Palatal prolapse as a signature of expiratory flow limitation and inspiratory palatal collapse in patients with obstructive sleep apnea

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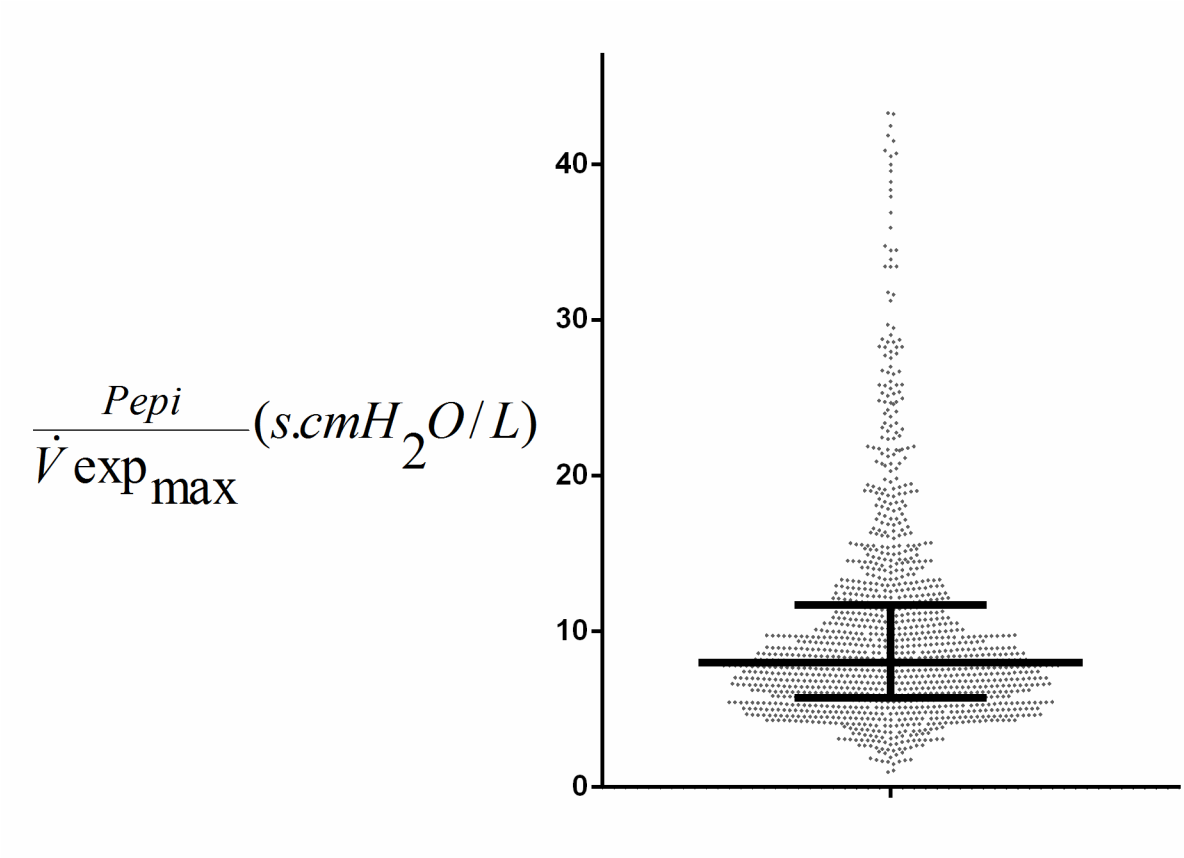

Figure S1: The scatter plot of the expiratory resistance at peak expiratory flow ($R_{aw/normal} = 8.0\ (5.7, 11.7)\frac{cmH_2O}{L/s}$).

Non-invasive Expiratory flow limitation index (EFLI): Palatal prolapse causes expiratory flow limitation and produces a distinct flow shape during expiration (Figure S2) that can be quantified objectively. Therefore, we sought to quantify this distinct expiratory flow shape in an automated manner.

