

Efficacy of Therapies for Postural Tachycardia Syndrome: A Systematic Review and Meta-analysis

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Abstract

Objective: To identify the evidence base and evaluate the efficacy of each treatment for postural tachycardia syndrome (POTS) in light of a recent consensus statement highlighting the lack of treatment options with clear benefit to risk ratios for this debilitating condition.

Methods: The CENTRAL (Cochrane Central Register of Controlled Trials), PubMed, and Embase databases from inception to May 2017 were searched using the terms *postural* AND *tachycardia* AND *syndrome*. A total of 135 full-text publications were screened after excluding duplicates (n=681), conference abstracts (n=467), and records that did not relate to POTS therapy (n=876). We included 28 studies with at least 4 patients with POTS in which symptomatic response was reported after more than 4 weeks of therapy. This review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Two investigators independently performed the data extraction and evaluated the quality of evidence.

Results: This study comprised 25 case series and 3 small randomized controlled trials that evaluated 755 and 103 patients with POTS, respectively. Interventions directed at increasing intravascular volume, increasing peripheral or splanchnic vascular tone, controlling heart rate, and increasing exercise tolerance demonstrate moderate efficacy (range, 51%-72%). Few data exist on their comparative effectiveness. Significant heterogeneities were seen in terms of patient age, symptom severity, and the measures used to evaluate treatment efficacy.

Conclusion: The current evidence base to guide optimal management of patients with POTS is extremely limited. More high-quality collaborative research with standardized reporting of symptom response and treatment tolerability is urgently needed.

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Postural tachycardia syndrome (POTS) is a chronic debilitating condition that can substantially affect quality of life (QOL), cognition, and psychosocial well-being.¹⁻⁴ Its prevalence has been estimated to be 170 cases per 100,000 individuals.⁵ The hallmark of POTS is a sustained heart rate increment of more than 30 bpm in adults (>40 bpm in children aged 12-19 years) during the first 10 minutes of head-up tilt (or upright posture) in association with symptoms of orthostatic intolerance (eg, presyncope, brain fog) and in the absence of orthostatic hypotension.^{6,7} Usually, POTS develops in childhood or early adult life and is seen predominantly in females.⁶

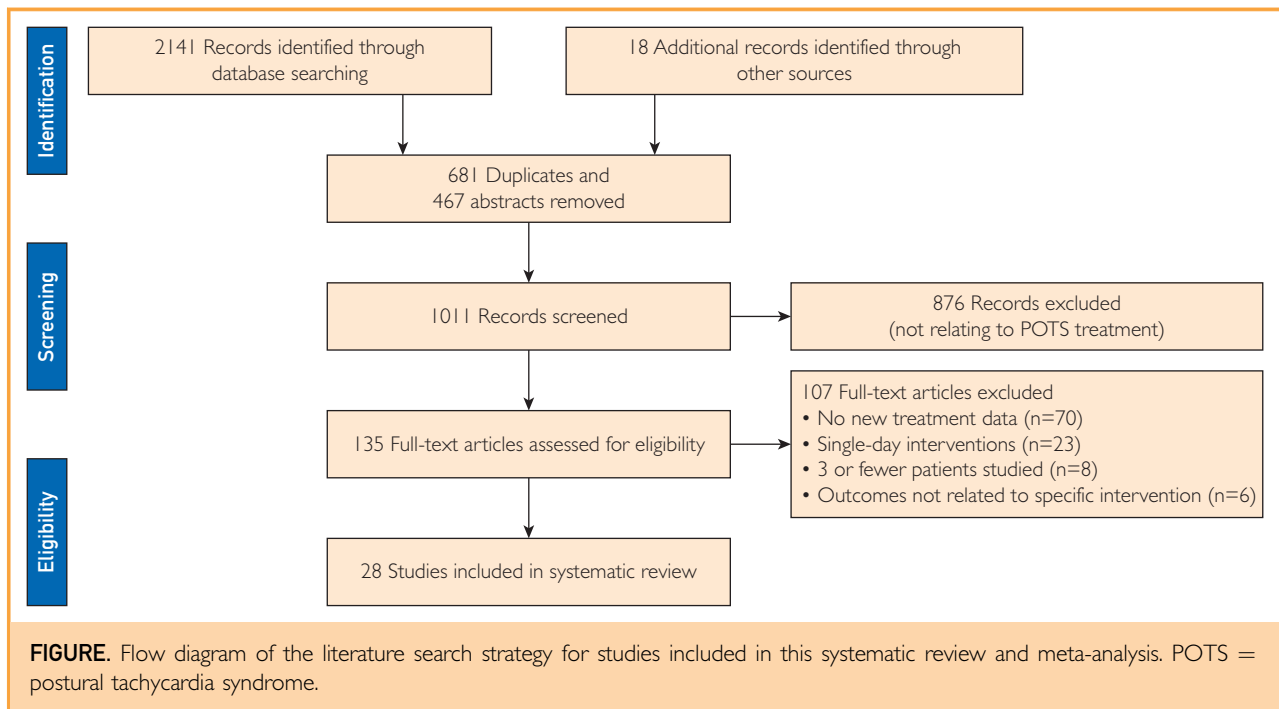
Patients with POTS commonly report symptoms of palpitations, dizziness, and visual disturbances that often improve when recumbent. Symptoms of fatigue and difficulties with cognition are often less responsive to postural maneuvers. Two main subtypes of POTS have been described, with neuropathic POTS involving reduced noradrenergic vasoconstriction in the extremities or the splanchnic vasculature and hyperadrenergic POTS involving excessive noradrenergic vasoconstriction, reduced calf blood flow, and prominent symptoms of sympathetic activation.^{1,8}

Recently, the Heart Rhythm Society released an expert consensus statement on



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the diagnosis and treatment of POTS.⁹ Strikingly, there was a lack of randomized controlled trial (RCT) data on POTS treatment, with most recommendations derived from consensus opinions or weaker studies. Furthermore, there was a distinct lack of management strategies with clear benefit to risk ratios for this condition (class IIa or higher according to the American College of Cardiology Foundation/American Heart Association Taskforce on practice guidelines). We, therefore, undertook a thorough systematic review and meta-analysis of the literature to clarify the current evidence base surrounding the treatment of POTS and evaluate the efficacy of the different options to guide further research directions.

METHODS

A search of the CENTRAL (Cochrane Central Register of Controlled Trials), PubMed, and Embase databases from inception to May 2017 using the terms *postural AND tachycardia AND syndrome* extracted 2141 records (Figure). A further 18 records were identified from the references of review articles. We then excluded duplicates (n=681), conference abstracts (n=467), and records that did not relate to treatment of POTS (n=876). The

full text of the remaining 135 articles was reviewed to identify original data regarding a symptomatic response to any specific therapy over at least 4 weeks.

The Heyland Methodological Quality Score was used to rate the quality of the RCTs. The score does not take into account the power of the study to identify a true difference between groups, but it does take into account patient selection, degree of blinding to intervention, whether groups were equal at baseline, whether co-interventions were adequately described and equal across groups, whether objective definitions of outcome measurements were used, and whether all patients were properly accounted for in the analysis (intention-to-treat). Case series were given a rating of 4 using the quality rating scheme modified from the Oxford Centre for Evidence-Based Medicine. Each of the included studies was assessed independently by 2 investigators (R.W. and D.H.L.). Discordant assessments were resolved by discussion. For each study, the following data elements were extracted: patient number, mean age and percentage of females in the study, study design, intervention (including dose, mode, and frequency of administration), duration of follow-up, symptomatic efficacy,

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