Use of pulse transit time as a measure of inspiratory effort in patients with obstructive sleep apnoea

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ABSTRACT: Pulse transit time (PTT) is the time taken for the arterial pulse pressure wave to travel from the aortic valve to a peripheral site. For convenience, it is usually measured from the R wave on the electrocardiogram to the pulse wave arrival at the finger. Pulse transit time is inversely proportional to blood pressure, and the falls in blood pressure which occur with inspiration (pulsus paradoxus) correspond to rises (lengthening) in pulse transit time. In awake normal subjects, the size of these inspiratory rises in pulse transit time correlate well with the degree of inspiratory effort. The aim of this study was to investigate whether inspiratory rises in pulse transit time could provide a quantitative measure of inspiratory effort in patients with obstructive sleep apnoea.

Eight patients with obstructive sleep apnoea, attending the laboratory for institution of nasal continuous positive airway pressure, took part in the study. Once asleep, airway pressure was varied between optimal treatment level and minimum pressure, to produce a range of inspiratory efforts whilst continuous recordings of oesophageal pressure and pulse transit time were made.

There was an excellent correlation between the size of the swings in oesophageal pressure and the size of the swings in pulse transit time (mean r=0.94).

Pulse transit time may, therefore, provide a clinically useful noninvasive and quantitative measure of inspiratory effort in patients with sleep-related breathing disorders. Eur Respir J., 1995, 8, 1669–1674.

Obstructive sleep apnoea (OSA) is characterized by repetitive periods of apnoea occurring during sleep due to collapse of the pharynx and obstruction of the upper airway [1]. Inspiratory efforts increase throughout the apnoea in an attempt to overcome the obstruction, and result in gradually larger pleural pressure swings. The eventual arousal from sleep, and the subsequent termination of the apnoea, is thought to occur usually as a result of these increasing respiratory efforts, rather than the accompanying hypoxia and hypercapnia [2, 3].

Recurrent transient arousals from sleep are probably responsible for the most debilitating symptom of OSA, daytime sleepiness [1], and it is the severity of the daytime symptoms which tend to guide the decision to treat this condition with nasal continuous positive airway pressure (nCPAP).

OSA lies at the severe end of a continuum of deterioration of upper airway patency during sleep. Lesser degrees of upper airway narrowing associated with snoring, increased inspiratory efforts and sleep fragmentation, may also result in decreases in daytime alertness [4–6]. It has even been suggested that there is a syndrome of increased upper airway resistance, causing increases in inspiratory effort and arousals from sleep, in the absence of either snoring or abnormal conventional sleep staging [7]. Thus, current evidence suggests that, because they are the main cause of sleep fragmentation, monitoring increases in inspiratory effort is an important part of a respiratory sleep study, and indeed some centres use it routinely in the diagnosis of sleep disorders [8].

The conventional technique for measuring changes in inspiratory effort is via oesophageal pressure, using either a balloon-tipped catheter or a catheter with a pressure transducer mounted on the end. This technique, however, has a number of disadvantages. Insertion of the catheter is uncomfortable and often unacceptable to the patient, and its presence may contribute to sleep disturbance during the sleep study. In addition, it is time-consuming to set up, requires a specialist technician, and inevitably increases the cost of the sleep study. There is also a growing need for simple techniques, suitable for domiciliary screening sleep studies, and it is difficult to envisage how oesophageal pressure monitoring could be incorporated into such studies. Other more indirect and qualitative measures of changes in pleural pressure which can be used in respiratory sleep studies include snoring and the detection of indrawing of the supraclavicular fossa or suprasternal notch. Rib cage and abdominal paradox can also be used, but this is at best only semiquantitative and tends to be less reliable in the obese.
The development of non-invasive beat-to-beat blood pressure (BP) monitors has allowed the BP profile to be investigated in sleep-related breathing disorders. The size of the falls in systolic blood pressure (SBP) occurring with inspiration (pulsum paradoxus) has been shown to correlate well with the degree of inspiratory effort [9]. All night beat-to-beat SBP tracings have been used successfully in the diagnosis of sleep-related breathing disorders because they contain this information on respiratory effort and also, via BP rises, an estimate of sleep fragmentation [10, 11]. Thus, beat-to-beat BP monitoring should be a useful technique to employ in a respiratory sleep study, however its main disadvantage is that this type of BP monitor is not portable and, therefore, could not be incorporated into a domiciliary sleep study.

Pulse transit time (PTT) is the time taken for the arterial pulse pressure wave (shock wave) to travel from the aortic valve to a peripheral site (usually the finger). The stiffness and tension in the arterial walls are the principle factors determining the speed of transmission of the pulse wave, and this in turn depends to a large extent on blood pressure. An increase in BP increases arterial wall tension and stiffness, thus, shortening PTT; and, conversely, a drop in BP lessens the stiffness and tension in the arterial walls, thus, lengthening PTT [12]. The difficulty in detecting the exact moment of opening of the aortic valve non-invasively has led to PTT being measured from a more easily detectable start point, the electrocardiographic (ECG) R wave. Measured in this way, the time delay between the R wave and the aortic valve opening (i.e. left ventricular isometric contraction time) is now added to the true PTT. Anything that affects BP, and therefore true PTT from the aortic valve, may also have an effect on the isometric contraction time, which may or may not be in the same direction as the BP effect [13]. It has already been shown that, as with oscillations in systolic blood pressure (SBP), the size of the oscillations in PTT during inspiration correlates well with the degree of inspiratory effort in awake normal subjects breathing through an added inspiratory threshold resistance [14]. It has also been demonstrated that much of the lengthening in PTT during an inspiratory effort is due to lengthening of the isometric contraction time, rather than lengthening of the true pulse transit time from the aortic valve to the finger [15].