To objectify and automate the recognition of palatal prolapse and expiratory flow limitation, several signal processing steps were taken. First, the expiratory phase of each breath

($\dot{V}_{exp}$) was identified using a previously validated technique for determining the onset and offset of each breath(1). Second, the index $\frac{\mathrm{rms}(\dot{V})^2}{\max(|\dot{V}|)^2}$ was quantified for each breath. The $rms(\dot{V})$ is the root-mean-square of expiratory flow and $\max(|\dot{V}|)$ reperesents the peak absolute value of expiratory flow. This index represents the average power of the expiratory flow signal normalized by the maximum expiratory flow. A low number indicates EFL, whereas a high number indicates no EFL. Therefore, to make the ratio higher for EFL breaths, it was subtracted from 1. We found that this index, when applied to expiratory flow ($\dot{V}_{exp}$), provided a reasonable separation (with an approximate detection accuracy of 85%) between EFL and non-EFL breaths (Figure S2, top row). Thus, to make the index more robust, a third signal processing step was taken: the expiratory airflow was divided into odd and even components. The odd component of the signal ($\dot{V}_{exp,odd}$) was obtained by adding the expiratory flow to its flipped (with respect to the mid expiration) and inverted version and dividing the result by 2, whereas the even part can be obtained by adding the expiratory flow to its flipped (with respect to the mid expiration) version and dividing the result by 2. We only used the odd component, $\dot{V}_{exp,odd}$, to calculate the expiratory flow limitation index ($EFLI = 1 - \frac{\mathrm{rms}(\dot{V}_{exp,odd})^2}{\max(|\dot{V}_{exp,odd}|)^2}$). The reason for only using the odd component is that it suppresses a flat and non-zero expiratory flow signal, which is usually seen in EFL breaths and not captured by this index when the whole expiratory flow is used (Figure S2, second column). The accuracy of detecting palatal prolapse was improved, as shown below. Figure S2 also shows how EFLI varies from a breath with no palatal prolapse (first column) to a breath with palatal ballooning (second and third columns) and to a breath with severe palatal prolapse (fourth column).

