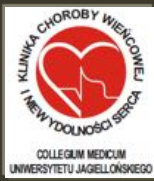


Changes of nitric oxide serum concentration during head-up tilt test in patients with vasovagal syncope

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Declaration of interest

I have nothing to declare

Introduction

- There are some studies demonstrating that the magnitude of the forearm vasodilation during syncope is larger than that which can be explained on the basis of sympathetic withdrawal alone
- Pronounced vasodilation during vasovagal syncope indicate the role of endothelium in its pathomechanism. The endothelial release of nitric oxide seems to be an important factor in the vasovagal syncope.

The aim of study

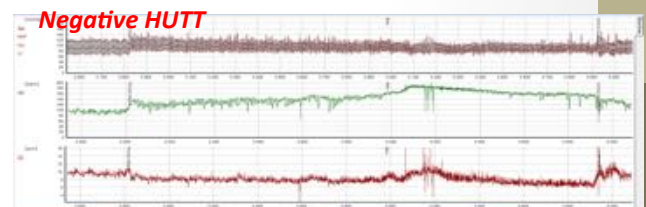
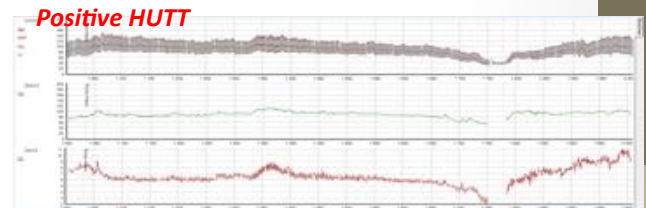
- The aim of study was evaluation of Nitric Oxide (NO) serum changes during head-up tilt-test in patients with vasovagal syncope (VVS).

Study population

- 25pts with VVS referred to HUTT
- Without disorders leading to endothelial dysfunction
(*like hyperlipidaemia, diabetes, arteriosclerosis, hypertension*)
- 11 men, 14 women,
- Aged 18-42 years (median of age: 21yrs).
- Cardio- and neurological causes of syncope were previously excluded in all studied pts

Methods

- In all pts HUTT, according to Westminster protocol, was done with sublingual nitroglycerine (NTG) provocation, in case of negative result of passive tilting.
- During HUTT continuous, non-invasive beat-to-beat monitoring of heart rate and blood pressure were performed using NEXFIN (Bmeyer) monitor.



Methods

- At least 30 minutes before HUTT antecubital vein was cannulated for blood samples collection.
- Serum concentration of nitrate (NO_3^-) and nitrite (NO_2^-) were evaluated

(blood samples were collected in heparinised tubes , centrifuged at 1500 g for 15 min in 4°C , than plasma samples were frozen at -80°C and stored until analysis.)

- Blood samples were taken before the HUTT, after completion of both – passive and active phases (after NTG provocation) and 15 minutes after finishing the test (syncope induction or protocol completion)

Methods

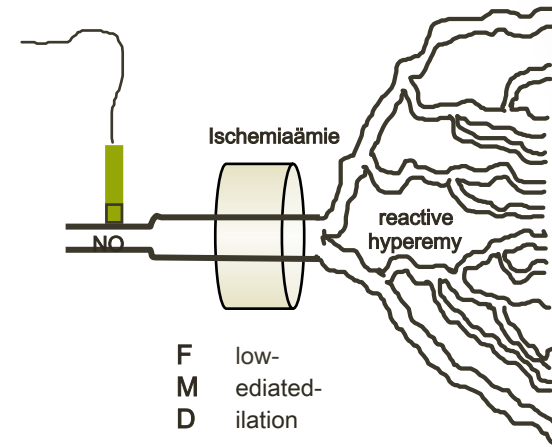
- The nitrate and nitrite concentration in plasma was measured by sensitive high-pressure liquid chromatography techniques
(ENO-20 NO_x Analyser; EiCom, Kyoto, Japan).
- Serum concentration of NO was evaluated as the difference before concentration of NO₂⁻ and NO₃⁻.
- Changes of NO serum concentrations during HUTT were analysed in relation to the type of vasovagal response during the test.

Methods

- The day before HUTT all pts underwent evaluation of endothelial function using ultrasound measurement of brachial artery diameter
- There were two parameters measured
 - Flow-mediated dilation (FMD) of the brachial artery after passive hyperaemia
 - Endothelium-independent vasodilation (EID) - result of direct extension of artery by nitroglycerin, used to determine the upper limit of arterial diastolic reaction.
- ROC curves analysis was used to evaluate the values of FMD and EID in prediction of positive result of HUTT.

