

Postural tachycardia syndrome:

multiple symptoms, but easily missed

The evolution of upright posture is usually considered an advantage in humans. For people with postural tachycardia syndrome (PoTS) it can present a daily challenge. Although orthostatic intolerance is often associated with older people, PoTS tends to affect young women who present with multiple, non-specific symptoms and significant functional impairment.¹

PoTS was characterised in 1993,² but previously existed under various names including irritable heart, soldier's heart, and idiopathic orthostatic intolerance. It is a heterogeneous group of disorders sharing similar characteristics as a consequence of abnormal autonomic nervous system response to assuming upright posture.

DEFINITION AND DIAGNOSIS

When humans stand up, approximately 500 ml of blood descends from the thorax into the abdominal cavity and limbs. A normal autonomic nervous system responds with immediate peripheral vasoconstriction, increase in heart rate of 10–20 beats per minute (bpm), and minimal change in blood pressure.¹

In patients with PoTS this mechanism does not respond appropriately; the exact pathophysiology remains unclear.³ A likely mechanism is inadequate vasoconstriction on standing, resulting in pooling of blood in splanchnic and peripheral vasculature. Heart rate and catecholamine levels increase further to compensate. Symptoms of cerebral hypoperfusion including dizziness and syncope occur, often in the presence of normal blood pressure.

Box 1. Diagnostic criteria for PoTS⁴

- Sustained heart rate increase of 30 beats per minute (bpm) or more within 10 minutes of standing or head up tilt (40 bpm age 12–19 years) in the absence of orthostatic hypotension
- Standing heart rate is often 120 beats per minute or more within 10 minutes of standing or head up tilt
- Orthostatic tachycardia may be accompanied by symptoms of cerebral hypoperfusion and autonomic over-activity that are relieved by decubency
- Criteria not applicable for low resting heart rate.

Ironically, some patients with PoTS have a hypertensive response to standing.¹

Diagnosis is usually made following a tilt table test or 10-minute stand test. The definition is arbitrary, but agreed by consensus (Box 1).⁴ Heart rate increases but, by definition, blood pressure does not necessarily drop. However, there is overlap with neurally mediated hypotension and some patients also subsequently experience a drop in blood pressure.⁵ Plasma noradrenaline levels are often elevated in the upright position.⁶

PoTS tends to affect people aged 15–50 years and is four times more common in females.¹ This may relate to peripheral vasodilator effects of female sex hormones and vasoconstrictive effects of testosterone. The prevalence in the UK is unknown⁴ but probably under-estimated due to overlap with other pathologies such as chronic fatigue, post-viral syndromes, and limited availability of knowledgeable healthcare personnel.⁷

NON-SPECIFIC SYMPTOMS

A plethora of symptoms are thought to result from hypoperfusion and compensatory increased catecholamine levels (Table 1). Many patients experience light-headedness, but 41.4% have transient loss of consciousness.⁶ Symptoms tend to be worse on standing or prolonged sitting and exacerbated by heat, food, and alcohol. Life expectancy is thought to be unaffected, but disability is considerable and equivalent to that found in congestive heart failure and chronic obstructive pulmonary disease.⁸

AETIOLOGY AND MANAGEMENT

Primary PoTS is often of abrupt onset and may follow pregnancy, surgery, immunisation, or trauma. There is some evidence of autoimmune aetiology. Many cases follow viral infections and these are more likely to be self-limiting. A 'developmental' form of primary PoTS affects teenagers (gradual onset around age 14 years) and 80% resolve within a few years. A genetic defect has been identified in some patients with the 'hyperadrenergic' form of PoTS.⁸

PoTS may be secondary to other underlying conditions such as deconditioning after prolonged bed rest or space flight. It is increasingly recognised in joint hypermobility syndrome

(indistinguishable from Ehlers-Danlos Syndrome — hypermobility type)³ and has been associated with other conditions including diabetes, amyloidosis, sarcoidosis, systemic lupus erythematosus, cancers, and toxins (alcohol, heavy metals, and chemotherapy). In some patients, PoTS may be a presenting feature of pure autonomic failure or multiple system atrophy.⁸

Management initially involves physiological methods including graduated exercise programmes, high fluid and salt intake (not in hyperadrenergic PoTS), and support tights.^{3,8} Triggers such as prolonged standing or sitting, alcohol, heat, and large meals should be avoided. Postural counter-maneuvres can abort a syncopal attack. Cognitive behavioural therapy helps patients adjust to long-term illness.

