Differential diagnosis of Transient Loss of Consciousness (TLOC)

Max J. Hilz

Department of Neurology, University of Erlangen-Nuremberg

Schwabachanlage 6, D-91054 Erlangen, Germany

E-mail: max.hilz@uk-erlangen.de

Oral Presentation Disclosure

	No, nothing to disclose
X	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
Genzyme	x	x						
Novartis	x		x					
Bayer	x		x					

Learning objectives

To enable participants to distinguish between various non-traumatic causes of transient loss of consciousness (TLOC), including syncope, epilepsy, pseudo-syncope and pseudo-seizures as well as rare causes of “TLOC”.

To enable participants to differentiate between three types of syncope, including **reflex syncope, syncope due to orthostatic hypotension, and cardiac syncope.**

Transient Loss of Consciousness

due to trauma (concussion)

not due to trauma

Key message

Syncope:

- **reflex syncope (66%)**
- **orthostatic hypotension (10%)**
- **cardiac syncope** (16%)

33-88% of TLOCs

1% of emergency department admissions

Epileptic seizures:

- primary generalized (tonic, clonic, tonic–clonic, atonic)
- secondary generalized

5-53% of TLOCs

Functional transient loss of consciousness:

- pseudoseizures
- pseudosyncope

Rare causes:

- vertebrobasilar transient ischemic attacks
- subclavian steal syndrome
- cataplexy
- excessive daytime sleepiness
- metabolic disorders (hypoglycemia)
- 'drop attacks'

(6%)

(Brignole 2006, van Dijk et al. 2009)

Transient Loss of Consciousness (TLOC)

Definition:

apparent loss of consciousness

rapid onset

temporary, self-limited

short duration (minutes)

spontaneous, complete recovery

absence of external cause

loss of postural control ➔ fall

(Thijs et al. 2004, van Dijk et al. 2009)

Syncope

temporary interruption of cerebral perfusion

➔ sudden, transient loss of consciousness,
loss of postural tone &
spontaneous recovery

1-6% of hospital admissions
~3% of emergency room visits

common in healthy young adults (12 - 48 %)

occurs once during lifetime in
up to 33% of general population

Prognosis depends on presence & severity
of underlying organic disease & injuries

(Shen & Gersh 1997)

Reflex syncope – neurally mediated syncope – neurocardiogenic syncope – vasovagal & situational syncope

Situations (e.g. micturition, coughing, defecation, swallowing, sneezing)

activate different afferent reflex branches

similar input into central structures of cardiovascular control

similar efferent autonomic pathways

⇒ sympathetic withdrawal, preload, ⇩

parasympathetic activity ⇧ *(Shen & Gersh 1997)*

most situations are associated with a Valsalva maneuver

⇒ changes in transthoracic pressure & respiratory pattern

(Aicardi et al. 1988)

pulmonary mechanoreceptors affect cardiovascular system

via respiratory center (brainstem) ⇒ trigger of situational syncope

(Shen & Gersh 1997)

Carotid sinus hypersensitivity (spontaneously rare <1% ?)

central baroreflex disturbance ?

1. **cardioinhibitory (70-75%)**

   asystole for at least 3 seconds

   (parasympathetic activation):

   transient sinus bradycardia, AV block

2. **vasodepressor (5-10%)**

   systolic blood pressure fall > 50 mm Hg

   (or 30 mmHg & presyncopal symptoms)

   sympathetic inhibition: hypotension

3. **mixed response**

   bradycardia & blood pressure fall

   (van Dijk et al; 2009)

Carotid sinus massage:

no syncope, but responses 1.- 3.