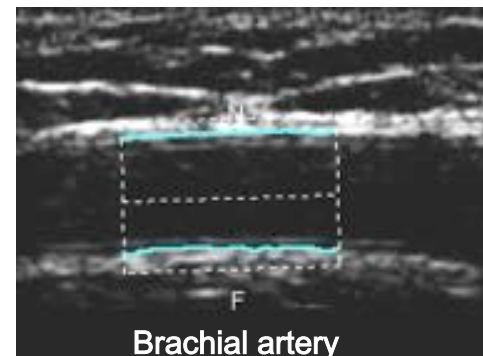
Evaluation of endothelium function

- FMD

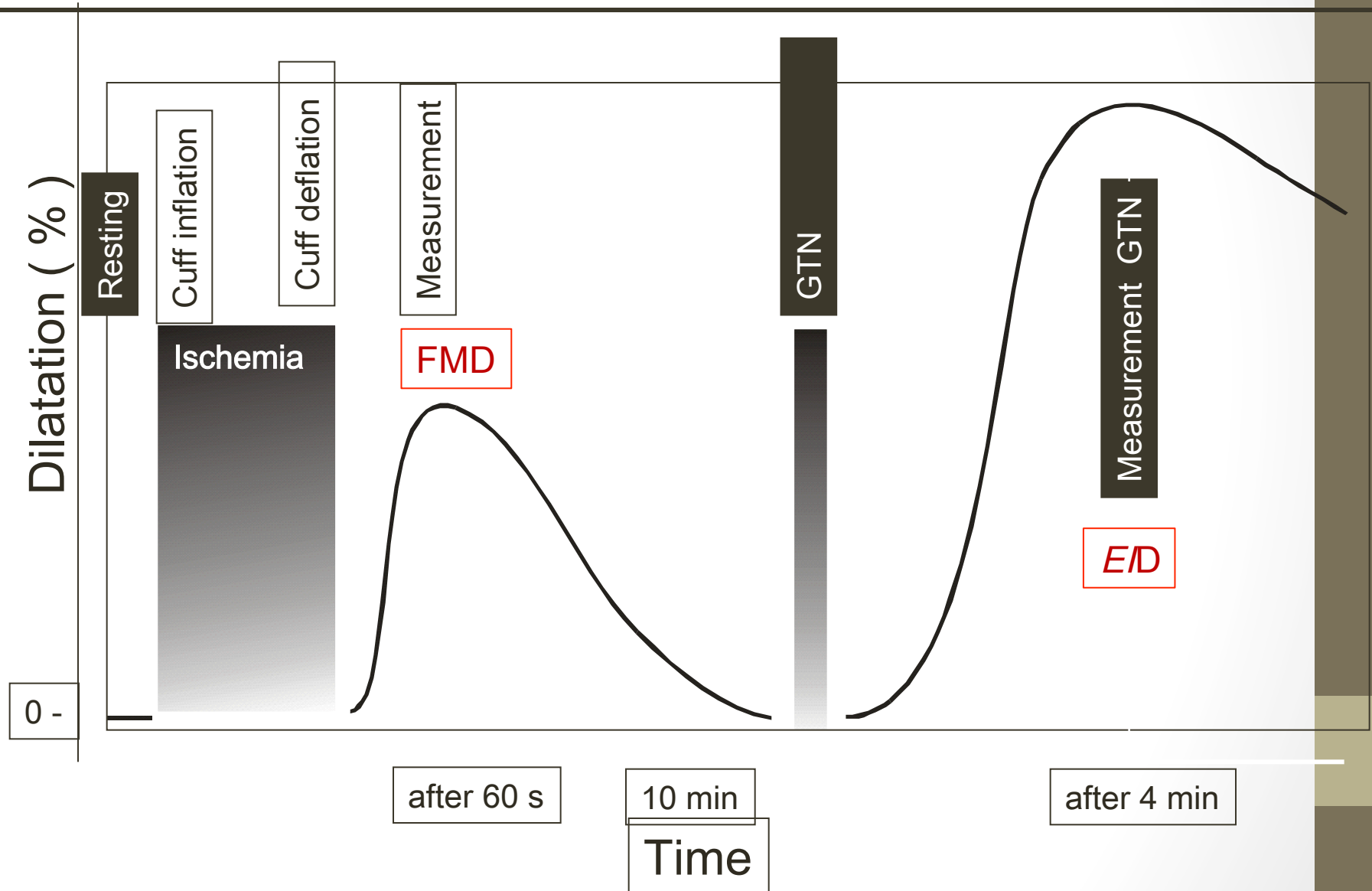


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