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Arterial flow waveforms, vascular tone, and chronic fatigue: A case report

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Abstract

We present the case of a patient with chronic fatigue secondary to Postural Orthostatic Tachycardia Syndrome (POTS) who had distinctive abnormalities in his arterial waveform morphology as assessed by pulse oximetry. Moreover, the patient's arterial waveform changed markedly from being supine to upright, suggesting that arterial flow patterns may be abnormal in our patient. Analysis of the waveform suggested a positional hypovolemia as the cause of his orthostatic intolerance. We review general aspects of arterial flow waveform analysis pertinent to health care providers and discuss the pathophysiology of POTS.

Keywords

Postural Orthostatic Tachycardia Syndrome; POTS; Pulse oximetry; Dicrotic notch; Dysautonomia; Pulse wave travel time

1. Introduction

Postural Orthostatic Tachycardia Syndrome (POTS) is defined as chronic orthostatic intolerance characterized by a sustained heart rate (HR) increment of 30 beats per minute (bpm) within 10 min of standing or head-up tilt in the absence of orthostatic hypotension (Freeman et al., 2011; Raj, 2013). The etiology of POTS is unknown, but it is clearly a heterogeneous disorder (Benarroch, 2012). In some cases, increased sympathetic tone

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associated with reduced peripheral vascular response may suggest a selective peripheral neuropathy (Bush et al., 2000). In other cases, POTS is associated with Chronic Fatigue Syndrome (CFS) (Rowe et al., 1995), and up to 30% of patients may have syncope (Pilcher and Saarel, 2014; Raj, 2013). Elastic tissue disorders such as Ehlers Danlos syndrome may also predispose to the development of POTS (Wallman et al., 2014).

Despite excellent work in this area (see, for example, Stewart and Montgomery, 2004), the hemodynamics of POTS are still incompletely characterized, and the possibility that patients with POTS may have different hemodynamic waveform signatures from normal individuals requires further exploration. The possibility also exists that these hemodynamic waveform signatures may vary amongst POTS patients with different pathophysiologic mechanisms.

In accordance with institutional IRB guidelines we present the case of an otherwise healthy young man with POTS who featured striking abnormalities of his pulse oximeter waveform, discuss the pathophysiology of POTS and review basic aspects of arterial waveform analysis. The patient reviewed this report and gave written permission for this publication.

2. Case presentation

A 32 year old male with a known history of CFS and POTS presented for magnetic resonance imaging of his brain. The patient's symptoms began at the age of 16 after a prodrome consistent with a viral illness. Prior to this episode, he had been perfectly healthy. Symptoms included severe daytime sleepiness, fatigue, difficulty concentrating, disrupted nighttime sleep, and worsening of symptoms after exercise. Physical exam findings and autonomic testing showed orthostatic tachycardia without hypotension on head up tilt, and acrocyanosis of dependent extremities. The patient had normal muscle strength and tone and relatively normal peak exercise tolerance. Medications included midodrine, fludrocortisone, and regular caffeine intake. The patient also reported being intolerant of beta blockade, which worsened his symptoms.

Routine monitors showed normal vital signs in the supine position with HR 74 bpm and blood pressure (BP) 130/72 mm Hg. At no time did the patient have a decrease in oxygen saturation from baseline (94–96% throughout the procedure), arrhythmias, or BP changes that were detectable with noninvasive BP monitoring.

While standing up, the patient immediately developed tachycardia at 100 bpm with a change in his pulse oximeter waveform to a distinct biphasic morphology (Fig 1, upper panel, upright) while BP remained unchanged. Both the tachycardia and the waveform abnormalities rapidly resolved upon resuming the supine position (middle panel, supine), and the patient underwent an uneventful MRI examination. When the patient stood up again, the biphasic morphology reappeared. However, when the patient squatted from a standing position, his heart rate slowed to 86 bpm and the waveform changed to resemble the supine tracing (lower panel, squatting). These specific waveform morphologies, and how they relate to this particular patient's POTS, are the focus of this case report. Quantitative waveform analysis was done by measuring peak-to-peak times between maximum ejection and reflection wave values and the times between the minimum preceding the ejection wave and

its maximum. All values were averaged over a 10-second interval and compared by ANOVA followed by Student–Newman–Keul's test for multiple comparisons (two-tailed, $\alpha = 0.05$); data are presented as mean $\pm$ standard error of the mean.

