Inappropriate Sinus Tachycardia, Postural Orthostatic Tachycardia Syndrome and Vasovagal Syncope

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VVS, POTS and IST

1. Many shared characteristics

2. Many shared symptoms”
   palpitations, lightheadedness, fatigue
   presyncope/syncope

3. Diseases of the young and predominantly in woman

4. Belong to the dysautonomia syndrome

Autonomic regulation of CV physiology is somehow messed up
Syncope

- Spontaneous, transient loss of consciousness associated with loss of postural tone.
- Usually results from global cerebral hypoperfusion
- Rapid onset, short duration and spontaneous, complete recovery
- Absence of clinical features of another form of transient loss of consciousness, e.g. epileptic seizure.
- Everyone has a cumulative lifetime incidence of syncope of 30-40%.

Postural Tachycardia Syndrome (POTS)

- Frequent symptoms occur with standing - palpitations, lightheadedness, weakness, etc
- Increase of heart rate by 30 bpm when moving from recumbent to standing position without orthostatic hypotension (>20/10 mmHg drop)
- Standing heart rate usually >120 bpm
- A systemic illness of young people (15-25 y/o) (symptoms may decrease after 20 y/o)
- Diagnosis of POTS and vasovagal syncope are not mutually exclusive

Inappropriate Sinus Tachycardia (IST)

1. Sinus heart rate >100 bpm at rest
2. Mean 24-hour heart rate >90 bpm
3. Distressing symptoms of palpitations
4. Mechanisms of IST are poorly understood
VVS, POTS and IST

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Autonomic regulation of CV physiology is somehow messed up
Standing upright requires a series of well-coordinated physiological responses
Physiological Responses to Standing Upright

1. Human is the only animal having to deal with this.

2. Heart can bump only the blood it receives. Faster HR alone cannot solve the problem.

3. Hydrostatic indifference point (HIP):
   The point in the vascular system that is independent of posture/position
   - arterial HIP: left ventricle
   - venous HIP: diaphragm

4. In supine position: only 25-30% blood volume in thorax
Physiological Responses of Standing Upright

When standing up: blood volume dropped 20-30% in the first 10” of standing

→ drop in cardiac filling pressure, stroke volume and arterial pressure

→ activate pressure-sensing mechanoreceptors:
  - high pressure receptors: in carotid sinus and aortic arch (baroreceptors)
  - Baroreflex: transmit BP information to the brain stem CV center
  - low pressure receptors: in heart and lung
The image illustrates the baroreflex pathway in the nervous system. It shows the connections between the carotid body, glossopharyngeal nerve (IX), and the sympathetic and vagus nerves. Key components include the Nucleus of Solitary tract, Dorsal motor Nucleus of vagus, Baroreflex afferent, Baroreflex afferent, Mechanoreceptor afferent, and Sympathetic ganglion. The diagram highlights the neural pathways that mediate blood pressure regulation through the baroreflex mechanism.
Physiological Responses of Standing Upright

Prolonged standing (e.g. >10 minutes):

- Increase in transmural capillary pressure in the dependent area of the body
- Increase in fluid filtration into tissue
- Lose up to 10% more plasma volume
Physiological Responses of Standing Upright

→ Fall in filling pressure: reduce the stretch of the mechanoreceptors in all chambers of heart:

- Sympathetic activation:
  • Increase vascular resistance of peripheral and splanchnic vascular bed.
  • Increase vascular resistance of skin, muscle and adipose tissue

If sympathetic activation did not lead to appropriate vasoconstriction → orthostatic intolerance or syncope
Syncope

1. Neurally mediated syncope (i.e. vasovagal syncope)

2. Syncope due to orthostatic hypotension
   - drop in SBP by 20 mmHg or DBP by 10 mmHg within 3 minutes of standing
   - Often caused by autonomic failure (diabetes, Parkinson’s disease, uremia, etc)

3. Cardiovascular syncope
   - Myocardial ischemia, arrhythmia, obstructive heart dz

All types of syncope result from sudden drop of cerebral perfusion due to hypotension and/or bradycardia and/or decreased peripheral vascular resistance.
Syncope

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Neurally Mediated Syncope

1. Vasovagal syncope: most common

2. Carotid sinus syncope

3. Situational syncope
   • micturition or post-micturition syncope
   • Defecation syncope
   • Cough syncope, etc
Vasovagal Syncope

- Occurs in an upright posture held for >30 seconds or with exposure to emotional stress, pain, or medical settings
- Features diaphoresis, warmth, nausea and pallor
- Associated with hypotension and relative bradycardia
- Followed by fatigue

Vasovagal Syncope

• By 60 y/o: 42% women and 32% men already had their 1st episode of syncope

• The incidence of VVS increases markedly around age of 11.

• The median age of the 1st syncope is 14 y/o.