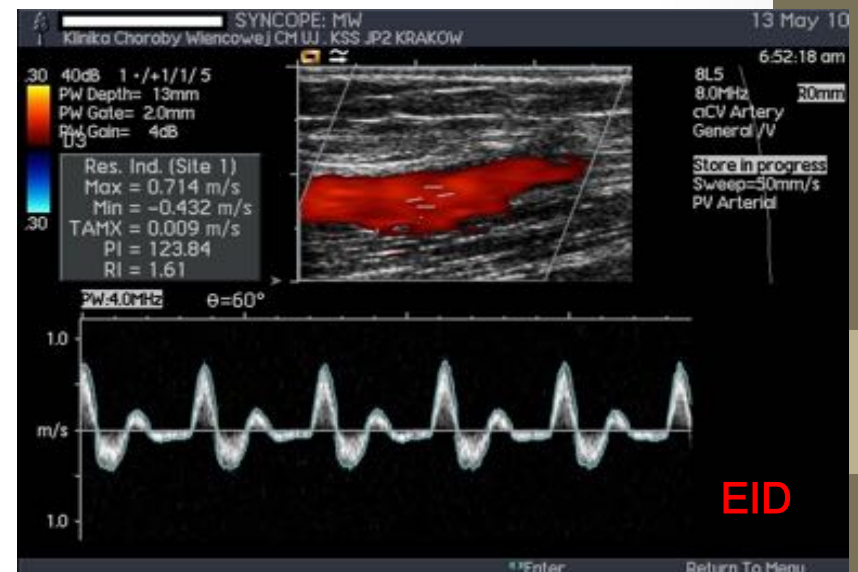
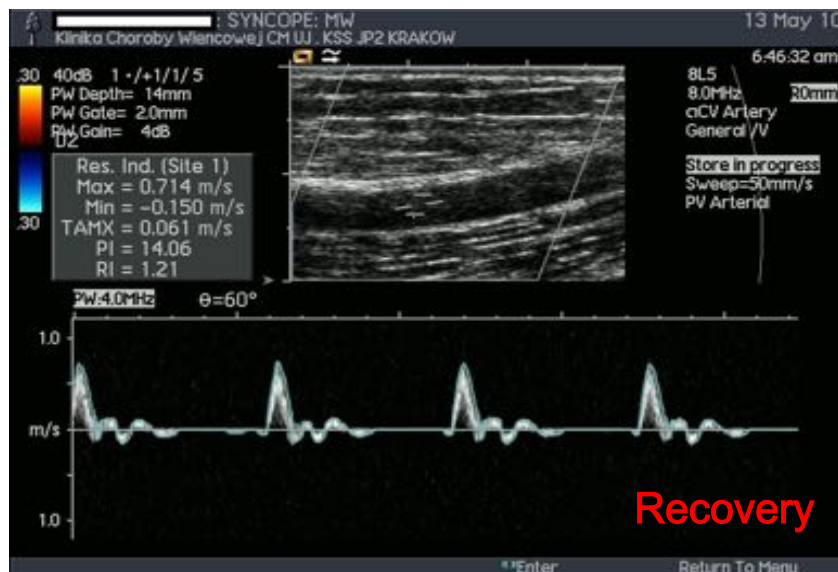
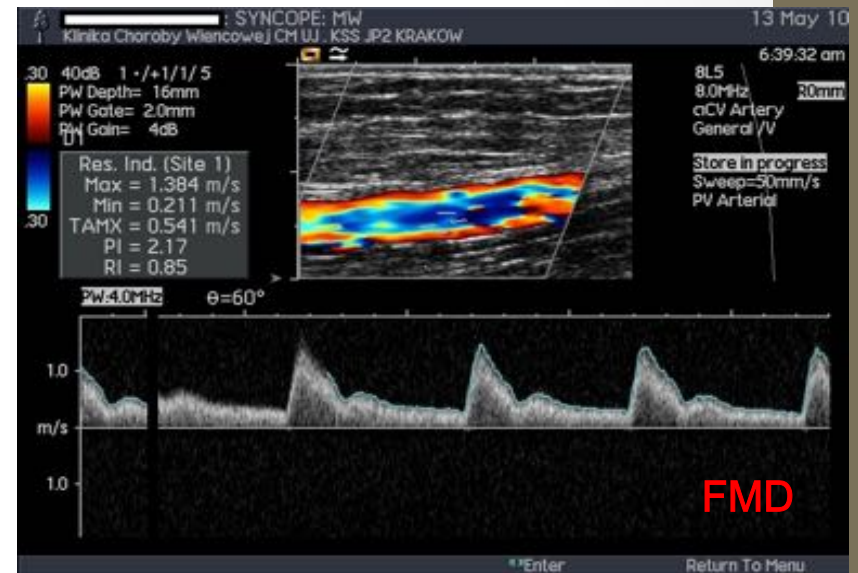
Mikro



