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PRACTICE POINTER

Orthostatic tachycardia after covid-19

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What you need to know

- Tachycardia on standing or minimal exertion may occur after covid-19 and may cause substantial functional impairment
- When assessing a patient with tachycardia, consider potential causes including autonomic dysfunction
- Measures to reduce tachycardia can greatly improve function and ability to return to activities and work

Patients with long covid—defined by the National Institute for Health and Care Excellence (NICE) as signs and symptoms that persist for more than four weeks (and especially more than 12 weeks) following acute covid-19[1 2]—may present in primary care with symptoms of palpitations (tachycardia) triggered by standing or minimal exertion.[3] These may be accompanied by dizziness, breathlessness, chest pain, sweating, bloating, fatigue, and other symptoms which may be caused by a dysfunction of the autonomic nervous system (dysautonomia).[4 -13] Patients can find these symptoms debilitating and they can affect function and mood. Limited evidence, variable diagnostic criteria, uncertainty around cause and pathogenesis, and the absence of licensed medications, have all contributed to making this a difficult condition to diagnose and manage. In this practice pointer, we offer an overview of orthostatic tachycardia following covid-19, including a summary of the key steps for diagnosis and management.

Prevalence estimates vary depending on sample and setting, but indicate that about 25% of long covid patients may have dysautonomia[14] and 2-14% will develop orthostatic tachycardia (postural orthostatic tachycardia syndrome) six to eight months after infection.[3 4 15 16] Box 1 provides more information on these conditions. The assessment and management is summarised in the infographic.

Box 1: Dysautonomia and postural orthostatic tachycardia syndromes

The autonomic nervous system is responsible for the unconscious regulation of many physiological processes, including heart rate, blood pressure, respiration, and digestion. The broad category of "dysautonomia" encompasses several conditions, from the intermittent "faint" (neurocardiogenic syncope) through more pervasive dysregulation (postural orthostatic tachycardia syndrome, where the autonomic system still works but is not so well regulated) to rare conditions of full blown autonomic failure, such as multiple system atrophy.[17]

In the context of long covid, the most frequently encountered dysautonomia is orthostatic intolerance syndrome, which includes postural orthostatic tachycardia and related conditions.[3 4] A sustained increase in the heart rate of 30 beats/min (or more than 40 in those aged 12-19) or to more than 120 beats/min for 10 minutes on standing is compatible with a diagnosis of postural orthostatic tachycardia syndrome when associated with symptomatic problems for at least three months.[18] Patients' postural symptoms may vary diurnally (eg, may be worse in the morning because of the circadian rise in cortisol)[19] and in response to triggers such as meals, warm environment, exertion, and alcohol.[4 5 9]

Diagnosing orthostatic tachycardia requires that orthostatic hypotension (a fall in blood pressure of more than 20 mm Hg systolic or 10 mm Hg diastolic within three minutes of standing) and other precipitants of tachycardia (eg, anaemia, dehydration, fever, sepsis, endocrinological conditions such as hyperthyroidism or Addison's disease, respiratory conditions such as pulmonary embolism, and cardiac conditions) have been excluded.[20 -23] Deconditioning owing to prolonged bed rest may contribute to orthostatic tachycardia but is not its primary cause.[21 24] Some patients attending long covid clinics with tachycardia do not meet the above criteria, but they present in a similar manner and respond to similar management strategies.[25]

Dysautonomia in long covid typically affects young, previously healthy individuals (aged 15-45), with a female sex predominance (80%). Association with covid-19 severity and comorbidities is uncertain, although hypertension, obesity, or immunosuppression have been implicated.[5 23 26 -31]

Possible pathophysiological mechanisms for dysautonomia include baroreflex impairment (eg, in the carotid bodies), immune mediated mechanisms, chronic inflammation and hypercoagulability caused by the infection, and direct autonomic nervous system injury by SARS-CoV-2.[5 20 21 24 27 31 32]

Other long covid symptoms that may have a similar pathophysiology (covered in our earlier long covid update[1]) are neurological, gastrointestinal, respiratory, throat (swallowing), and musculoskeletal.[6 -13] In some patients, the diagnosis of dysautonomia is easy to make but in others it remains in doubt. A key component of care for the latter is managing the uncertainty.

