Introduction:
Impaired cerebrovascular reactivity (CAR) after traumatic brain injury (TBI) is a marker for disease severity and poor outcome. It is unclear how dynamic changes in body temperature and fever impact CAR and outcome.

Methods:
We calculated the pressure reactivity index (PRx) using the CENTER-TBI high-resolution intensive care unit cohort, as a moving correlation coefficient between intracranial pressure (ICP) and mean arterial pressure (MAP). Minute and hourly values of PRx and temperature were averaged in patients with simultaneous recording of ICP and ABP. Demographic data was based the Core Registry (V2.0). Linear mixed models were calculated based on minute-by-minute data using R with lme4 V1.1-21 and ggeffects V0.9.0. Generalized estimating equation models were used to analyze changes during effervescence (increase of temperature of >1°C within 3 hours).

Results:
We assessed high frequency physiological data during 567 days of 102 patients admitted to the ICU with predominantly a closed injury type (N=94/102). Median age was 46 years (IQR 29-62), baseline GCS was 6 (IQR 3-9), and 27% had at least one unreactive pupil. The main measurement site for temperature was the urinary bladder 55/102 (54%). Half of the patients (49/102) developed fever (>1h with mean T ≥ 38.3°C) with a total of 834h fever and a median of 9h fever (IQR 4-24) per patient. Of 110 effervescence episodes 30 (27%) reached the febrile threshold of 38.3°C which was associated with an increase in PRx from 0.09 (±SD 0.25) at baseline (2h before) to 0.26 (±SD 0.3) during the febrile peak (p=0.014) (Figure 1-A). Linear mixed models showed a quadratic relationship between PRx and temperature (p<0.001) with an increase in predicted PRx with febrile and hypothermic temperatures (Figure 1B).

Conclusion:
The association of increasing body temperature with worsening of CAR supports prevention of fever in severe TBI. Prospective studies are needed to further differentiate between mechanisms involved (i.e. inflammation) and central autonomic dysregulation.
Figure 1. A) Changes in mean PRs during episodes of effervescence (1°C within 3 hours); B) Predicted relationship between PRs and temperature based on mixed linear models.