Flow mediated dilation – Protocol



FMD and EID



Results

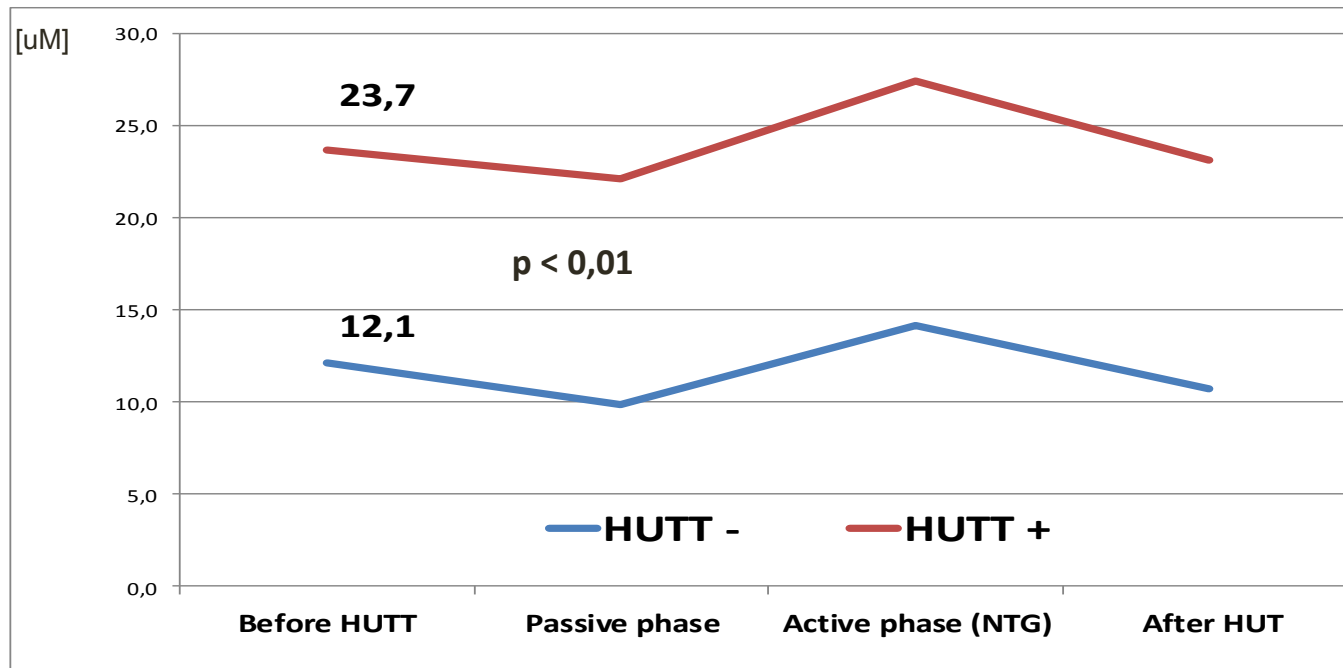
HUTT was positive in 21 pts (84%)

- 5 pts. (20%) had cardioinhibitory response,
- 14 pts. (56%) – mixed response
- 2 pts. (8%) – vasodepressive response

All pts required NTG provocation during HUTT

Results

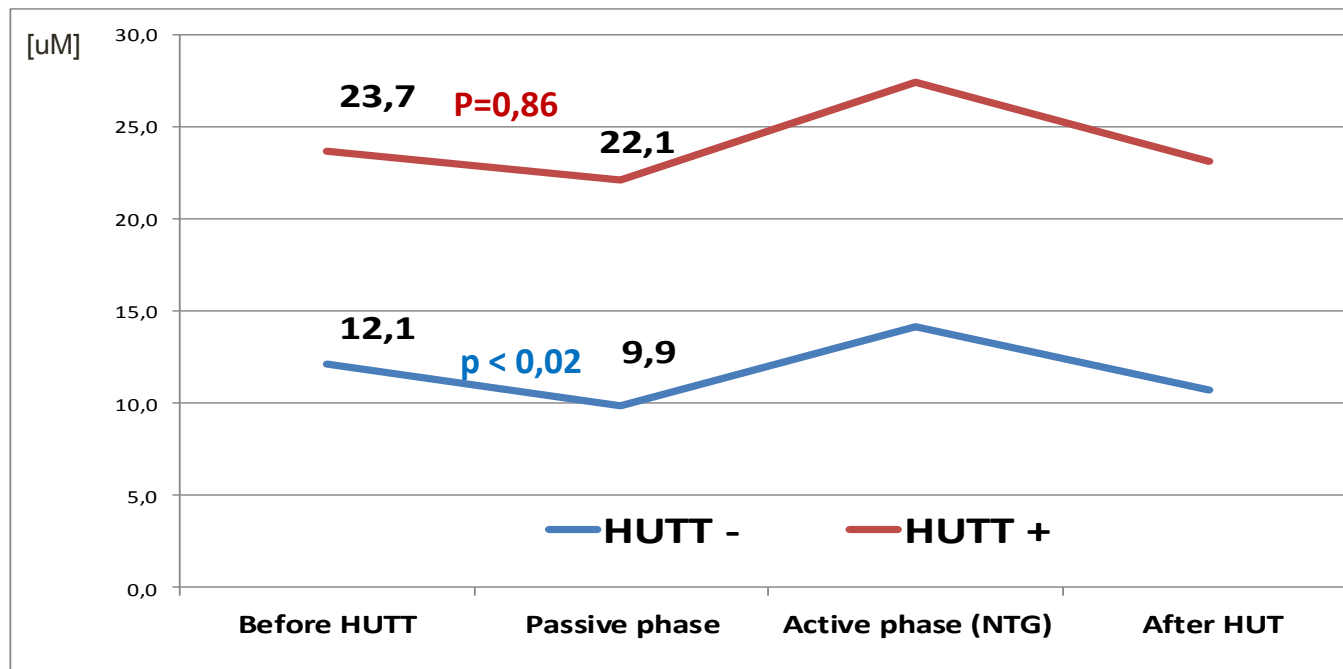
Before the test serum NO concentration in pts with negative HUTT was significantly lower in relation to pts with positive HUTT (12,2 vs 22,6 uM).