How does tachycardia present in patients with long covid?

Box 2 gives some case histories of patients in whom orthostatic tachycardia was suspected.

Box 2: Presentations of tachycardia following covid-19

All cases are fictional, but are based on multiple similar cases.

Case 1

Eight weeks after acute covid-19, a previously well 48 year old woman presented to her GP with new symptoms of fatigue, breathlessness, brain fog, difficulty standing,

and bursts of palpitations after minimal exertion. She described associated intermittent left sided chest pain, so was referred to cardiology. An echocardiogram and brain natriuretic peptide test yielded normal results; therefore she was discharged with no clear explanation for her symptoms. Her GP referred her to a long covid clinic, where a detailed history revealed that her symptoms occurred on standing. Postural tests showed an increase in heart rate of 20-25 beats/min, with no change in blood pressure on standing—suggestive but not diagnostic of postural orthostatic tachycardia syndrome. She was advised that she was probably "on a spectrum of postural orthostatic tachycardia syndromes" and was given suggestions for non-pharmacological measures. These improved her symptoms and wellbeing, and she did not need medications for symptomatic relief.

Case 2

A 31 year old woman with a history of asthma presented with four months of debilitating symptoms following acute covid-19. She had left sided intermittent chest pain, shortness of breath, severe physical and mental fatigue, muscle pains, and palpitations. A previous emergency admission had excluded pulmonary embolic disease, and showed a normal chest x ray image and normal results from blood tests and electrocardiogram (ECG). On detailed history, her shortness of breath and tight chest pains often co-occurred with palpitations and were worse on standing and light exertion. An ambulatory ECG correlated diary instances of breathlessness and palpitations with episodes of sinus tachycardia up to 134 beats/min, despite her being largely confined to the house by fatigue, and she had no other dysrhythmia. On the NASA lean test, the maximum heart rate increase was 25 beats/min, and the test was terminated after six minutes because the patient felt unwell, without hypotension. Although these changes did not meet the formal criteria for orthostatic tachycardia, features of the history suggestive of dysautonomia informed the management strategy. Despite starting non-pharmacological measures and reducing use of salbutamol, the tachycardia persisted. β-blockers were contraindicated, and she was started on ivabradine following discussion with the patient on its side effects. These measures allowed the patient to increase gradually the amount of exertion she could tolerate, and ivabradine was discontinued after a few months.

Case 3

Following a bout of covid-19, a 42 year old man developed intermittent palpitations and a jittery feeling, which he initially attributed to mild anxiety. He attended his GP, who found that his anxiety-provoking palpitations were usually associated with standing; he had no other symptoms of anxiety. Postural tests showed an increase in heart rate of 20 beats/min on standing, with no change in blood pressure. After an explanation of the likely cause, the patient did not wish to have medication. He agreed to try non-pharmacological measures such as pacing and avoiding situations that might exacerbate his "fight-flight" response. His symptoms partially resolved over six months.

In these case histories, the first patient presented unambiguously with palpitations on standing. The second patient had multiple cardiorespiratory symptoms which were extensively investigated, but the eventual diagnosis was made on the basis of the history. Palpitations were present but overshadowed by other symptoms, so the patient did not volunteer them, and the activity that precipitated her symptoms was not heavy exertion but standing up. The third patient presented with anxiety symptoms precipitated by a sudden and dramatic rise in his heart rate on standing; his "electric shock" sensation is commonly reported in patients with orthostatic tachycardia.

Clinical assessment

Carefully assess any patient with possible acute cardiac symptoms for red flag symptoms such as those of cardiac ischaemia.[4 33] When considering dysautonomia as a cause of tachycardia, document whether the patient's palpitations occur on standing or with minimal exertion, and whether they are associated with dizziness, nausea, or chest tightness. A detailed history may point to the diagnosis and save the patient unnecessary investigations, as illustrated by the case histories in box 2).

