UNIKLINIK RWTH AACHEN

Treating orthostatic intolerance in ME/CFS

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Conflicts of interest

Memberships:

- Deutsche Gesellschaft für Neurologie (DGN)
- Arbeitsgemeinschaft Autonomes Nervensystem e.V. (AG ANS)
- Otto Loewi Gesellschaft
- Deutsche Kontinenz Gesellschaft e.V.
- Deutsche EDS Initiative e.V., MWB
- POTS und andere Dysautonomien e.V., MWB

Sponsoring:

- Nutricia und Shire, Takeda, Centogene, StandingUpToPots, Boso Medical, Parkinson Fonds International, Conterganstiftung, Angelman e.V.

Case presentation

Medical history:

- 29 years old female
- infection with EBV: tonsillar swelling and fever, dizziness
- bed ridden: dizzines, weakness, vertigo, nausea and orthostatic tachycardia
- two syncopes
- postprandial nausea
- paresthesia and burning pain in the extremities
- recumbence over time, but persistent orthostatic dizziness and paresthesia when first visiting outpatient clinic

Prior diagnoses and testing results:

- sinus tachycardia even in childhood
- heart frequency up to 140/min in 24h-ecg
- cardiac ultrasound, electrophysiological diagnostic and cerebral MRI: no results

Neurological investigation:

- pupils with reduced reaction to light
- distally reduced temperature and pain sensitivity

Diagnosis in syndromes of orthostatic intolerance (OI)

Detailed orthostatic history

+

Standing test

(active, passive or tilt table testing)

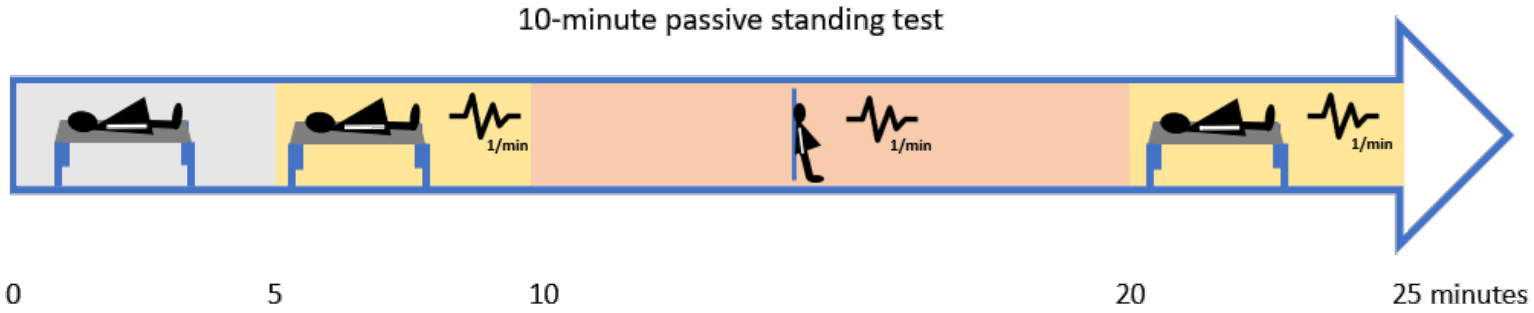


illustration by Fiona Fischer, ANS Ambulanz

Standardized orthostatic testing in order to assess autonomic cardiovascular neuropathy

- ✓ no medication
- ✓ sober (no tea/coffein/nicotine/meal in the morning)
- ✓ no compression garments
- ✓ lie down for at least 10 min before the test.

Diagnosis in syndromes of orthostatic intolerance (OI)

postural orthostatic tachycardia syndrome (POTS)

- heart frequency raises more than **30 beats/min** (40beats/min in adolescents) during 10 min standing time
- and/or heart frequency **> 120 bpm** orthostatic
- and symptoms of orthostatic intolerance for at least **3 months**
- **no** accompanied orthostatic **hypotension**

orthostatic hypotension (OH)

