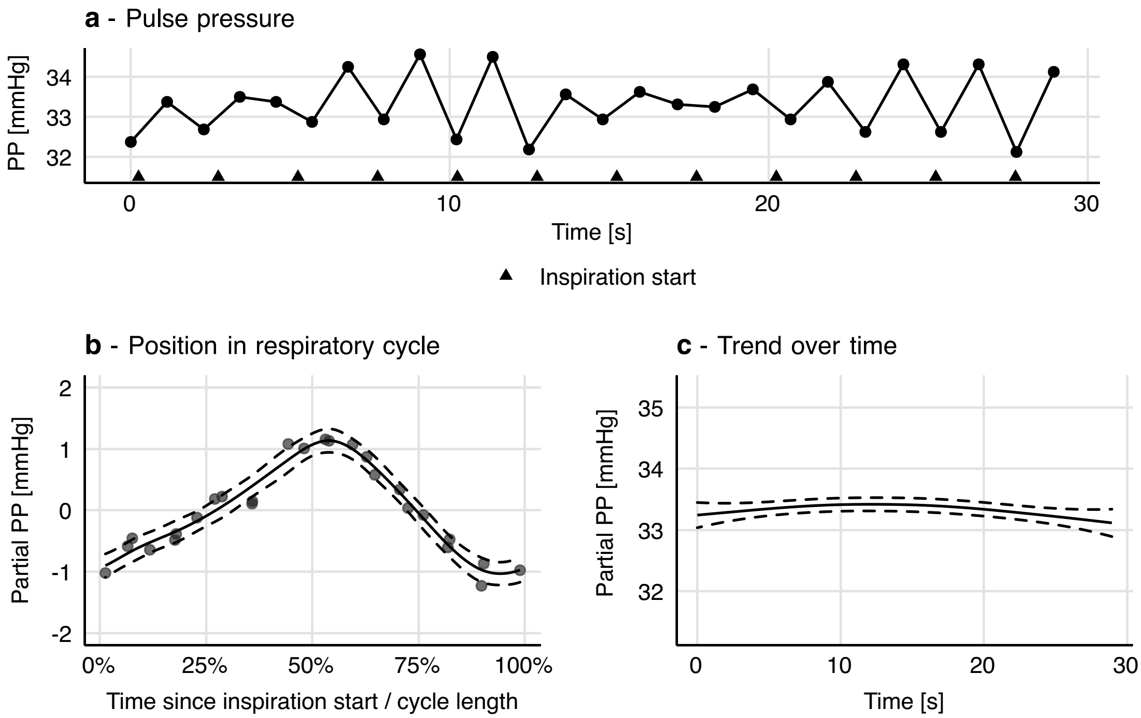

Fig. 3 This patient has a heart-rate-to-respiratory rate ratio just beyond 2:1 (52:24). **a** From the pulse pressure (PP) plot, it is difficult to assess pulse pressure variability (PPV), and it seems to be changing. **b** When PP is modelled as a smooth function of each beat's position in the respiratory cycle, a tight relationship between respiration and PP is revealed. Dashed curves represent 95% confidence intervals

After fitting the model, we can inspect the model by plotting the smooth functions over a relevant interval (usually the interval containing the original observations) (see Fig. 2c and d). In our model of pulse pressure, $f\left(pos_{ventilationcycle}\right)$ represents the variation in pulse pressure with each respiratory cycle. Thus, we can use $f\left(pos_{ventilationcycle}\right)$ to calculate PPV.

$$PPV = \frac{max\left(f\left(pos_{ventilationcycle}\right)\right) - min\left(f\left(pos_{ventilationcycle}\right)\right)}{\alpha},$$

where $pos_{ventilationcycle}$ is between 0 and 100%.

Since α is the mean PP, this is equivalent to the classic formula for PPV:

$$PPV = \frac{PP_{max} - PP_{min}}{\left(PP_{max} + PP_{min}\right)/2}.$$

Calculation of a confidence interval for PPV is described in Online Resource 1.

Essentially, a GAM facilitates the "step" from panel b to panel c in Fig. 2, where the highly deterministic effect of heart–lung interactions on pulse pressure is uncovered. Calculating PPV from a GAM model takes every beat in our sample into account. This makes the PPV estimate less sensitive to outliers (min and max being inherently very sensitive to outliers). Also, PPV estimated from individual respiratory cycles will tend to be lower than PPV calculated from a GAM, by a somewhat random amount. Heart beats occur at varying positions in the respiratory cycle; often not at the positions giving both the maximum and minimum pulse pressure. This is especially important in conditions with few beats per ventilation [17] (see Fig. 3). Details about the shape and phase of $f\left(pos_{ventilationcycle}\right)$ may also contain important information about the heart–lung interaction, though this has not yet been investigated.

2.3 Example 2: Central venous pressure

Hemodynamic waveforms are affected by both the heart and the lungs. The CVP waveform has a fast period with the length of one cardiac cycle and a slower period with the length of one respiratory cycle. For each cardiac cycle, well-defined features represent atrial contraction (*a*), tricuspid valve closing (*c*), ventricular contraction (*x'*), atrial filling during ventricular systole (*v*) and tricuspid valve opening (*y*) [18, 19] (CVP landmarks are shown in Fig. 4b). If the patient is on a ventilator, the entire CVP waveform will rise with the inspiration and fall with the expiration (see Fig. 4a). A third effect is the interaction between the cardiac cycle and the respiratory cycle. A cardiac cycle during inspiration produces a CVP waveform that is different from what is produced during expiration. Lastly, a number of factors