Clinical examination (cardiovascular, respiratory, and neurological) should be oriented to identify acute conditions that require urgent management, and alternative diagnoses (box 1), such as ischaemic heart disease, pulmonary embolism, anaemia, endocrinological conditions, and drug side effects.[4 5 9 24 34]

Tailor investigations to the history and clinical findings. Blood tests (such as full blood count, renal and kidney function, C reactive protein, vitamin B12, folate, ferritin, thyroid function, glucose, calcium, and morning cortisol), chest x ray imaging, ECG, and 24 hour ambulatory blood pressure and heart rate monitoring may be indicated.[21 23 24 29 35] A normal ECG excludes resting arrhythmia and (if clinical examination is normal) also makes structural heart disease unlikely.[18]

How to test for postural orthostatic tachycardia syndrome in primary care

If the history suggests orthostatic tachycardia, orthostatic tests may be considered to complete the diagnosis.[23] Those listed below can be undertaken safely in primary care. Instructions for completing these tests are given in the supplementary materials.

In the active stand test, blood pressure and heart rate are measured after five minutes of rest supine, then immediately on standing, and at regular intervals for 10 minutes.

In the NASA lean test, after resting supine the patient leans against a wall (shoulder blades touching the wall, heels around 20 cm away) and blood pressure and heart rate are measured every minute for 10 minutes. This posture reduces some of the effect of the skeletal muscle pump.

Symptoms occurring during either test should be recorded and the clinician should be vigilant in case the patient feels unwell or faint.

These clinic based tests capture only a single point in time. However, orthostatic tachycardia may go unnoticed because of daytime variability and absence of triggers. The adapted Autonomic Profile test, completed by the patient at home with their own blood pressure machine, records information on symptoms, postural blood pressure, and heart rate at various points throughout the day.[36] Although its diagnostic accuracy against the NASA or active stand test for orthostatic tachycardia has yet to be established, it may produce valuable information to support the diagnosis and identify triggers, thereby informing management strategies. The decision to carry out this test should be made on a case-by-case basis.

The head-up tilt test is a specialist investigation for dysautonomia performed in secondary or tertiary centres.[37] The test was designed to investigate causes of loss of consciousness and is the agreed way to investigate fainting in laboratory conditions. The patient is placed on a table with a motorised tilt function, and blood pressure and heart rate taken supine and tilted head up at around 60° for up to 45 minutes. If syncope or pre-syncope occurs, the patient is quickly returned to the supine position. This specialist test is not necessary for a straightforward diagnosis of orthostatic tachycardia but is useful for investigating specific symptoms (for example, unexplained syncope).

What non-drug treatments are available?

Research on management of orthostatic tachycardia in long covid is still scarce. The recommendations in this article are supported by available evidence and the experience of clinicians and patients working in LOCOMOTION, a national quality improvement

collaborative.[38] As illustrated in cases 1 and 3 in box 2, patients are often reassured when they receive an explanation of what is causing their symptoms. For those requiring intervention, consider non-pharmacological or conservative measures in the first instance. These include:

- Liberal fluids (2-3 L a day) and (in the absence of contraindications such as high blood pressure) salt (around 10 g a day, for example, add 1-2 teaspoons a day to food)[4]
- Avoid triggers such as alcohol, prolonged standing, heavy meals, and warm places[5]
- Wear waist-high compression hosiery[22]
- Try physical reconditioning if tolerated, starting with isometric exercises that increase venous return, such as crossing legs, squatting, and clenching buttocks. If isometric exercises are tolerated, patients can engage in seated or supine aerobic gradual rehabilitation programmes in combination with resistance exercise such as cycling on a recumbent exercise bike or swimming[4 21 22];
- Encourage patients to keep active but to pace themselves.