Drug treatment is aimed at increasing blood volume (fludrocortisone, desmopressin, erythropoietin), vasoconstriction (midodrine, methylphenidate, octreotide), reducing tachycardia (beta blockers, ivabradine), improving central cardiovascular control (selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, clonidine), and facilitating synapse transmission (pyridostigmine). The available drugs are all currently unlicensed for this indication.^{5,6,8}

MISDIAGNOSIS AND MISTRUST

PoTS can be misdiagnosed for a number of reasons. Patients may repeatedly present with a multitude of symptoms (Table 1), often without obvious clinical findings: typical 'heart-sink' patients. Although severely incapacitated, they often appear well. Patients may not recognise the significance of symptoms or be reluctant to divulge them for fear of the clinician's response. In consultations, blood pressure and heart rate measurements are usually taken with patients in the seated position, when recordings may be normal.

There is little knowledge of PoTS within the medical community and it is often misdiagnosed as anxiety, panic attacks, vaso-vagal syncope, chronic fatigue syndrome, or inappropriate sinus tachycardia. Consequently, diagnosis of PoTS is commonly delayed by several years.⁶ Patients are often extensively and expensively investigated, to no avail.

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Table 1. Most common symptoms reported by patients with PoTS and percentage affected⁶

| Symptoms | Patients, % |
|---------------------|-------------|
| Light-headedness | 77.6 |
| Palpitations | 75 |
| Pre-syncope | 60.5 |
| Weakness | 50 |
| Fatigue | 48 |
| Syncope | 41.4 |
| Nausea | 38.8 |
| Tremulousness | 7.5 |
| Sleep disturbance | 31.6 |
| Headache | 27.6 |
| Shortness of breath | 27.6 |
| Chest pain | 24.3 |
| Bloating | 23.7 |
| Diarrhoea | 7.8 |

Experienced physicians³ and patient support groups^{11,12} are aware that patients often acquire inappropriate psychiatric diagnoses and consequently, distrust of doctors is common. Interestingly, using an anxiety assessment tool that relies on cognitive symptoms as opposed to somatic ones, PoTS patients have a tendency to lower anxiety levels than controls.¹

As a result of orthostatic intolerance, patients can become wheelchair users or bed-bound and are often unable to continue in education or employment (25%). However, 80–90% will respond to treatment⁸ and 60% will return to previous levels of functioning.³

GPs' ROLE IN POTS

A diagnosis of PoTS should be considered in patients (especially young women) with a combination of unexplained symptoms. The most common are dizziness, palpitations, and tiredness which are usually worse with upright posture. GPs should have a high index of suspicion in joint hypermobility syndrome, chronic fatigue syndrome, and diabetes.

Conditions with similar symptomatology must be excluded and underlying causes of PoTS considered. Investigations may include full blood count, biochemical profile, glucose, thyroid function, calcium, serum cortisol, and catecholamine levels.⁹ All

patients with syncope should have a 12-lead electrocardiography using automated interpretation.¹⁰ A normal 24-hour ambulatory blood pressure monitor recording may not exclude PoTS; monitors that can be triggered to record blood pressure and heart rate during symptoms are helpful.^{2,9}

The stand test is useful.¹ In a safe environment, heart rate and blood pressure are recorded after resting supine, sitting, immediate standing, then at 2, 5, and 10 minutes of standing still, stopping if the patient becomes symptomatic. Look for acrocyanosis (puffy, bluish discoloration of lower legs which occurs in almost 50% of patients and is thought to be due to venous pooling).¹ A sustained increase in heart rate of >30 bpm suggests PoTS and referral should be considered.

Many secondary care physicians, including general cardiologists, are unaware of PoTS and such referrals can be a very frustrating experience for patients. If PoTS is suspected, referral should be made to an electrophysiologist, syncope clinic (often found in neurology, cardiology, or medicine for the elderly departments), or autonomic (neurovascular) unit. There are lists of doctors with an interest on the STARS¹¹ and PoTS UK¹² support group websites.

Much research is necessary to understand the pathophysiology and best management of this recently recognised disorder. Education is needed to increase awareness among healthcare professionals and improve referral pathways. However, successful treatment is already available for many of those who receive the correct diagnosis.

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