➔ **"Carotid sinus hypersensitivity"**

Syncope:

➔ **"induced carotid-sinus syncope"**
(requires longer lasting asystole or prominent blood pressure drop)

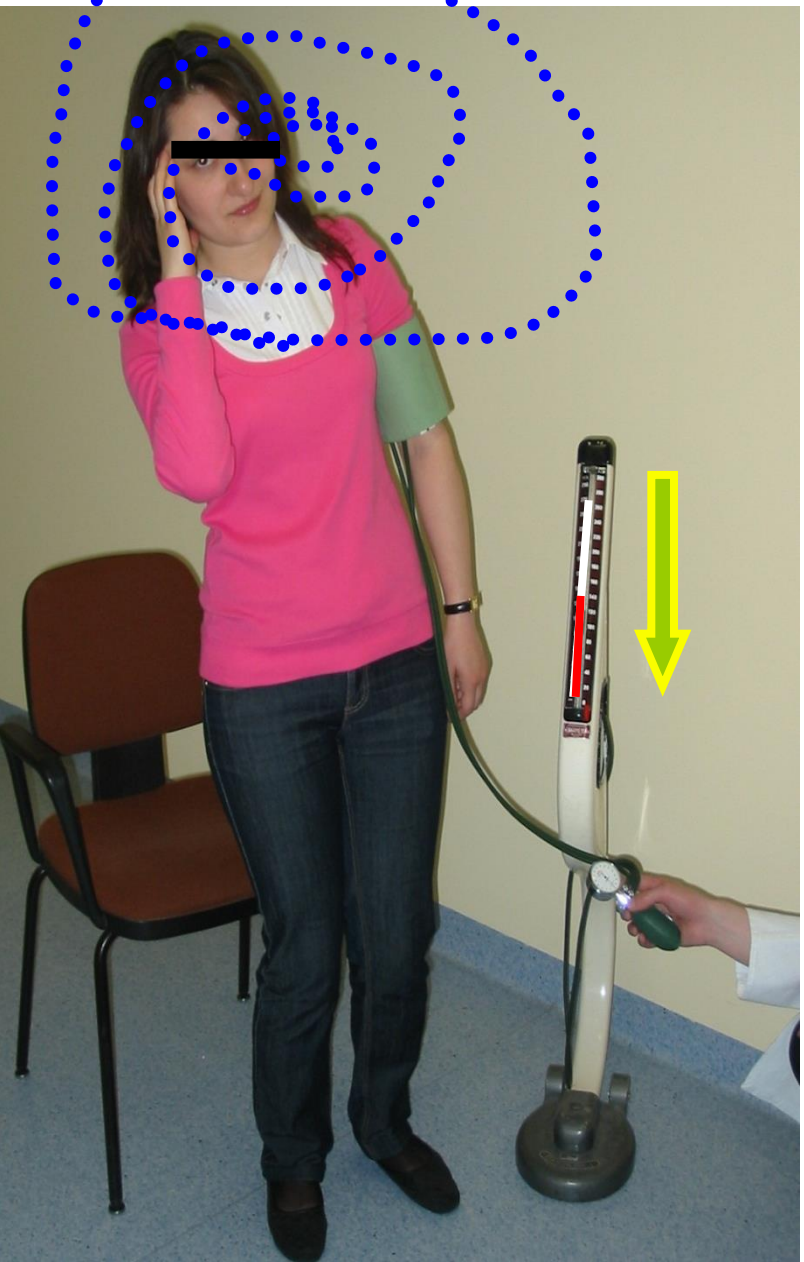
(van Dijk et al; 2009)

Good prognosis of reflex syncope

- no increased cardiac or neurological morbidity or mortality

- HOWEVER:
  - risk of trauma
  - psychologic problems,
  - problems at school,
  - problems at work
  - driving is prohibited !!

Syncope due to orthostatic hypotension



blood pressure fall within 3 min.

after standing-up / 60° passive head-up tilt:

(systolic ≥ 20 mmHg / diastolic ≥ 10 mmHg)

(Am. Autonomic Society & Academy of Neurology,1996)

Symptoms:

- weakness, dizziness, blurred vision
- difficulties to concentrate
- coat-hanger-like neck pain
- nausea, palpitations