If tolerated (but not otherwise), the patient should gradually increase the length and intensity of activity. However, as covered in a previous article in this series,[1] worsening of symptoms following physical or mental activity is a common feature of long covid[31 39 40] and necessitates caution along with careful pacing, starting with low level gentle exercise. Some patients may require pharmacological measures in combination with conservative measures to engage in any physical activity.[27]

What drugs could be tried?

If non-drug measures are not effective and symptoms are markedly affecting the patient's personal and professional life, pharmacological options may be indicated, depending on the patient's medical history and clinical findings. Evidence from clinical trials is limited, therefore no licensed medications are available for orthostatic tachycardia in any country. However, consensus guidelines and published literature list several drugs for symptomatic relief.[18 25] Most are aimed at controlling heart rate and increasing peripheral vasoconstriction and intravascular volume. They include[5 21 -24 29]:

- β-blockers such as propranolol, to alleviate tachycardia, reduce the "on edge" feeling, and help any concurrent migraines
- The If channel blocker ivabradine, which reduces heart rate without affecting blood pressure
- Anticholinesterase inhibitors such as pyridostigmine, which reduce heart rate without vasodilation
- Peripheral vasoconstrictors such as midodrine, which increase venous return to the heart (exclude supine hypertension before prescribing)
- Central adrenergic inhibitors such as clonidine and α-methyldopa, which can help with tachycardia caused by the catecholamine surge on standing
- Volume expanders such as fludrocortisone, which require monitoring of blood pressure and fluid retention.

Because these medications are being used off label, local restrictions on their use may apply and specialist advice or referral should be considered before commencement. Based on clinical experience in the LOCOMOTION team, these medications should be discontinued if they prove ineffective after a trial period of four to six weeks. At this point, discuss alternative pharmacological and non-pharmacological measures, or the need for further tests. Our experience suggests that failure to respond to one medication does not predict failure to respond to others.

When clinically appropriate, discontinue medications that could intensify tachycardia, or reduce the dose. These drugs include serotonin and noradrenaline reuptake inhibitors, such as duloxetine, and tricyclic antidepressants (particularly at high dose). Similarly, avoid medications that cause hypotension such as diuretics, opiates, nifedipine, and nitrates.[9]

To monitor the effectiveness of treatments, repeat the NASA lean test or active stand test, or track the patient's resting heart rate along with relevant symptoms at follow-up consultations.

What can patients do for themselves?

No evidence is available from randomised trials for lifestyle measures in orthostatic intolerance syndromes linked to long covid, but clinicians and patients have identified measures that appear to aid recovery, avoid symptom exacerbation, and improve wellbeing. These include:

- Minimising stress and activities that are physically, mentally, or emotionally demanding[41]
- Optimising sleep by adopting a sleep time routine, avoiding blue light from electronic screens one hour before going to bed, and reducing intake of alcohol and caffeine[42]
- Pacing, where the patient uses self-awareness to manage fluctuations in their condition, identifying "good days" in which more activities may be undertaken, and "bad days" when more rest is needed, thereby avoiding the "crashes" associated with long covid[41 43]
- Improving diet to reduce bloating (eg, small frequent meals) and optimise the gut microbiome: eating a healthy, Mediterranean style diet with up to 30 different plant based ingredients per week, and limiting intake of red meat, sugar, and processed foods[44]
- Using relaxation techniques such as meditation, mindfulness, yogic breathing, and complementary therapies such as acupuncture.[43]

Postural orthostatic tachycardia syndrome and its variants can be disabling and demoralising. Peer support can be invaluable. Box 3 offers some resources aimed primarily at patients, but which may also be helpful to health professionals.

Box 3: Resources for patients

Postural orthostatic tachycardia syndrome support group

- PoTS UK (www.potsuk.org) is the national charity dedicated to advising patients in the investigation and management of orthostatic intolerance syndromes. It is run by patients, many of whom are healthcare professionals, and provides up-to-date advice and resources on the condition and organises meetings and events for patients and healthcare professionals. It has a medical advisory board of internationally recognised clinicians.