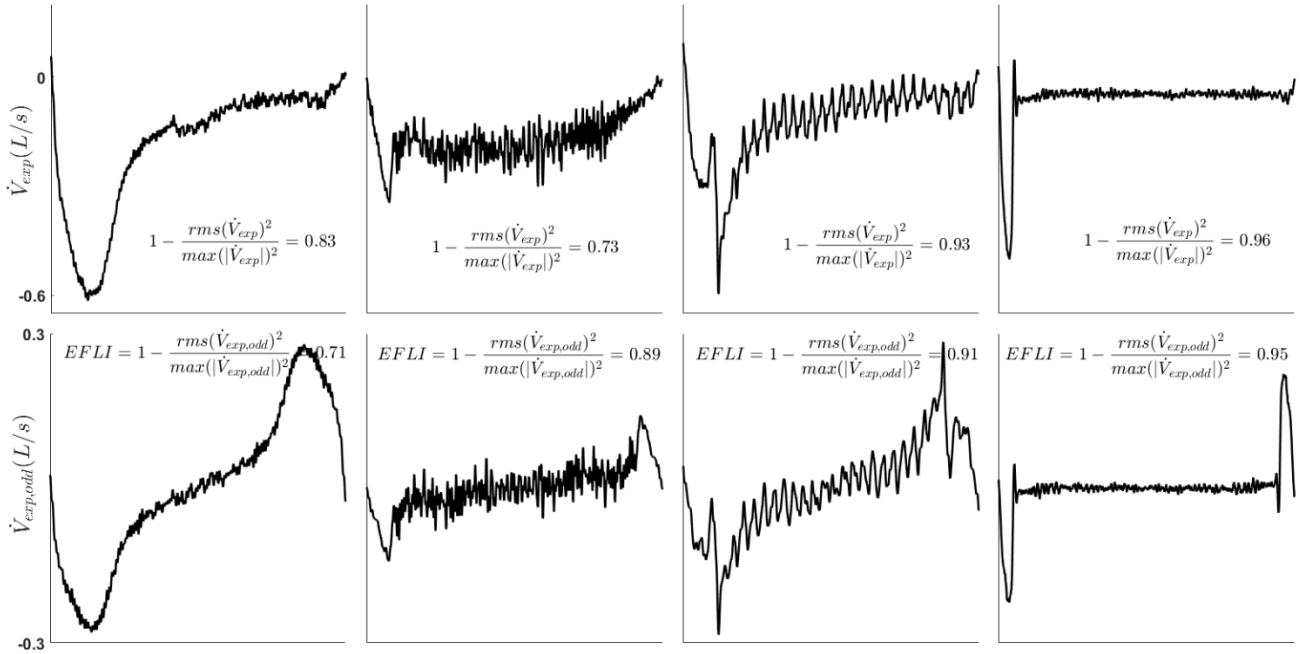

Figure S2: The top row shows the expiratory flow ($\dot{V}_{exp}$) of a normal expiration (first column), a breath with ballooning of palate causing mild expiratory flow limitation and high frequency fluttering (second column), a breath with ballooning of palate causing moderate expiratory flow limitation and intense low frequency fluttering (third column), and lastly a breath with a nearly complete palatal prolapse and severe expiratory flow limitation (last column). $EFLI$ is higher for breaths with expiratory flow limitation as compare to those without EFL.

Example traces: Figure S3(a) demonstrates example breaths that were associated with palatal prolapse during expiration, resulting in an increase in epiglottic pressure and an abrupt and severe reduction in expiratory flow through the nose. This phenomenon produced distinct expiratory flow shapes (Figure S3(a)) that were quantified automatically by the EFLI. In contrast, breaths without palatal prolapse, shown in Figure S3(b), had "normal" and non-flow limited expiratory flow, resulting in lower values of EFLI (EFLI<0.8).