• Most people with VSS had their 1st syncope before 40 y/o

What Went Wrong in VVS

• Instead of sympathetic activation and vasoconstriction, vasodilatation occurs

• How brain processes the neural trafficking of reduced BP is messed up.
  - Mechanoreceptors to brain stem
  - CV center and vagal motor nuclei in brain
  - Responses of the peripheral vascular bed to sympathetic activation
  - Excessive parasympathetic activation

<table>
<thead>
<tr>
<th><strong>Vasovagal Syncope</strong></th>
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<tr>
<td>- Mostly mixed cardio-inhibition and vasodepressor responses</td>
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<td>- Occasionally see pure cardio-inhibitory syncope:</td>
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<tr>
<td>- abrupt heart rate decrease to &lt;40 bpm with or without asystole</td>
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<tr>
<td>- depressed AV conduction</td>
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<td>- Occasionally see pure vasodepressive syncope:</td>
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<td>- significant hypotension with &lt;10% change in heart rate</td>
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Diagnosis of Vasovagal Syncope

• Mainly based on clinical history
  - Happens after prolonged standing or sitting
  - can be triggered in supine position by pain or stress
  - In contrast to syncope due to orthostatic hypotension, VVS occurs at least 3-5’ after standing
  - often has prodromal features (e.g. flushing, nausea, sense of warmth)

Diagnosis of Vasovagal Syncope

• Tilt-table testing:
  - try to reproduce presyncope or syncope by introducing progressive orthostatic stress
  - up to 60-80 degree over 20-40 minutes
  - If history suggests VVS, TTT has a 70-80% sensitivity and 90% specificity

Be patient! It may take 40 minutes to induce VVS

Stage 1: Lie down and relax with monitors attached.
Stage 2: Dr tilts the bed, reads the monitors and watches your reactions.
Stage 3: Dr lies you down again when they have the info needed, or you've had enough.
Stage 4: Lie down and recover.

Po Says: Be patient. Second helpings come to those who wait.
Tilt-Table Testing

• A positive response:
  - Clinically reminiscent presyncope or syncope associated with hypotension and usually bradycardia
  - A syncopal episode associated with BOTH sinus bradycardia and AV block: more likely to be VVS
  - nitroglycerin, isoproterenol and adenosine have been used to increase sensitivity of TTT but at the expense of specificity.

Tilt-Table Testing

• Results of TTT is specific but sensitivity is unknown
• Very helpful in differentiating VVS, POTS, OH:
  - Syncope from orthostatic hypotension occurs very early in TTT
  - VVS: BP and HR are maintained for a while until reaching the breakpoint
  - POTS: HR increases early and gradually during TTT with minimal change in BP (in contrast to orthostatic hypotension)

Management of Vasovagal Syncope

- Challenges: episodes often are interspersed with long quiescent periods without recurrence
  - Education, promoting salt, fluid intake
    - Class I indication
  - Isometric physical counterpressure maneuvers:
    - Best for patients with clear prodrome
    - Risk free, should always be part of the therapy
    - Class IIa indication
Management of Vasovagal Syncope

- Pharmacological Therapies:
  - β-blockers:
    - Not effective in young patients
    - May be effective in patients older than 40 y/o
    - Class IIb indication
  - Fludrocortisone (retain salt and water)
    - Maybe effective in patients with severe sx
    - Class IIb indication
Management of Vasovagal Syncope

- Pharmacological Therapies:
  - Midodrine: α-receptor agonist: vasoconstrictor
    - May be effective in patients with severe sx
    - Class IIb indication
  - Serotonin transporter inhibitors:
    - Serotonin in the brain stem regulation of HR and BP
    - Effect on preventing syncope is unclear
Management of Vasovagal Syncope

• If TTT is negative:
  - implantable loop recorder can be used.
  - For elderly patients with unexplained syncope, ILP should be considered earlier.

These patients tend to have profound bradycardia (asystole or high-degree AVB as the cause of unexplained syncope)

Except for this specific group of patients with prolonged asystole or AV block, pacemaker implantation is not indicated for VVS

Pacemakers for Syncope

- >40 y/o with recurrent syncope and a documented pause ≥ 3” during syncope or asymptomatic pause ≥ 6”  
  (Class IIa)
- Pediatric patients with recurrent syncope and documented asystole refractory to medical therapy  
  (Class IIb)
- Adenosine-sensitive older patients with unexplained syncope without a prodrome (normal ECG, no structural heart disease)  
  (Class IIb)

Postural Tachycardia Syndrome (POTS)

- Frequent symptoms occur within 10’ of standing - palpitations, lightheadedness, weakness, etc
- Increase of heart rate by 30 bpm when moving from recumbent to standing position without orthostatic hypotension (>20/10 mmHg drop)
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- Diagnosis of POTS and VVS are not mutually exclusive