➔ **syncope**

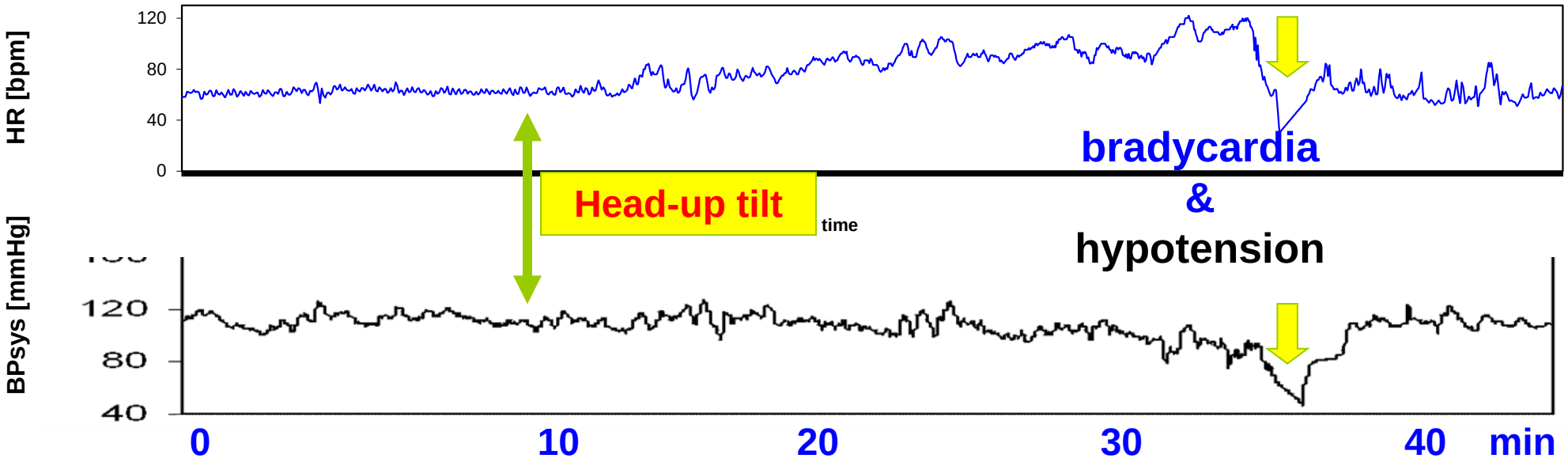
minimal heart rate response,

excessive hypotension during Valsalva,

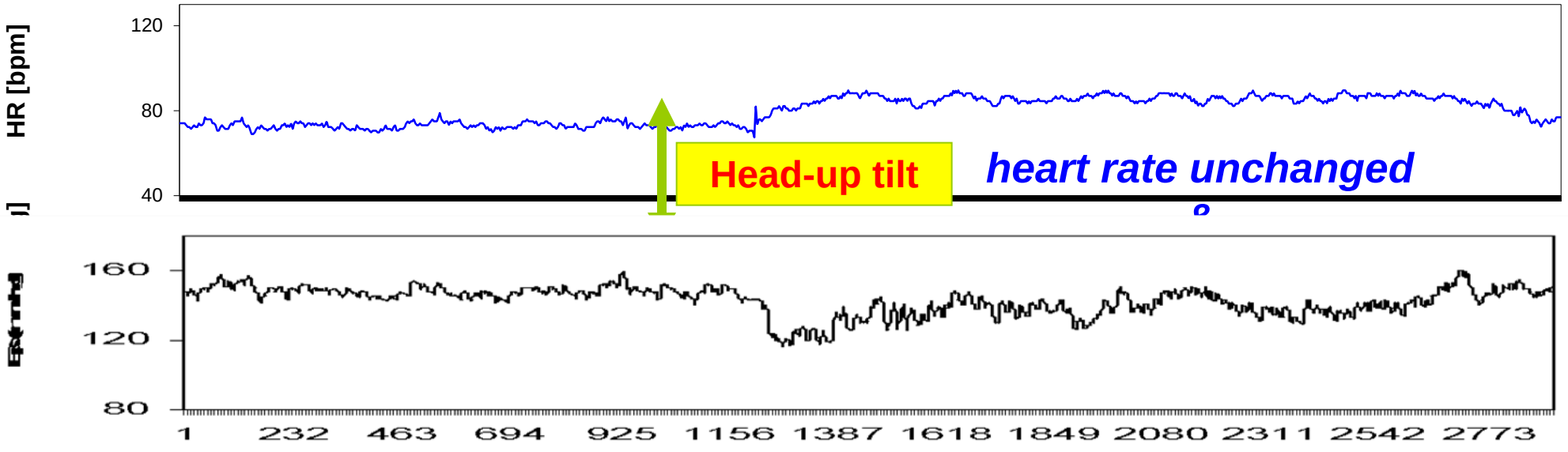
pathologic findings with autonomic tests,

often neurologic or internal diseases (e.g. diabetes mellitus, MSA)