Serum NO concentration during HUTT

Results

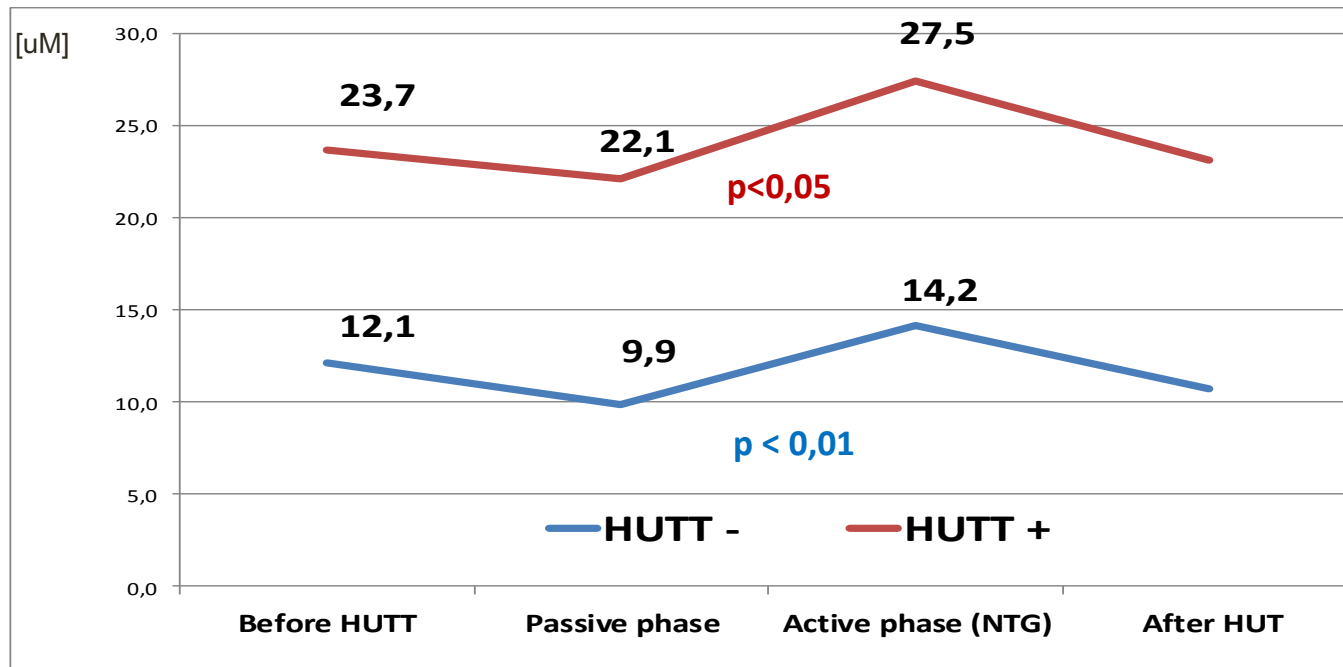
After completion of passive phase of HUTT significant decline of NO concentration was noticed in HUTT-negative pts., whereas pts with positive HUTT revealed non-significant trend to decrease.



Serum NO concentration during HUTT

Results

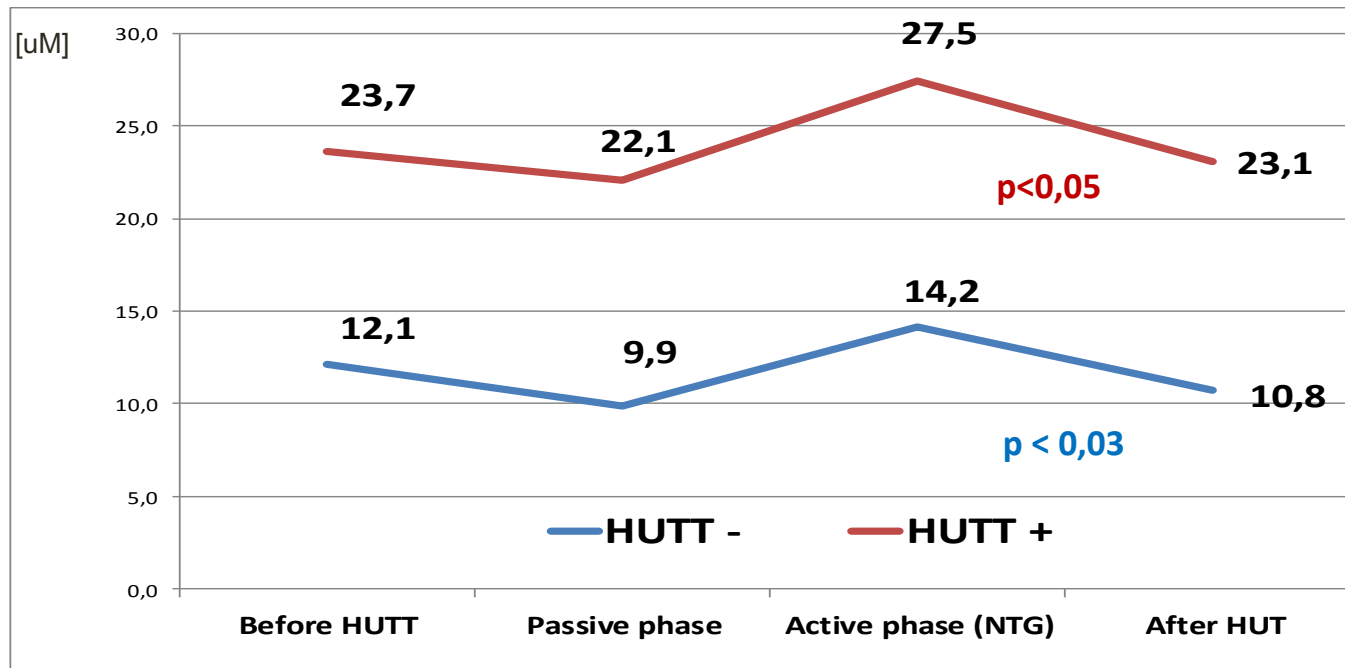
After sublingual NTG administration, increase of NO concentration was observed in both HUTT negative and HUTT positive pts.