General dysautonomia resources

- www.stopfainting.com and www.dysautonomiainternational.org contain a wealth of accessible information to promote patient education and engagement during treatment.

General long covid resources

- Long Covid Support (https://www.longcovid.org/) is a registered charity, formed by people with long covid. The trustee and advisory boards include medical professionals, who are leaders in long covid care and research. It runs a tightly moderated peer support group and can offer support for tachycardia in the context of wider manifestations of long covid. The organisation hosts an active programme of online social and wellbeing activities.

When should patients be referred to a specialist?

Consider referral if the diagnosis is in doubt after an active stand or NASA lean test, to gain advice about use of off-label medication, or if the patient has a severe or atypical symptom pattern (eg, unexplained syncope) that persists despite non-pharmacological and pharmacological measures in the absence of alternative diagnosis.[29] Orthostatic tachycardia syndromes are probably neurologically mediated (via neural pathways controlling heart rate and blood pressure), but the most appropriate referral path is usually to a cardiologist, since symptoms (and potential differential diagnoses) are mostly cardiovascular, and pharmacological management tends to be with cardiac drugs. If the patient has other symptoms of dysautonomia, consider the appropriate specialty.

What is the outlook for the patient?

Long term prognosis of orthostatic tachycardia in long covid is uncertain. Based on clinical experience shared in the LOCOMOTION quality improvement collaborative, it appears to vary depending on the patient's comorbidities and treatment received.[4,5] The course of postural orthostatic tachycardia syndrome caused by non-covid conditions (and especially those where the precipitant is known, such as Epstein-Barr virus) is to improve over time, but recovery can be slow and incomplete. Residual symptoms persisted in 85% of a cohort six to eight months after covid-19, regardless of treatment[5]; however, this and other studies suggest that approximately 50% of patients recover within one to three years, and lifestyle measures can aid recovery.[23,25]

Like other symptoms of long covid, those associated with dysautonomia often remit and relapse, particularly when exacerbated by intercurrent illness, stress, and overexertion, so the patient should expect an uneven recovery course. Many will benefit from a flexible, patient centred tailored plan to return to work.

Education into practice

If a patient reported palpitations six months after an acute episode of covid-19:

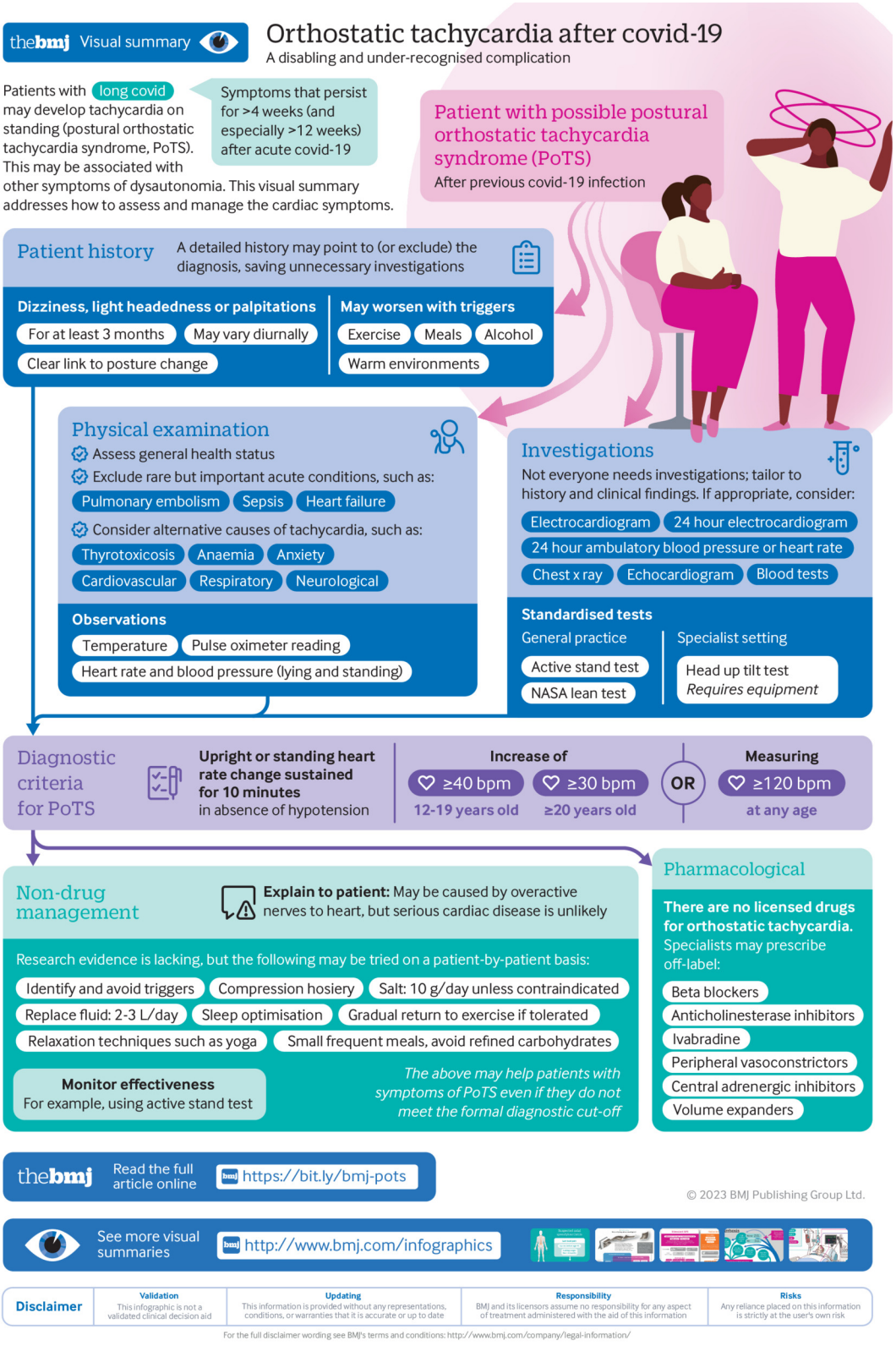
- What questions would you ask them, what would you look for in the clinical examination, and what tests (if any) would you order?
- What would prompt you to refer to a specialist?
- If your findings indicated a diagnosis of postural orthostatic tachycardia syndrome, how would you explain this condition to the patient and what advice would you give?

How patients were involved in the creation of this article

Patients (author NR and members of the advisory group) are part of the LOCOMOTION quality improvement collaborative. NR has lived experience of tachycardia in long covid and is networked with others with lived experience via the patient advisory group for LOCOMOTION, as well as to patient support groups, the Long Covid Support charity, and various other research studies. The paper was read by three additional patients with long covid and modified in response to their feedback, mainly by reducing jargon and ensuring emphasis on pacing.

How this article was created

This article builds on a general introduction to long covid for primary care clinicians.[1] The authors are part of an interdisciplinary team with expertise in clinical management of long covid in primary and secondary care, specialist cardiology for dysautonomia, systematic review, and lived experience of long covid. The idea for the paper emerged from a long covid quality improvement collaborative (part of the NIHR funded LOCOMOTION study[38]), which brought together 30 clinicians from 10 long covid services in the UK to share case histories and analyse service provision. Clinical experiences and literature known to participants were shared and discussed at the collaborative. A targeted literature search was conducted with specialist librarian support, with a primary focus on dysautonomia following covid-19, but also including selected seminal articles on dysautonomia. In all, 153 articles were retrieved from Embase and Scopus and 50 articles were considered relevant. Specialists in the condition were contacted and asked to suggest additional references. We also took account of patient facing literature and websites. Published sources, clinical experiences, and patient input were combined by narrative synthesis.



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