Neurally mediated syncope



Orthostatic hypotension due to autonomic failure



Convulsive syncope

brief, tonic-clonic movements of individual muscle groups

at times quite difficult to differentiate from epileptic seizures

can occur independently from the etiology of syncope.

differentiation by simultaneous Video-EEG-recording (rarely available)

serum prolactin levels are unreliable

as prolactin levels increase after epileptic seizure & after syncope

better differentiation by serum creatine kinase:

creatine kinase increases only after seizure.

(blood sample must be drawn within 3 hours after seizure/syncope !)

Epileptic seizures

epileptic aura *(e.g. epigastric aura with rising sensation in abdomen, unpleasant smelly, „ Déjà-vu “ phenomenon)*

emission of a initial cry

automatisms, supposedly normal actions

ictally symmetric and rhythmic motor jerks

in epilepsy, **but not in syncope,** jerks can begin unilaterally & before the fall.

Jerks are coarse, symmetrical, rhythmic.

eyes usually open (also during syncope !)

gaze directed towards one side, pronounced head deviation,

cyanotic facial color (also occurs in cardiac syncope, but is less common in reflex syncope !)

epileptic seizure duration usually > 1 min

(van Dijk et al. 2009)

JG van Dijk, RD Thijs, DG Benditt, W Wieling. Nat. Rev. Neurol. 2009;5:438–48.

Functional ‘psychogenic‘ Pseudo-epilepsy

„*Psychogenic nonepileptic seizures (PNES)“*

frequently misdiagnosed as epilepsy
(20% in tertiary epilepsy clinics)
women >> men; young > old individuals,
high frequency of attacks,
multiple somatic symptoms,
no somatic explanation

psychological problems,
stress (acute, chronic),
history of abuse
(physical and/or sexual)

repeated evaluations
(outpatient / inpatient clinics)

eyes almost always closed !
less often trauma
(HOWEVER: observed in > 50% of cases!)
rarely tongue biting & incontinence

Alternating movements,
“arc de cercle”
pelvic thrusting
movements change in nature,
wax and waning severity

frequently induced by verbal suggestion or various provocations

JG van Dijk, RD Thijs, DG Benditt, W Wieling. Nat. Rev. Neurol. 2009;5:438–48.

(Functional or psychogenic) “Pseudo-syncope”

mimicks loss of consciousness !

not characterized by jerks

eyes closed

triggered eventually while lying down,

eventually on a tilt table test,

<u>absence</u> of low blood pressure and/or

low heart rate

➔ rules out syncope !

Duration: many minutes

(longer than in syncope)

can recur dozens of times in one day

slow recovery, weeping might occur

up to 6% of presumed syncope episodes!

different muscle tone than in truly unconscious person

(e.g. passively raised leg does not drop flaccidly

but is briefly held up)

evtl. sudden & active eye closure upon

passive opening of eyelids reflexive gaze movements:

eyes turned upwards, downwards or away from observer

ice water irrigation ➔ intense nystagm in awake person

in comatose person : more commonly deviation of eyes)

<u>heart rate, blood pressure & EEG normal</u>

neurological signs not compatible

with true unconsciousness

Pseudo-unconsciousness lasts too long

to be confused with syncope !

(Thijs et al. 2004, van Dijk et al. 2009)

TIA in vertebrobasilar territory

inadequate cerebral blood flow

rarely complete loss of consciousness,

unconsciousness occurs only if ascending reticular activating system (ARAS) is affected

➔ **only TIAs in vertebrobasilar territory might cause TLOC !**

typical acute focal neurological signs

diplopia, dysarthria, vertigo, hemiparesis

75% of TIAs last > 5 minutes

= too long for syncope !

Rule of thumb:

TIAs cause neurological deficit without unconsciousness.