3. Discussion

In this case report we describe distinct abnormalities in pulse oximetry waveform morphology in a patient with POTS. Since these are absent in normal individuals we conclude that they are a result of our patient's pathophysiology.

While changes in regional blood flow have been described in POTS (Stewart et al., 2004), changes in arterial flow waveform morphology in CFS or POTS have not yet been described. We hypothesize that these waveform changes may allow further elucidation of the mechanisms underlying this patient's disorder. Furthermore, should these waveform changes be observable in other patients with POTS, the possibility exists that they may offer a noninvasive method to help with diagnosis and titrating treatment of the disorder in general.

Pulse oximeters, developed for clinical use in Japan in 1972, were adopted as a standard of care monitor in the US in 1987. Today, they are used by health care providers in many different practice settings, and are considered basic monitors in the operating room and the intensive care unit. Pulse oximeters work by transilluminating tissue with light of both visible (660 nm) and infrared (910 nm) wavelengths. Located opposite the light source, photodetectors measure the amount of light passing through the tissue in-between. Pulsatile blood flow causes rhythmic changes in local tissue blood volume which create an oscillating pattern of light absorption. From these data, the pulse oximeter is also able to determine the relative portion of hemoglobin that is saturated with oxygen.

While their primary purpose is to monitor the oxygen saturation of arterial hemoglobin, many oximeters graphically display an arterial waveform. In our case, this waveform was of specific interest because it changed markedly as the patient went from supine to standing, suggesting a significant difference between supine and upright blood flow patterns.

The classic arterial waveform in the finger includes a dicrotic notch present in the descending portion of the ejection wave (arrow in Fig 1, supine). One commonly taught etiology of the dicrotic notch is that it is a manifestation of aortic valve closure. However, this explanation is incomplete. While the closure of the aortic valve generates a transient reversal of blood flow in the aorta which can contribute to the shape of the notch, the traditional arterial flow waveform consists of two superimposed waves, a primary ejection pulse wave and its reflection from the lower extremities. As the primary wave meets the impedance of the lower extremity vasculature, a portion of the pulse wave energy is redirected back towards the heart and upper extremities as a second pulse that arrives in the upper extremity after the primary wave. The overlap of both waves generates the classic biphasic shape that is influenced greatly by the timing of the second wave (O'Rourke and Avolio, 1980).

Arterial stiffness and/or a high vascular tone increase the speed of the reflected wave. The faster the travel time, the earlier the wave reflected from the lower extremities arrives in the

finger, and the closer together the two waves appear (O'Rourke et al., 1980). Conversely, with low tone more time elapses between the two readings, increasing the spacing between the two with a deepening notch in the downslope of the wave. Indeed, in extremely low SVR states the reflected wave may appear as a completely separate wave or even slur with the upslope of the following pulse wave, generating a “backwards” dicrotic notch. This pulse transit time has been studied as a marker of cardiovascular disease and risk. While most of the literature regarding transit time addresses the travel time between the carotid and femoral arteries, the concept has been validated in analyzing the dicrotic notch as a measurement of pulse wave travel time (Hermeling et al., 2009).

Another factor influencing the shape of the arterial wave is volume status, and changes in the wave characteristics have been documented in simulations using lower body negative pressure as a mechanism of temporarily depleting central blood volume (Convertino, 2012). The changes in the waveform shape with hypovolemia can be similar to those seen with lower vascular tone in that there are two distinct peaks in the pulse wave, independent of vascular tone. Decreases in stroke volume, as well as increased inotropy and chronotropy can all shorten the duration of the ejection wave, and in hypovolemic states the two waves are therefore less likely to overlap as the wave and its reflection become more narrow, which is true at any wave travel time. This leads to less overlap and more distinct visualization of the two in hypovolemic states.