Serum NO concentration during HUTT

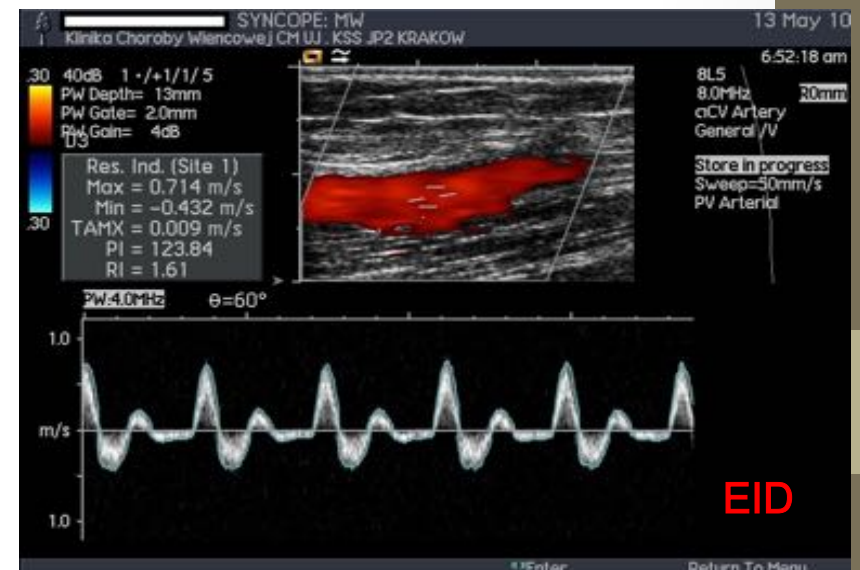
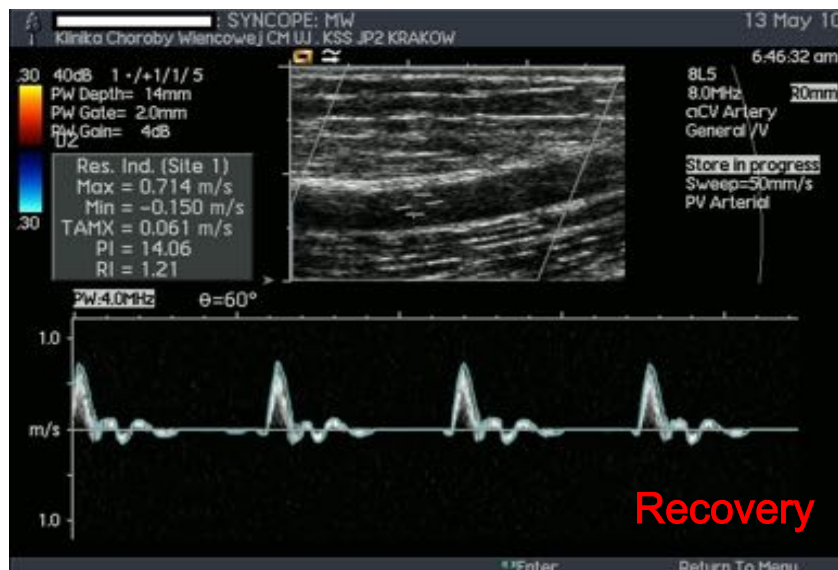
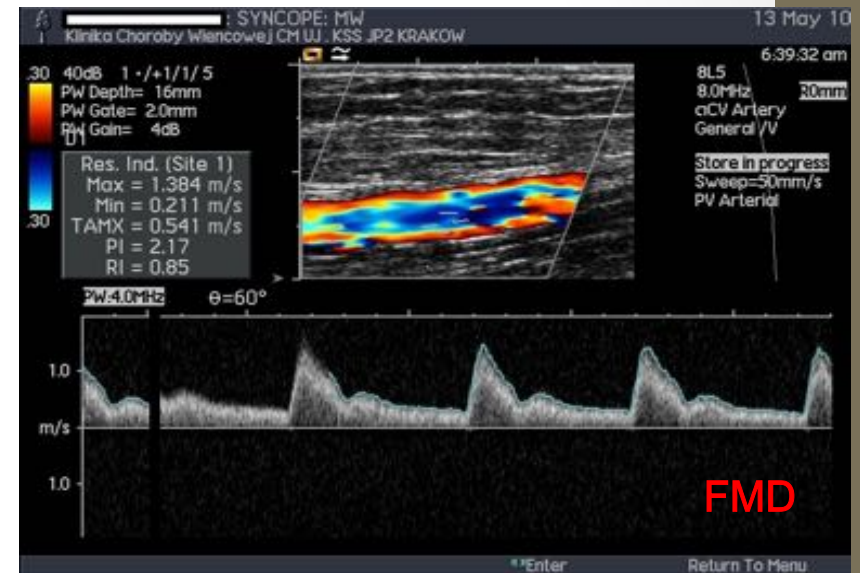
Results