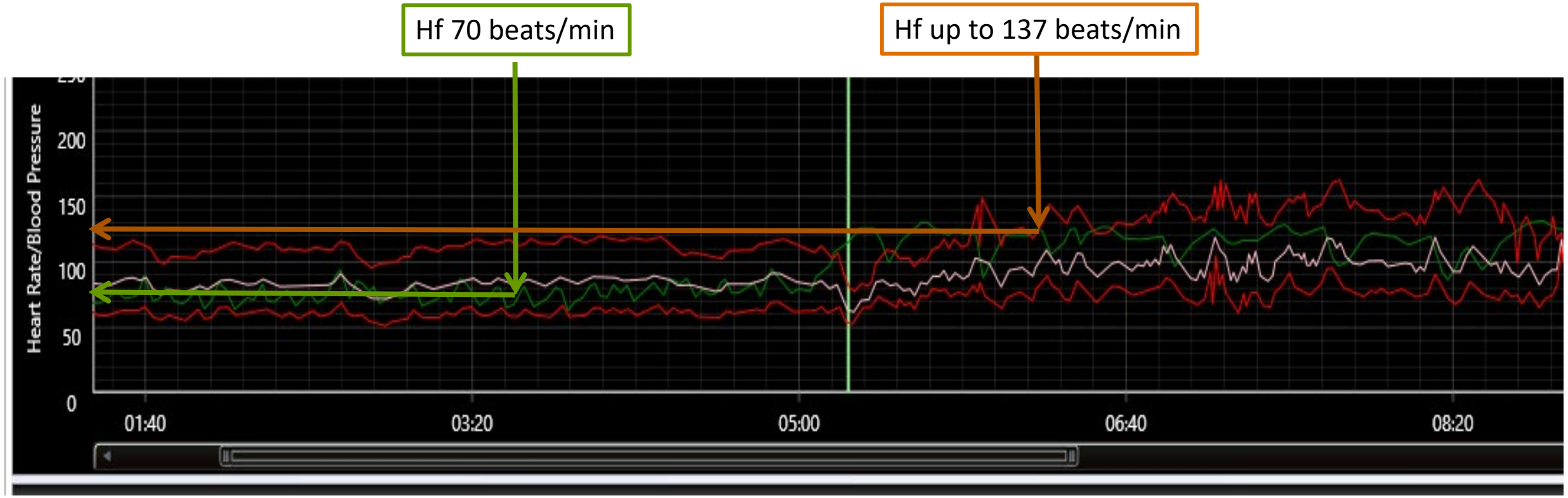
- blood pressure falls systolic more than 20mmHg and/or diastolic more than 10mmHg during 3 minutes standing time
- and symptoms of orthostatic intolerance

postural symptoms without tachycardia (PSWT)

- symptoms of orthostatic intolerance during standing
- criteria of POTS not fulfilled

Rai, 2020

Case presentation: tilt table

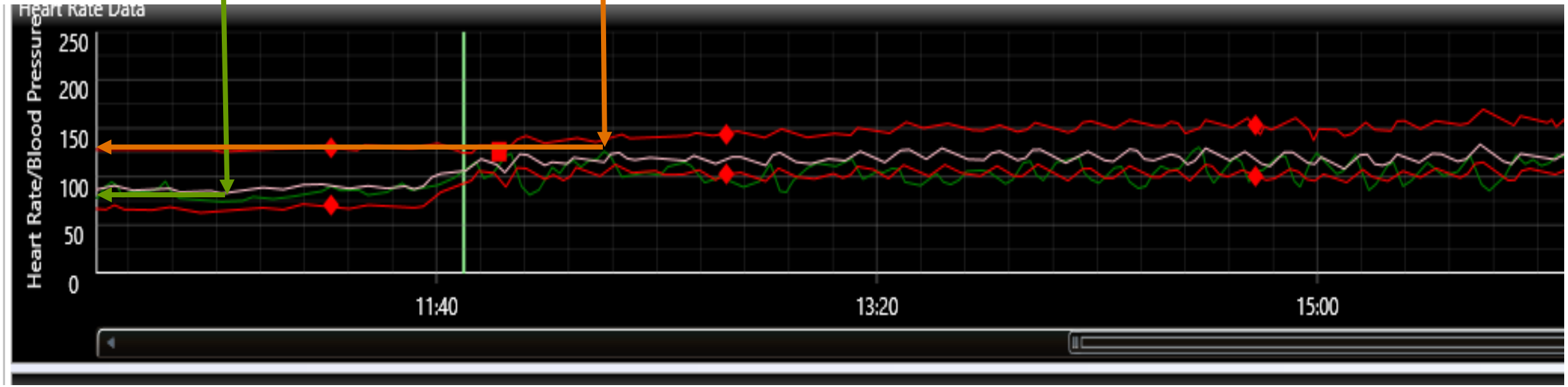


→ **hyperadrenergic POTS (**with small fiber neuropathy, autoimmune triggered)