Mechanisms underlying POTS

1. Peripheral autonomic denervation:
   • Maybe preceded by viral infection, pregnancy, surgery, trauma, electrical injuries
   • Up to 50% POTS patients had restricted autonomic neuropathy of small postganglionic nerves esp. feet and toes
   • Reduced splanchnic and peripheral vascular resistance
   • Venous pooling in the lower extremities and splanchnic beds

Mechanisms underlying POTS

2. Hypovolemic:  
   - Blood volume can be reduced by 50% when standing up in POTS patients

3. Hyperadrenergic POTS:  
   - SBP increases >10 mmHg when standing upright for 10 minutes.
   - Prominent sympathetic symptoms: anxiety, tremor
   - May have elevated standing serum norepinephrine level
   - Hypersensitive to isoproterenol challenge

Mechanisms underlying POTS

4. Deconditioning:
   - Exercise training may help

5. Secondary POTS:
   - Autonomic neuropathy from diabetes, cancer, lupus etc.
   - Drug-induced POTS:
     - alcohol, vasodilators
     - tricyclics, monoamine oxidase, etc
   - Must identify and treat secondary POTS first

Diagnosis of POTS

1. History, exam with orthostatic vital signs, ECG (often enough to make the diagnosis)
   - Acral cyanosis (venous cooling)
2. TTT: with BP/HR recording over time: very helpful
3. Echo, Holter to exclude other CV diseases
4. CBC, thyroid function to exclude other non-CV diseases
5. Not helpful tests:

- Thermoregulatory sweat test (abnormal sweat pattern) to detect autonomic neuropathy
- supine/standing epinephrine and norepinephrine levels
Treatment for POTS

1. Regular, structured and progressive exercise program e.g. recumbent bike (Class IIa)

2. Saline infusion for short-term clinical decompensation (Class IIa)

3. Consume 2-3 L of water and 10-12g of NaCl daily (Class IIb)

4. Flodrocortisone, daytime midodrine or low dose propranolol (Class IIb)

5. Pyridostigmine: peripheral acetylcholine esterase inhibitor (Class IIb)

6. Ablation has no role in managing POTS (w/o tachycardia: POTS patients will faint)
Inappropriate Sinus Tachycardia (IST)

1. Sinus heart rate >100 bpm at rest
2. Mean 24-hour heart rate >90 bpm (HR slows now at night)
3. Distressing symptoms of palpitations
4. Mechanisms of IST are poorly understood
   • Sinus node automaticity
   • β-receptor hypersensitivity
   • β-receptor autoantibody
   • Decreased parasympathetic activity
## Symptoms of IST (despite HR)

- Palpitations
- Breathlessness
- Atypical Chest Pain
- Dizziness / Syncope
- Extreme fatigue
- Anxiety / Depression
- Myalgia / Abdominal discomfort
- Low risk of tachycardia mediated cardiomyopathy
## Diagnosis of IST

1. History, physical exam and ECG (Class I)

2. CBC and thyroid function (Class IIA) and exclude secondary causes of IST

3. 24-hour Holter, drug screen (Class IIB)

4. Tilt table testing:

   - IST and POTS patients may have similar sx
     - POTS: only induced by orthostatic stress
     - IST: induced by both physical and emotional stress
Diagnosis of IST

5. Diagnostic Electrophysiologic Study

- Only reserved for patients with symptoms suggestive of focal atrial tachycardia
  - Rapid onset and off set of “sinus” tachycardia
  - Tachycardia and sinus rhythm P waves look different
Diagnosis of POTS vs. IST, VVS

1. Hyperadrenergic POTS is very similar to IST:
   - POTS patients rarely have a supine HR > 100 bpm
   - POTS patients display a much greater postural change in heart rate

2. TTT:
   - POTS patients: HR is normal in supine position but increases gradually with tilt
   - IST patients: HR is fast in supine position and increases rapidly with tilt
Treatment for IST

1. Find and treat reversible causes of sinus tachycardia (Class I)
   - symptoms, not heart rate is the focus of Tx

2. β-blockers, Ca blockers: usually not very effective

3. Ibravadine: a blocker of the pacemaker current (I_f) (Class IIa, off label use)

4. Sinus node modification by ablation:
   - Not recommended
5. Experimental ablation protocol at OU:

- EP study to exclude focal atrial tachycardia; if focal AT is induced → ablate it
- For true IST → ablate the sympathetic nerve innervating the sinus node and/or ablate the autonomic ganglion relays this sympathetic nerve
Conclusion

• VVS, POTS and IST are part of the dysautonomia syndrome

• The normal CV response to various stress (e.g. orthostatic stress) was messed up somewhere in the autonomic nervous system

• No effective therapy yet