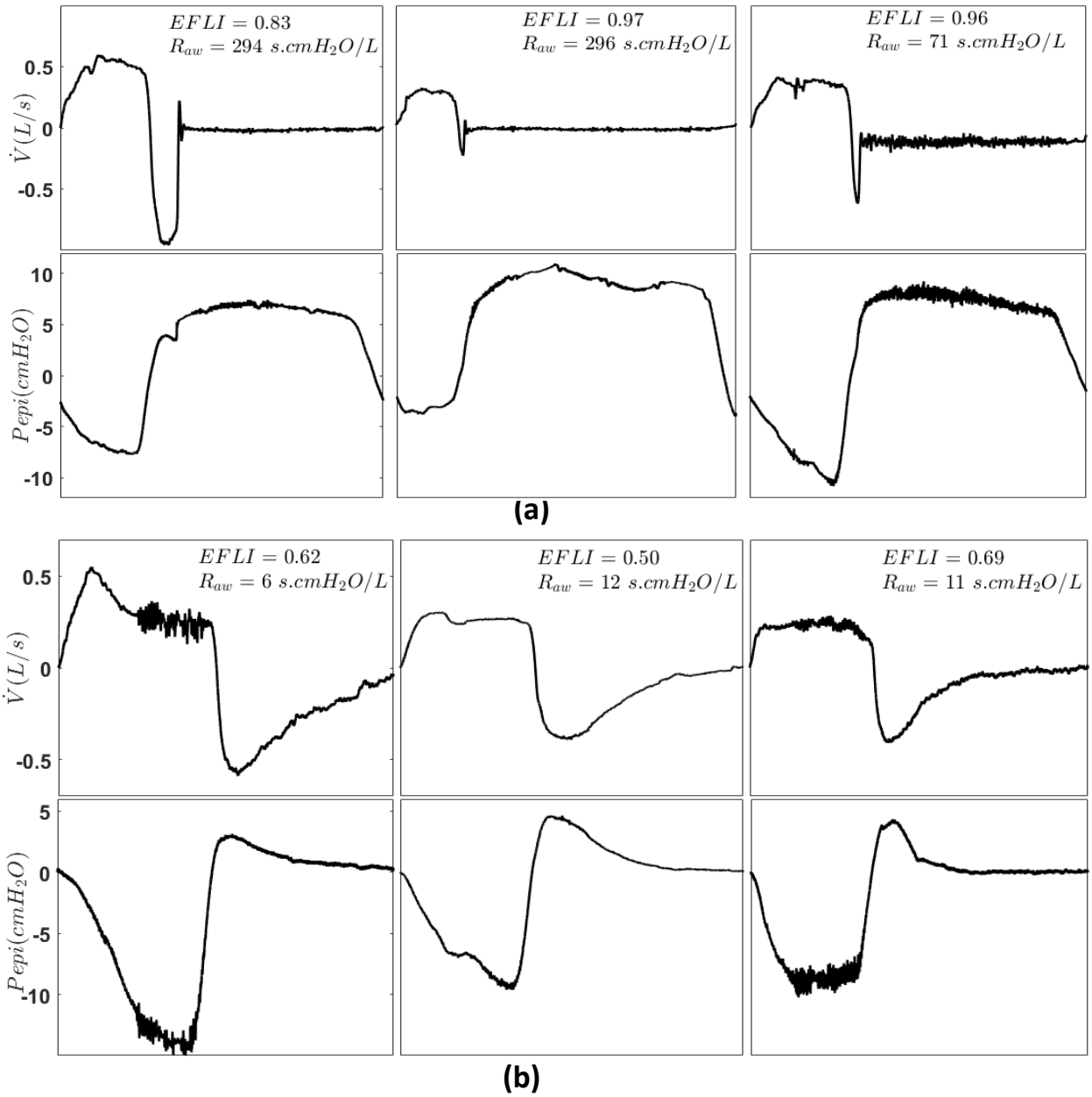

Figure S3: (a) Example breaths associated with EFL and palatal prolapse. There is no nasal flow despite an increase in deriving pressure which causes the redirection of expiratory flow through the mouth. This resulted in high values of airway resistance at peak epiglottic pressure (R_{aw}) during expiration (calculated from nasal flow ($\dot{V}$)and epiglottic pressure ($Pepi$)). EFL, caused by palatal prolapse, can be identified from expiratory flow limitation index ($EFLI$) proposed in this study (i.e. $EFLI > 0.8$). (b) Example breaths without EFL, resulting in low values of R_{aw} (i.e. <20 $\frac{cmH_2O}{L/s}$) and $EFLI$ (i.e. < 0.8)