After the test, NO concentration decreased below the value observed prior to HUTT.

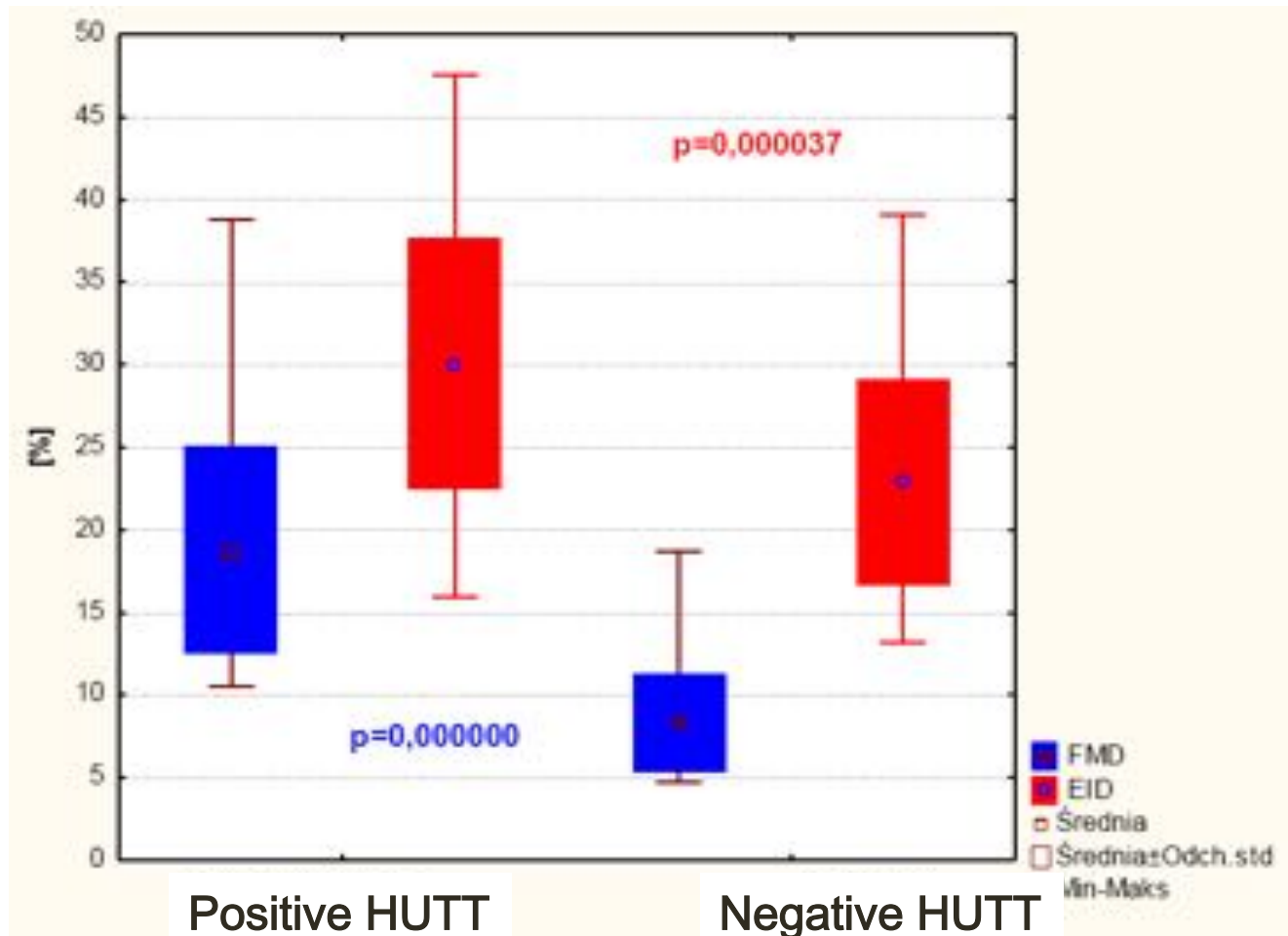


Serum NO concentration during HUTT

FMD and EID



FMD and EID in pts. with VVS



Results

- There were no relations between serum NO concentration and type of vasovagal response to the orthostatic stress.
- There were no relations between FMD and EID values and type of vasovagal response to the orthostatic stress.