Syncope causes unconsciousness without neurological deficit.

Subclavian-Steal-Syndrome:

arterial stenosis or occlusion

low blood pressure beyond stenosis

blood diverted from another artery to low-pressure region

subclavian artery stenosis

post stenotic artery receives blood from ipsilateral vertebral artery

➔ hypoperfusion in vertebrobasilar territory

Symptoms manifest during vigorous activity of affected arm

Blood pressure difference between arms

Unknown whether or how often unconsciousness occurs due to subclavian steal syndrome.

(Thijs et al. 2004)

Other disorders

Metabolic causes

hypoxia, hypoglycemia, hypocapnia

➔ decreased energy supply

➔ coma

(Kapoor et al. 1989, Linzer et al. 1990, Salins et al. 1992 , Shen & Gersh 1997)

'drop attacks'

[confusing term describing any sudden fall]

- middle-aged women

  (in rare cases men)
- sudden fall
- patients land on their knees & hands
- no loss of consciousness
- unknown cause

Cataplexy

loss of muscle tone due to emotions

(e.g. laughter, unexpected situation)

At times residual muscle tone stops fall!

Patient is unable to respond

but completely conscious & aware

NO AMNESIA !

(but patient may fall asleep

& forget attack)

frequently associated with

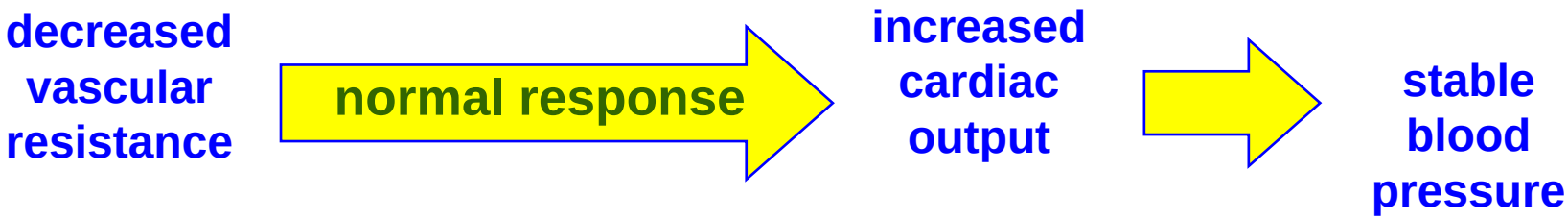
Narcolepsy:

➔ excessive daytime sleepiness

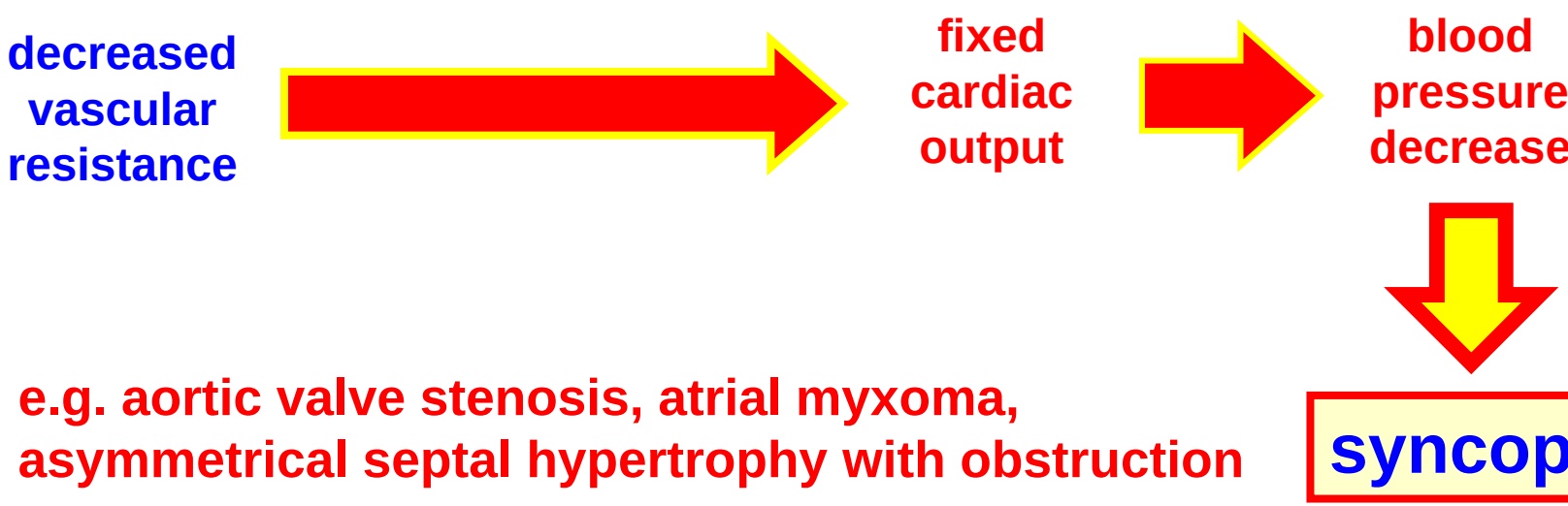
(Thijs et al. 2004; van Dijk et al. 2009)