Our patient was young and had no known cardiovascular disease. *Qualitatively*, his pulse wave travel time (Tsuchikura et al., 2010) was slow enough and the ejection wave duration short enough to result in minimal to no overlap between the primary and reflected waves as he stood upright (Fig. 1) suggesting inappropriately low vascular tone, hypovolemia, or both. Although we are limited in quality and quantity of the data gathered as our patient encounter was in a clinical rather than an experimental setting, further retrospective *quantitative* waveform analysis revealed that the time between the two wave peaks significantly decreased from 275 ± 3 ms to 249 ± 4 ms ($p < 0.05$) and that the upslope time of the ejection pulse wave decreased from 164 ± 2 ms to 151 ± 5 ms ($p < 0.05$) when the patient went from supine to upright, respectively. This suggests that the waves becoming more distinct was primarily due to decreased stroke volume secondary to a gravitationally mediated downward translocation of blood volume rather than due to an increase in the actual wave reflection time. The latter had in fact slightly decreased suggesting an increase in vascular tone, even if this increase was inappropriately insufficient to maintain stroke volume and prevent orthostatic tachycardia.

With squatting of the patient, we seemingly observed a *qualitative* trend back towards a normal waveform shape. However, when measured, the waveform reflection time remained decreased (242 ± 4 ms) compared to supine ($p < 0.05$) which did not differ from standing. In contrast, the upslope time increased to 172 ± 3 ms during squatting, a significant increase compared to standing ($p < 0.05$) but not to supine. Leg compression, as occurs during a squat, alters hemodynamics in two potential ways that interestingly coincide with the hypothesis regarding our patient's hemodynamic perturbation. First, if the point of wave reflection is distal to the femoral artery, forceful compression of the thighs may shift the reflection point proximally to the site of compression, generating an earlier arrival of the

pulse wave. Second, squatting may result in a bolus of venous blood volume to the central circulation via mechanical compression of the lower extremities. As the timing between the peaks of the ejection and reflected waves was similar between standing and squatting, but the width of the wave increased significantly, we hypothesize that increased venous return was the primary mechanism responsible for the normalization of the waveform during squatting. We note, however, that the two mechanisms are potentially highly interrelated, adding to the difficulty concluding which mechanism might dominate in our patient, given the limited data of our brief clinical encounter.

Experimentally, real time cardiovascular monitoring during the squatting maneuver via a Swan–Ganz catheter and/or transthoracic echocardiography, the latter having the advantage of being noninvasive, would allow assessment of central blood volume and/or cardiac output in POTS patients performing these maneuvers, and may help elucidate the mechanisms in play. From our observations in this particular case, we believe that the observed changes in the shape of the arterial pulse wave are directly related to the patient's POTS, though we were unable to find literature previously describing such changes. Supporting these hypotheses is the fact that the patient was intolerant of beta blockade but had attenuation of his symptoms with an oral alpha agonist which has been shown to improve venous return and assist in orthostatic tolerance (Cruz, 2000).

A more detailed waveform analysis including, for example, higher oscillations associated with central hypovolemia (as described by Rickards et al., 2011) was not possible due to the retrospective character and limited quantity and quality of our data recordings.

In conclusion, we observed distinct changes in pulse oximetry derived waveforms when our patient known to have POTS changed his position from supine to upright and again from upright to squatting, consistent with an inappropriately low increase in vascular tone and subsequent onset of intrathoracic hypovolemia when upright. The patient's chronic orthostatic intolerance may closely reflect arterial flow pattern changes. To our knowledge this is the first report dissecting arterial waveforms in a POTS patient. If corroborated in systematic studies, such a practice may be helpful in better defining the mechanism of POTS in patients with different presumed etiologies. Our case also illustrates an important example of how simple arterial waveform analysis can aid health care providers in diagnosing changes in cardiovascular status in the clinical setting.

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Fig. 1.

The patient's pulse oximeter waveforms upon standing (upper panel), when resuming the supine position (middle panel), and when squatting (lower panel). Note the prominent biphasic nature of the flow pattern when standing and the more traditional waveform with a dicrotic notch (arrow) present in the descending portion of the wave when supine. Squatting reversed the appearance of the prominent waveform from supine to upright.