Results

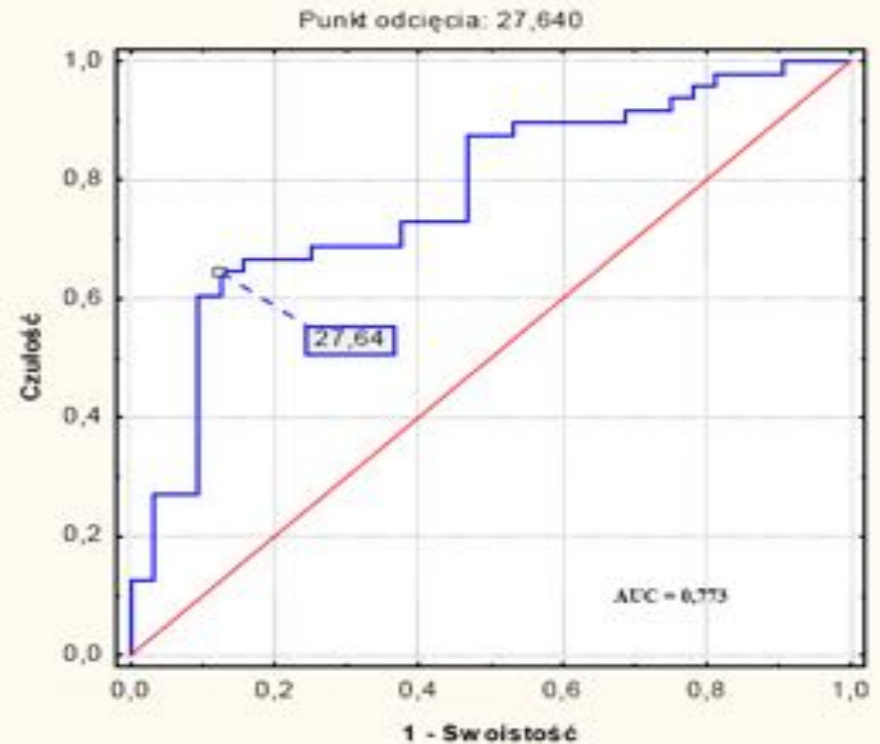
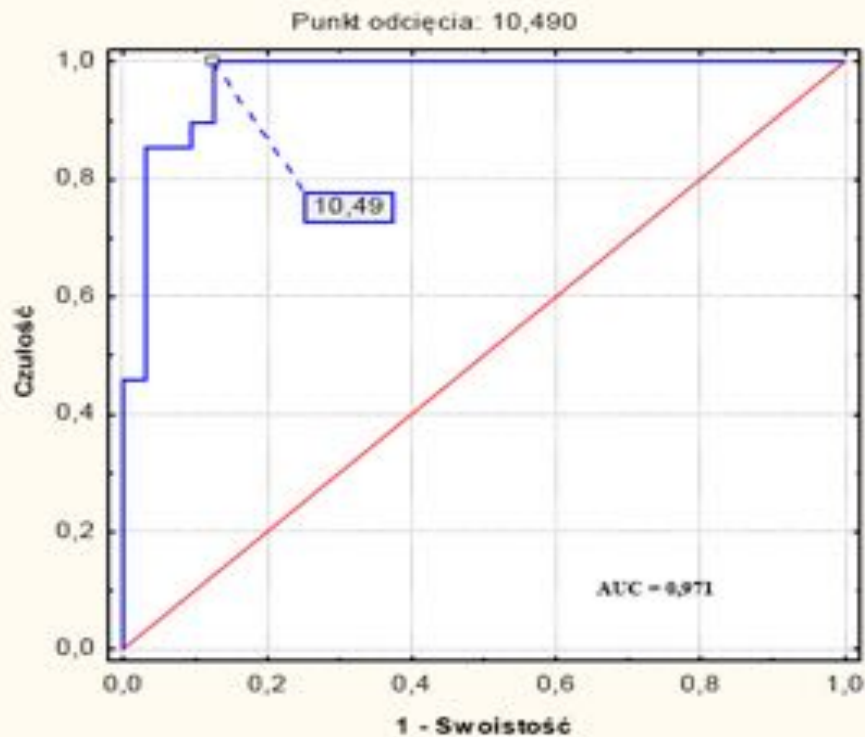
- Significant correlation was observed between NO concentration during HUTT (all phases) and values of FMD and EID

(k ranged *from 0,282 to 0,326* $p < 0,02$)

FMD and EID in pts. with VWS

Value of FMD in prediction positive result of HUTT

Value of EID in prediction positive result of HUTT



Conclusions:

Serum nitric oxide concentration decreased during the passive phase of HUTT, then significantly increased after NTG provocation and finally decreased below initial values. This changes were much more pronounced in patients with negative result of the HUTT

Conclusions:

Syncope induction during HUTT was related to significantly higher values of serum nitric oxide concentration, as well as higher values of both: FMD and EID in relation to the HUTT-negative patients.

Conclusions:

Endothelial dependent changes of nitric oxide concentrations seem to play an important role in the pathomechanism of vasovagal response to orthostatic stress in patients with vasovagal syncope.



Thank you for your attention