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RESEARCH LETTER

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Early versus late postural tachycardia: a re-evaluation of a syndrome

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Abstract Postural tachycardia syndrome (POTS) involves an HR-rise within 10 minutes of head-up tilt. Hypokinetic circulation, older age, and ACE-inhibitor or Angiotensin-Receptor Blockers were associated with "Late" POTS (after 10 minutes of tilt) versus "Early" POTS (within 10 minutes of tilt).

Key words postural tachycardia syndrome · syncope · orthostatic intolerance · tilt table test

Introduction

Postural tachycardia syndrome (POTS) is a form of orthostatic intolerance associated with symptoms ranging from palpitations to syncope [2] and commonly affects daily activities [3]. POTS has been defined as a rise in heart rate (HR) by 30 bpm or to 120 bpm within the first 10 minutes of head-up tilt (HUT) [2, 3]. In the purest sense, POTS is diagnosed only in the absence of other conditions that could alter circulatory autonomics [4]; this can be thought of as "primary" or idiopathic POTS. "Secondary" POTS would refer to a similar rise in HR that may be due to underlying conditions or primarily circulatory disturbances that could alter autonomics, such as diabetes or medications.

The definition of POTS uses a 10-minute cut-off during HUT. It is unclear if there is a mechanistic difference between a 30-bpm HR-rise seen within 10 minutes (Early-POTS) versus an HR-rise seen after 10 minutes (Late-POTS). A "Late" rise in HR is very frequently seen and its meaning has not been fully elucidated. The present study analyzes the circulatory-kinetic and blood volume differences in Early- versus Late-POTS. No distinction was made between primary or secondary POTS.

Methods

Data was analyzed from a prospectively collected registry database in a study approved by the Institutional Review Board. During the year 2006, analysis was done on all patients diagnosed with POTS, both primary and secondary, who came to the Syncope Clinic as part of their work-up for orthostatic intolerance. Patients had symptoms ranging from palpitations to syncope; $n = 190$ (159 were women) out of a total of 1,044 patients with HUT tests done that year, with ages ranging from 19 to 84 years old. Standard HUT-protocol included monitoring of vitals signs during supine-rest, 30° tilt (2-minutes), 45° tilt (2-minutes), 70° tilt (45-minutes), and supine-recovery (5-minutes); no isoproterenol was used. All patients included in this analysis received additional blood volume and circulatory-kinetic testing.

Blood volume was measured using a I-131-HSA tagged human serum albumin technique [1] using a Daxor BVA-100 system (Daxor Corporation, NY, USA). If the actual blood volume was within 8% of normal predicted blood volume then it was deemed normal. Otherwise it was deemed either hypervolemic or hypovolemic.

Evaluation of circulatory-kinetics was done using 99 m Technetium-RBC radionuclide imaging [5]. Pulmonary mean transit-time, cardiac index and total peripheral resistance were calculated. Hypokinetic circulation was defined as a combination of a low cardiac index (<2.8), prolonged pulmonary mean transit time (>9 seconds), and high total peripheral resistance (>32). Hyperkinetic circulation was defined as a combination of a high cardiac index (>3.1), shortened mean transit-time (<7 seconds), and low peripheral resistance (<29).

Demographics, medications, and results from the blood volume and circulatory-kinetics testing were analyzed. Multiple analyses of variance were done and Fishers post hoc tests were done to assess any interactions. A $P < 0.05$ was significant.

Results

Ninety-seven patients had Early-POTS; 93 patients had Late-POTS (Table 1). The number of women in each group was similar. There was an association between increased age and Late-POTS (38.8 ± 15 yo in Early-POTS versus 45.5 ± 14.4 yo in Late-POTS, $P = 0.002$). Age was included as a covariate in subsequent analyses. Beta-blocker use in the two groups was similar. Angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) uses were different; more subjects in the Late-POTS group were using an ACE-I or ARB ($P = 0.034$). There was a non-significant trend toward diuretics use and having Late-POTS ($P = 0.059$). Usage rates were no different for other medications though the numbers were small. In comparing a hypokinetic circulation to normokinetic circulation (Table 2), a hypokinetic circulation was associated with having Late-POTS, $P = 0.046$. In comparing a hypokinetic circulation to a hyperkinetic circulation, a hypokinetic circulation again was associated with Late-POTS, $P = 0.036$. In comparing a normokinetic circulation to a hyperkinetic circulation, no difference was found. Only a hypokinetic circulation was associated with Late-POTS. In terms of blood volume, no difference was found between the two groups. In general, the HR trend varied between patients before it met Late-POTS criteria.

Table 1 Demographics

	Early POTS	Late POTS
Total # patients	97	93
# Women	84	75
Age (years ± SD)	38.3 ± 15	45.5 ± 14.4*
Medications (# patients taking)		
Beta-blocker	12	18
ACE-I/ARB	3	10*
Calcium-channel blocker	4	5
Diuretic	3	9**
Fludrocortisone/hydrocortisone	9	4
Isosorbide dinitrate	0	1
Midodrine	5	5
Pyridostigmine	1	0
Clonidine	2	0

ACE-I angiotensin-converting enzyme inhibitor, *ARB* angiotensin-receptor blocker

* $P < 0.05$, ** $P = 0.059$

Table 2 Circulatory kinetics and blood volume

	Early POTS	Late POTS
Total # patients	97	93
Circulatory kinetics (# patients)		
Hyper-kinetic	37	30
Hypo-kinetic	7	16*
Normal	53	47
Blood volume (# patients)		
High (>8% predicted)	9	12
Low (<8% predicted)	27	26
Normal	61	55

* $P < 0.05$

Discussion

Older age, ACE-I or ARB use, and a hypokinetic circulation were individually found to be associated with Late-POTS. Blood volume was not significant between the two groups.

There may be a difference in the mechanism of POTS in younger versus older patients; whereas POTS in younger patients may be due to an imbalance of sympathetic versus parasympathetic tone, older patients may be more prone to other, perhaps circulatory or more subtle, autonomic neural dysfunction problems. Though ACE-I and ARB use was not separated; it may be that the bradykinin effect of ACE-I when associated with venodilation causes HR to rise later, resulting in Late-POTS. If a hypokinetic circulation is presumed to be due to a high vagal tone, it may take longer to override with an increase in sympathetic tone, or, conversely, a withdrawal of vagal tone may take longer, thus exhibiting Late-POTS. Lastly, the use of a more encompassing term such as accentuated postural tachycardia to describe the HR-rise seen in POTS (whether primary or secondary) can be considered.

Limitations

Firstly, symptoms were not evaluated for this article and may be different between Early and Late-POTS. Secondly, ACE-I and ARB use was not separated; though both medications act on the renin-angioten-

sin-aldosterone pathway, their mechanisms are not exactly the same. Thirdly, the recommended therapy was not evaluated for this article. In our institution, therapy is influenced by results of blood volume and circulatory-kinetic testing. Since hypokinetic circulation was associated with Late-POTS, it may be that therapy is different for Late versus Early POTS. Lastly, no distinction was made between primary and secondary POTS.

Conclusions

Significant differences were found between Early- and Late-POTS suggesting that they are two distinct entities with different mechanisms. Implications regarding symptoms, therapy, and prognosis need further study.

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