasing patient fear avoidance and is the active ingredient in this structured intervention? Or is it the decrease in anxiety that parents experience in the program through the structured parenting sessions that is the key to successful rehabilitation of these teens? Future research that targets the components of the interdisciplinary program will be able to determine the relative contributions of each to the program's overall success.

Conclusions

This study provides the first follow-up data regarding orthostatic symptoms following interdisciplinary treatment for adolescents with Postural Orthostatic Tachycardia Syndrome (POTS) and is the first study to assess the durability of treatment gains for this population. For patients with

debilitating symptoms, an intensive treatment approach is effective in returning patients to school and improving their level of functioning, autonomic symptoms, and coping. An intensive rehabilitation program may be an effective structure for the treatment of severely debilitated patients with Postural Orthostatic Tachycardia Syndrome (POTS).

Corresponding author:

Barbara K. Bruce, PhD, Department of
Psychiatry and Psychology, Mayo Clinic,
4500 San Pablo Road,
Jacksonville, Florida 32224.
Phone: 904 953-3061. Fax: 904 953-0461.
Email: bruce.barbara@mayo.edu

Acknowledgements

Dr. Barbara K. Bruce had full access to all data
in the study and takes responsibility for the
integrity of the data and the accuracy of the
data analysis.

Funding:

No sources of financial or material support or
assistance were received in support of this
research project.

Conflict of Interests:

There are no authors' potential conflicts of
interest including relevant financial interests,
activities, relationships and affiliations

References

1. Bhatia R, Kizilbash SJ, Ahrens SP, et al. Outcomes of Adolescent-Onset Postural Orthostatic Tachycardia Syndrome. *J Pediatr*. Jun 2016;173:149-53. doi: 10.1016/j.jpeds.2016.02.035
2. Raj SR, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): Priorities for POTS care and research from a 2019 National Institutes of Health Expert Consensus Meeting—Part 2. *Autonomic Neuroscience*. 2021;235:102836.
3. Goldstein DS. The possible association between COVID-19 and postural tachycardia syndrome. *Heart rhythm*. 2021;18(4):508-509.
4. Kanjwal K, Jamal S, Kichloo A, Grubb BP. New-onset postural orthostatic tachycardia syndrome following coronavirus disease 2019 infection. *The Journal of innovations in cardiac rhythm management*. 2020; 11(11): 4302.
5. Miglis MG, Prieto T, Shaik R, Muppidi S, Sinn D-I, Jaradeh S. A case report of postural tachycardia syndrome after COVID-19. *Clinical Autonomic Research*. 2020; 30(5): 449-451.
6. Johnson JN, Mack KJ, Kuntz NL, Brands CK, Porter CJ, Fischer PR. Postural orthostatic tachycardia syndrome: a clinical review. *Pediatric neurology*. Feb 2010; 42(2): 77-85. doi: 10.1016/j.pediatrneurol.2009.07.002
7. Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society*. Apr 2011; 21(2): 69-72. doi: 10.1007/s10286-011-0119-5
8. Singer W, Sletten DM, Opfer-Gehrking TL, Brands CK, Fischer PR, Low PA. Postural tachycardia in children and adolescents: what is abnormal? *J Pediatr*. Feb 2012; 160(2):222-6. doi: 10.1016/j.jpeds.2011.08.054
9. Raj SR. The Postural Tachycardia Syndrome (POTS): pathophysiology, diagnosis & management. *Indian pacing and electrophysiology journal*. Apr 01 2006; 6(2): 84-99.
10. Benrud-Larson LM, Dewar MS, Sandroni P, Rummans TA, Haythornthwaite JA, Low PA. Quality of life in patients with postural tachycardia syndrome. *Mayo Clin Proc*. Jun 2002; 77(6): 531-7. doi: 10.4065/77.6.531
11. McTate EA, Weiss KE. Psychosocial Dimensions and Functioning in Youth With Postural Orthostatic Tachycardia Syndrome. *Clin Pediatr (Phila)*. Sep 2016; 55(10): 979-82. doi: 10.1177/0009922815616890
12. Kritzberger CJ, Antiel RM, Wallace DP, et al. Functional disability in adolescents with orthostatic intolerance and chronic pain. *J Child Neurol*. May 2011; 26(5): 593-8. doi: 10.1177/0883073810390366
13. Benrud-Larson LM, Sandroni P, Haythornthwaite JA, Rummans TA, Low PA.

Correlates of functional disability in patients with postural tachycardia syndrome: preliminary cross-sectional findings. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association*. Nov 2003; 22(6): 643-8. doi: 10.1037/0278-6133.22.6.643

14. Grubb BP. Postural tachycardia syndrome. *Circulation*. May 27 2008; 117(21): 2814-7. doi: 10.1161/circulationaha.107.761643

15. Pederson CL, Brook JB. Health-related quality of life and suicide risk in postural tachycardia syndrome. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society*. Apr 2017; 27(2): 75-81. doi: 10.1007/s10286-017-0399-5

16. Kizilbash SJ, Ahrens SP, Bruce BK, et al. Adolescent fatigue, POTS, and recovery: a guide for clinicians. *Curr Probl Pediatr Adolesc Health Care*. May-Jun 2014; 44(5): 108-33. doi: 10.1016/j.cppeds.2013.12.014

17. Winker R, Barth A, Bidmon D, et al. Endurance exercise training in orthostatic intolerance: a randomized, controlled trial. *Hypertension*. Mar 2005; 45(3): 391-8. doi: 10.1161/01.HYP.0000156540.25707.af

18. Joyner MJ. Exercise training in Postural Orthostatic Tachycardia syndrome: blocking the urge to block β -receptors? *Hypertension*. 2011; 58(2): 136-137.