Cardiac syncope – HIGH RISK !

Cardiac syncope due to structural heart disease



In structural heart disease



e.g. aortic valve stenosis, atrial myxoma, asymmetrical septal hypertrophy with obstruction

(Shen & Gersh 1997)

Cardiac syncope – HIGH RISK !

Rhythmogenic Syncope

Bradycardia

- sinus node dysfunction
- atrioventricular node dysfunction, grade 2 & 3
- malfunction of pacemaker or implantable cardioverter–defibrillator
- drug-induced

Tachycardia

supraventricular or ventricular

- familial ion channel disease
  - Brugada syndrome,
  - long QT syndrome
  - (Romano-Ward syndrome)
- defibrillator malfunction
- drug-induced (OFTEN !)

Van Dijk et al, 2009.

TLOC patient must have specialist cardiovascular assessment within 24 hours if there is any of the following red flags:

- Transient loss of consciousness during exertion
- new or unexplained breathlessness
- heart failure
- family history of sudden cardiac death in patients younger than 40 years and/or an inherited cardiac condition
- a heart murmur
- any of the electrocardiographic abnormalities on the right (box):

- inappropriate persistent **bradycardia**
- **conduction abnormality**
  (e.g., complete right or left bundle branch block or any degree of heart block)
- left or right **ventricular hypertrophy**
- long **QT interval** (corrected >450 ms)
  & short QT interval (corrected <350 ms)
- **pathological Q waves**
- **ventricular pre-excitation**
- any **ventricular arrhythmia** (including ventricular extrasystoles)
- **Brugada syndrome**
- **paced rhythm**
- any **abnormalities in ST-segment or T-wave**, especially abnormal T- wave inversion

Westby M, et al. BMJ. 2010;341:c4457.

References

Brignole, M., R. Sutton, et al. (2006). "Early application of an implantable loop recorder allows effective specific therapy in patients with recurrent suspected neurally mediated syncope." Eur Heart J 27(9): 1085-1092.

Hilz MJ. (2015) Synkopen. In: Hacke W, Bendszus M., Ringleb P, Schwab S., Wick W (eds.): Lehrbuch der Neurologie, 14th ed.. Springer, Heidelberg, (in print)

Hilz, M. J., H. Marthol, et al. (2002). "[Syncope - a systematic overview of classification, pathogenesis, diagnosis and management]." Fortschr Neurol Psychiatr 70(2): 95-107.

Kaufmann, H. (1997). "Neurally mediated syncope and syncope due to autonomic failure: differences and similarities." J Clin Neurophysiol 14(3): 183-196.

Thijs, R. D., W. Wieling, et al. (2004). "Defining and classifying syncope." Clin Auton Res 14 Suppl 1: 4-8.

van Dijk, J. G., R. D. Thijs, et al. (2009). "A guide to disorders causing transient loss of consciousness: focus on syncope." Nat Rev Neurol 5(8): 438-448.

Westby M, Bullock I, et al. (2010). Guideline Development Group. TLOC—initial assessment, diagnosis, and specialist referral: summary of NICE guidance. BMJ. 2010;341:c4457.