Tilt table 2: patient with ME/CFS

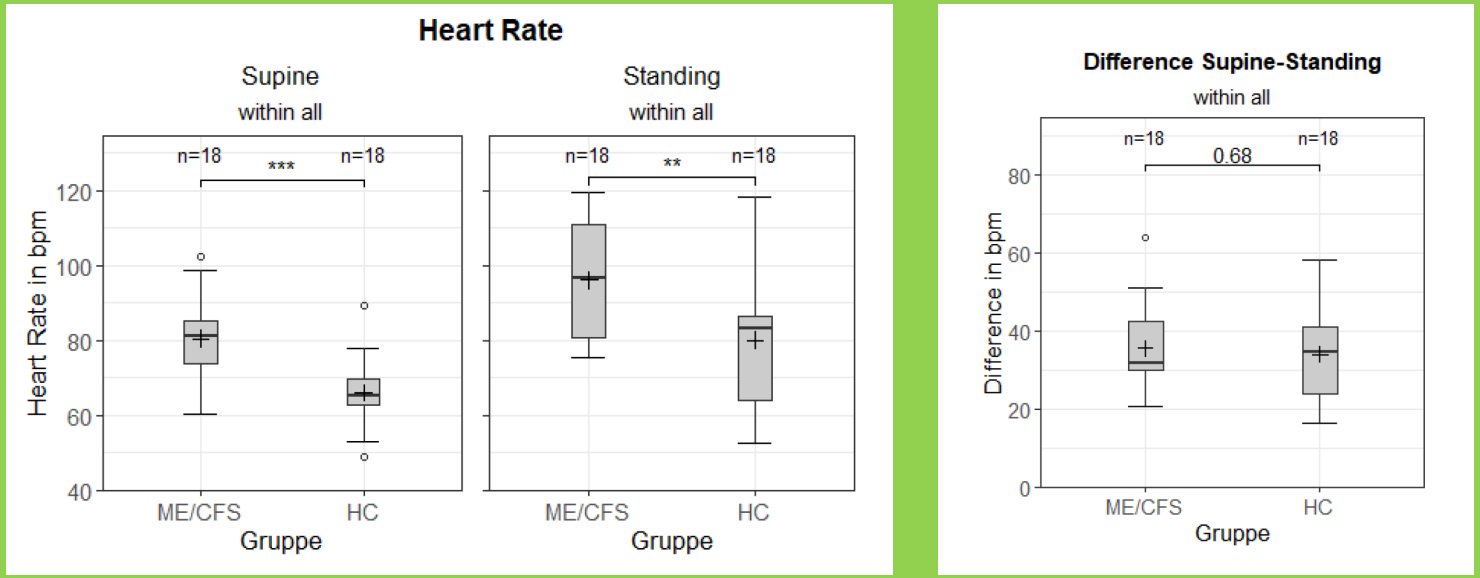
Hf 90 beats/min

Hf up to 130 beats/min, mostly over 120 beats/min



reduced standing time of only 7 minutes

Own results



(Leone…Behrends, Maier, 2023)

18 adolescents with ME/CFS vs 18 HC:

- supine and standing HR significantly higher in ME/CFS than in HC ($p<0.001$)
- no significant difference of heart rate between supine and standing