19. Moon J, Kim DY, Byun JI, et al. Orthostatic intolerance symptoms are associated with depression and diminished quality of life in

patients with postural tachycardia syndrome. *Health Qual Life Outcomes*. Oct 12 2016; 14(1): 144. doi: 10.1186/s12955-016-0548-x

20. Bruce BK, Weiss KE, Harrison TE, et al. Interdisciplinary Treatment of Maladaptive Behaviors Associated with Postural Orthostatic Tachycardia Syndrome (POTS): A Case Report. *J Clin Psychol Med Settings*. Jun 2016; 23(2): 147-59. doi: 10.1007/s10880-015-9438-3

21. McDonald C, Koshi S, Busner L, Kavi L, Newton JL. Postural tachycardia syndrome is associated with significant symptoms and functional impairment predominantly affecting young women: a UK perspective. *BMJ open*. Jun 16 2014; 4(6): e004127. doi: 10.1136/bmjopen-2013-004127

22. Bruce BK, Harrison TE, Bee SM, et al. Improvement in Functioning and Psychological Distress in Adolescents With Postural Orthostatic Tachycardia Syndrome Following Interdisciplinary Treatment. *Clin Pediatr (Phila)*. Mar 15 2016; doi: 10.1177/0009922816638663

23. Junghans-Rutelonis AN, Craner JR, Ale CM, Harbeck-Weber C, Fischer PR, Weiss KE. Youth with chronic pain and postural orthostatic tachycardia syndrome (POTS): treatment mediators of improvement in functional disability. *Journal of clinical psychology in medical settings*. 2018; 25(4): 471-484.

24. Bruce BK, Ale CM, Harrison TE, et al. Getting Back to Living: Further Evidence for

the Efficacy of an Interdisciplinary Pediatric Pain Treatment Program. *The Clinical journal of pain*. Aug 31 2016;

doi: 10.1097/AJP.0000000000000433

25. Hechler T, Kanstrup M, Holley AL, et al. Systematic Review on Intensive Interdisciplinary Pain Treatment of Children With Chronic Pain. *Pediatrics*. Jul 2015; 136(1): 115-27. doi: 10.1542/peds.2014-3319

26. Sletten DM, Suarez GA, Low PA, Mandrekar J, Singer W. COMPASS 31: a refined and abbreviated Composite Autonomic Symptom Score. *Mayo Clin Proc*. Dec 2012;87(12): 1196-201. doi:10.1016/j.mayocp.2012.10.013

27. Suarez GA, Opfer-Gehrking TL, Offord KP, Atkinson EJ, O'Brien PC, Low PA. The Autonomic Symptom Profile: a new instrument to assess autonomic symptoms. *Neurology*. Feb 1999;52(3):523-8.

28. Treister R, O'Neil K, Downs HM, Oaklander AL. Validation of the composite autonomic symptom scale 31 (COMPASS-31) in patients with and without small fiber polyneuropathy. *European journal of neurology*. Jul 2015; 22(7): 1124-30. doi: 10.1111/ene.12717

29. Robinson-Papp J, Sharma SK, George MC, Simpson DM. Assessment of autonomic symptoms in a medically complex, urban patient population. *Clinical autonomic research: official journal of the Clinical Autonomic Research Society*. Feb 2017; 27(1):25-29. doi: 10.1007/s10286-016-0384-4

30. Claar RL, Walker LS. Functional assessment of pediatric pain patients: psychometric properties of the functional disability inventory. *Pain*. Mar 2006; 121(1-2): 77-84. doi: 10.1016/j.pain.2005.12.002

31. Kashikar-Zuck S, Flowers SR, Claar RL, et al. Clinical utility and validity of the Functional Disability Inventory among a multicenter sample of youth with chronic pain. *Pain*. Jul 2011; 152(7): 1600-7. doi: 10.1016/j.pain.2011.02.050

32. Walker LS, Greene JW. The functional disability inventory: measuring a neglected dimension of child health status. *J Pediatr Psychol*. Feb 1991;16(1):39-58.

33. Weissman MM, Orvaschel H, Padian N. Children's symptom and social functioning self-report scales. Comparison of mothers' and children's reports. *The Journal of nervous and mental disease*. Dec 1980; 168(12): 736-40.

34. Roberts RE, Andrews JA, Lewinsohn PM, Hops H. Assessment of depression in adolescents using the Center for Epidemiologic Studies Depression Scale. Peer Reviewed. *Psychological Assessment: A Journal of Consulting and Clinical Psychology*. 1990; 2(2): pp. doi: 10.1037/1040-3590.2.2.122

35. Faulstich ME, Carey MP, Ruggiero L, Enyart P, Gresham F. Assessment of depression in childhood and adolescence: an evaluation of the Center for Epidemiological Studies Depression Scale for Children (CES-

DC). *The American journal of psychiatry*. Aug 1986; 143(8): 1024-7.

doi: 10.1176/ajp.143.8.1024

36. Bruce B, Weiss K, Ale CM, Harrison T, Fischer PR. Development of an Interdisciplinary Pediatric Pain Rehabilitation Program: The First 1,0000 Consecutive Patients. *Mayo Clin Proc*. 2017 In Press;

37. Townsend CO, Bruce BK, Hooten WM, Rome JD. The role of mental health professionals in multidisciplinary pain rehabilitation programs. *J Clin Psychol*. Nov 2006;62(11):1433-43. doi: 10.1002/jclp.20322

38. Kluck BN, Junghans-Rutelonis AN, Jones AE, Fischer PR, Weiss KE. Adolescent Chronic Fatigue and Orthostatic Intolerance: Relationships Between Parental Attributes and Child Functioning. *Clin Pediatr (Phila)*. Jul 15 2016; doi: 10.1177/0009922816644730