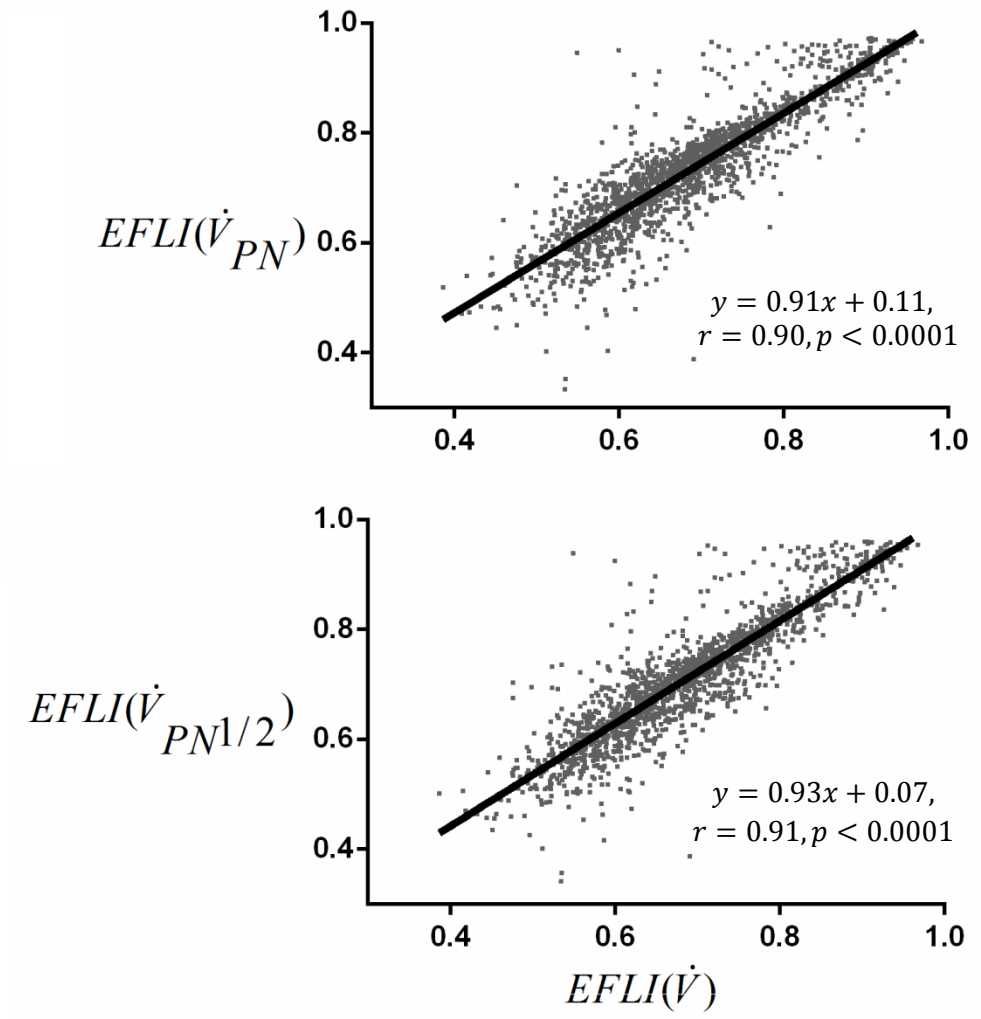

Figure S4: The EFLI obtained from pneumotach flow ($\dot{V}$) were strongly associated with their corresponding values obtained from both the nasal pressure ($\dot{V}_{PN}$) (top panel) and the linearized nasal pressure ($\dot{V}_{PN^{\frac{1}{2}}}$) (bottom panel).