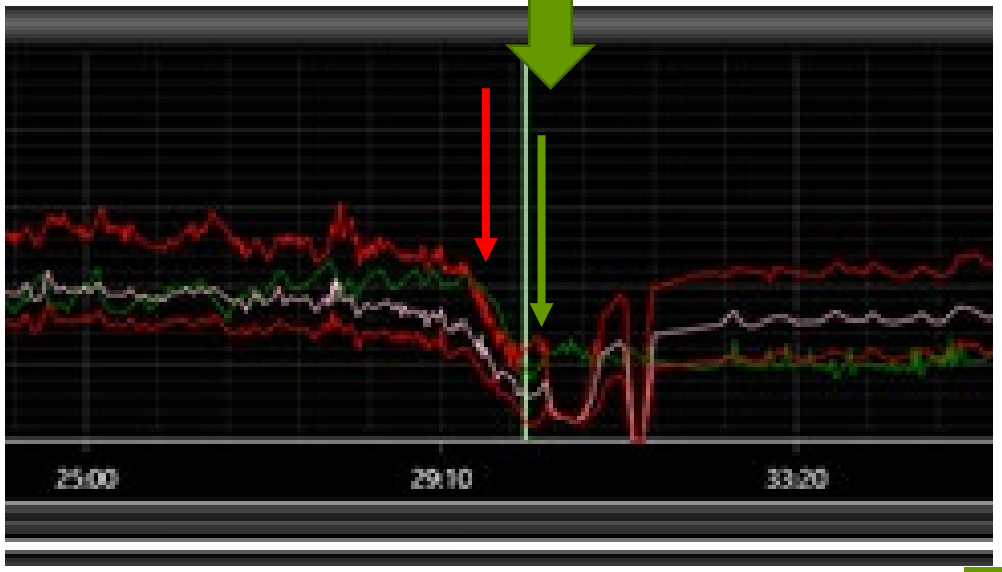
Tilt table 3

Blood pressure 130mmHg sys

HF up to 117 beats/min, mean 85 beats/min

Hf 60 beats/min

blood pressure 135 mmHg sys



Drop of blood pressure:
61/30 mmHg and hf 34 beats/min +
syncope after 20 min standing

→ neurocardiogenic syncope

Tilt table 4

Hf about 50beats/min

HF about 60beats/min

Tilt table:

symptoms during the whole time: dizziness, eyes get closed, tiredness, vision problems

→ postural symptoms without tachycardia (PSWT)

Raj et al., 2020. Canadian consensus on POTS

Therapy of POTS

@Haubrich, ANS

Education

- 50 % sponatenous remission in 1–3 years (Bhatia et al. 2016)
- Trigger: long standing, volume depletion, heat
- Typical prodromi and possibily to avoid syncopes
  (lying down, counter maneuvers)

Basis therapy

- Avoid lying in bed
- Stand up slowly
- Small, frequent meals
- Raise blood volume: drink 2-3 l/day, NaCl 8-12 g/day
- Compression stockings and abdominal binder
- Treat related conditions (Ehlers-Danlos syndromes, small fiber neuropathy, pain, mast cell disorder, anemia, vitamin B12 depletion)

- Train calf and abdominal muscles, standing training, endurance training (if possible depending on ME/CFS!!)
- exercise examples: | pots-dys (pots-dysautonomia.net), Exercise Examples - PoTS UK

Diehl, 2022, Synkopen, S1-Leitlinie, 2020

Fu, 2018: Exercise and non-pharmacological treatment of POTS

Medications in POTS

@Haubrich, ANS

If symptomatic therapy does not help, **start in very slow dose**!

- saline 1-4 capsules each day
- midodrine 2,5 (-10mg) 1-3/day, not later than 6 p.m.
- mestinone 10 (-60) mg 1-3/day. (AE diarrhea)
- fludrocortisone 0,1-0,3mg (AE myocardial fibrosis)

Hyperadrenergic POTS:

- betablockers (propranolol 10-20 mg 3-4/day (h)
- carvedilole 3,125 mg 1-2/day, labetalole 100-200 mg 2/day (h)
- ivabradine 2,5 mg 1-2/day (h)
- clonidine 0,1 mg
- methyldopa, 125-250 mg up to 2/day
- bupropione 150-300 mg/day
- escitaloprame 10 mg/Tag
- desmopressine 0,1 mg z.N.

- Short term: NaCl i.v. (Ruzieh, 2017: Effects of Intermittend intravenous saline infusion in POTS)

Raj, 2020 und Diehl, 2022, Synkopen, S1-Leitlinie, 2020

Therapy of neurocardiogenic syncopes

Education

- Same as in POTS

Physical

- Drink 2–2,5 liters of water and eat more salt
- Compression stockings and abdominal binder when standing
- Counter maneuvers
- Standing training
- Sports

@Haubrich, ANS

Medication

- midodrine (3 × 2,5–10 mg/d) when arterial hypotension (Ward et al. 1998; Perez-Lugones et al. 2001; Kaufmann et al. 2002)
- Beta blocker mostly not helpful (Flevari et al. 2002; Sheldon et al. 2006a)
- Atomoxetin? (Sheldon et al., 2022)

Pace maker

- Only in therapy refractory syncopes with asystolia more than 3 sec and in patients older than 40 years)
  (Brignole et al. 2012; von Scheidt et al. 2019a)

Diehl, 2022, Synkopen, S1-Leitlinie, 2020

OI in ME/CFS Summary

- PoTS has many faces and causes
- diagnosis via detailed medical history + standing test/ tilt testing

  → OH, POTS, PSWT or neurocardiogenic syncope?
- exclude cardiac disease
- basic therapy symotomatic: volume, saline, compression garments and avoid deconditioning
- medications: off label
- treat comorbid diseases: small fiber neuropathy, Ehlers-Danlos syndromes, MCAS, pain
- **ME/CFS: PEM as big challenge**

Literature

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