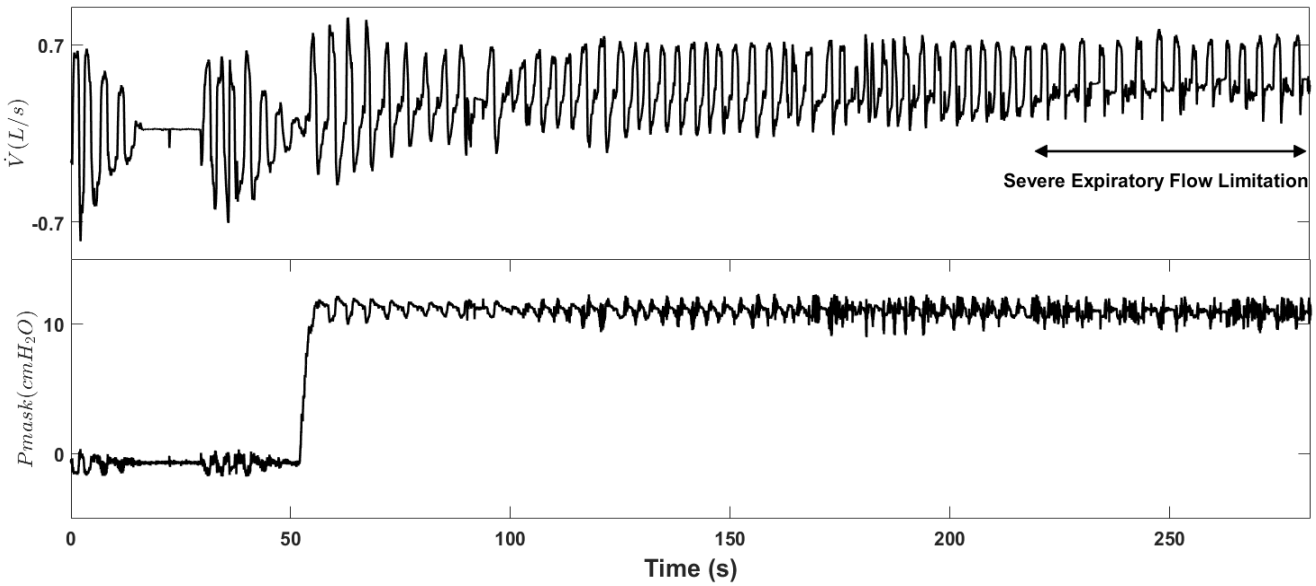

Figure S5: In some patients, palatal prolapse (detected by EFLI) also appears on high CPAP levels (e.g. >10 cmH_2O).

Calculation of lung volume from chest and abdomen band movements:

Quantitative DC-coupled thoracoabdominal respiratory inductance plethysmographic (RIP) signals (Nox A1, Nox Medical, Reykjavík, Iceland) were acquired at 25 Hz in 10 patients during sleep at the same time as we recorded oronasal airflow via a pneumotach and other polysomnographic signals. Calibration of the respiratory belts was performed using the equation $RIPvol(t) = \alpha \times [L_{th}(t)/k^{0.5} + L_{ab}(t) \times k^{0.5}]$, where $L_{th}(t)$ and $L_{ab}(t)$ represent the inductances of the thoracic and abdominal respiratory belts respectively, k represents the relative contribution of the abdomen versus thoracic circumference to the changes in lung volume (i.e. a value of k=2 indicates that a changes in abdominal belt inductance (L_{ab}) must first be multiplied by 2 to reflect the same change in lung volume seen at the thorax), and α is a scaling factor in units of L/H (H is the symbol for henry, the unit of inductance). The power of 0.5

(square root term) was used (rather than RIPvol(t) = $a\times[L_{th}(t)+L_{ab}(t)\times k)]$ so that changing k would have a relatively minimal effect on the magnitude of the signal. For each 5-min window of recording, a custom automated algorithm calculated true tidal volumes for each breath (integrated pneumotachograph volume) and estimated tidal volumes based on the RIPvol signal (see above equation). Values for *a* and *k* were adjusted to best fit the true tidal volumes using linear regression. Fits with $R^2<0.4$ were excluded. A moving time average of *a* and *k* parameters was generated across the night to handle potential changes in RIP calibration across the night (2 hours). Values of *k* were $\log_{10}$ transformed before averaging, then untransformed ($y=10^x$) afterwards (as appropriate for the ratio measure, i.e. k=0.5 and k=2 are equally different from 1 on a log scale). The moving time average was also weighted based on the goodness of fit (R^2).

Of note, the calibrated RIPvol signal represents dynamic changes in lung volume across a short period of time; it is not intended to reflect absolute volumes (i.e. one would not use it to calculate functional residual capacity, but one could calculate vital capacity). The end expiratory lung volume (EELV) from RIPvol signal was used to examine the effect of EFL on EELV.

REFERENCES

1. Azarbarzin A, Sands SA, Taranto-Montemurro L, Oliveira Marques MD, Genta PR, Edwards BA, et al. Estimation of pharyngeal collapsibility during sleep by peak inspiratory airflow. SLEEP. 2016;In press.