Since PTT can be calculated and stored by a small portable device similar in size to an ambulatory BP monitor, it would be a particularly suitable technique for use in domiciliary screening sleep studies. The aim of this study was, therefore, to establish whether respiratory oscillations in PTT could provide a clinically useful quantitative measure of changes in inspiratory effort in patients with obstructive sleep apnoea.

Material and methods

Study subjects

Recordings were made on 10 patients with OSA who were booked to attend the sleep laboratory for institution of nCPAP. One patient was unable to sleep during the study and a technical failure occurred with the equipment in a second patient. Data are, therefore, presented on the eight patients in whom complete recordings were available. They were all male, with moderate to severe OSA (mean >4% arterial oxygen saturation (SaO_2) dip rate 43 (range 13–68) dips h⁻¹), and their mean age was 44 yrs (range 34–58 yrs).

Techniques

Pulse transit time. An RM10 solid state recorder (Parametric Recorders, London, UK) with ECG and pulse modules was used to calculate and store PTT. The RM10 samples both the ECG and pulse at 500 Hz. PTT is calculated as the time interval between the ECG R wave and a point on the pulse waveform (detected by a photoplethysmographic finger probe) which is 25% of the height of the pulse wave. PTT is typically about 250 ms, and is measured to an accuracy of 2 ms. PTT values (available with every heart beat) were oversampled at 5 Hz.

Intra-oesophageal pressure. Intra-oesophageal pressure (Poes) was measured by means of an oesophageal balloon (P.K. Morgan Ltd, Kent, UK). The standard laboratory technique for placement of the balloon was used, passing it via the nasal airway into the oesophagus after application of topical local anaesthetic to the nasal mucosa. The balloon was initially placed 40 cm from the nasal entrance, filled with 0.5 cm³ air (by instilling 1 cm³ then withdrawing 0.5 cm³), and connected via a pressure transducer to an external in-put module on the RM10 recorder. The Poes signal was viewed and minor alterations to the balloon position were made in order to produce clear respiratory pressure swings. Once the balloon had been correctly positioned, the pressure transducer was calibrated by the use of an air-filled syringe and a water manometer. Poes was sampled at 5 Hz.

Nasal continuous positive airway pressure. The patient was fitted with an appropriately sized nasal mask and the Poes line was passed out through one of the mask ports. A Sleep Easy II CPAP machine with externally adjustable valve (Respironics Inc.) was used for the CPAP titration. A continuous display of pressure within the mask was obtained by connecting a digital manometer to the second mask port.

Sleep monitoring. Electroencephalographic activity (EEG) (C3, A2 or C4, A1) was recorded at 100 Hz by the EEG module on the RM10. An infra-red video recording was made and processed in real time for body movement and sound. These were displayed continuously together with oxygen saturation and pulse rate (Ohmeda 3700 pulse oximeter) by the Visi-Lab sleep monitoring system (Stowood Scientific Instruments, Oxford, UK).

Protocol

The recording took place during the routine sleep study for titration of nCPAP. After introduction to the nCPAP
system and fitting of the correctly sized nasal mask, all other monitoring equipment was attached. The patient was allowed to fall asleep with the nCPAP set at a comfortable level (usually about 2 cmH₂O). The RM10 was connected to a lap-top computer (Commodore C286-LT) to provide a continuous display of EEG, PTT and $P_{oes}$. A continuous display of body movement, $S_{ao₂}$, pulse rate and sound was also available from the Visi-Lab system. The patient was observed using the closed-circuit infra-red camera. Once the patient was asleep (verified by EEG) and having obstructive apnoeas (verified by direct observation, $S_{ao₂}$ dips and sound), nCPAP was gradually increased until the obstruction was completely abolished and the patient was breathing normally. The nCPAP was then decreased from this level at 3 min intervals in steps of 1 cmH₂O to produce a range of inspiratory efforts until complete obstruction recurred. At this point, the nCPAP was turned up to the optimal treatment level again and stepped down at 3 min intervals for a second run. The patient was then woken briefly for removal of some equipment, and then left to sleep for the remainder of the night at the appropriate nCPAP level.

**Analysis**

The data from the RM10 was transferred to a personal computer. For each patient, sections of the PTT and $P_{oes}$ tracings comprising about 20 breaths at each nCPAP level were analysed. For each breath, the change in $P_{oes}$ and PTT during inspiration (inspiratory swing) was calculated as the peak to trough difference (fig. 1). Because a PTT value is only available with every QRS complex, and the heart rate is, thus, not sufficiently faster than the rate of breathing to prevent undersampling, a given maximum PTT value may or may not correspond to the $P_{oes}$ nadir (fig. 2a). Thus $P_{oes}$

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**Fig. 1.** – One minute section of an intra-oesophageal pressure ($P_{oes}$) and pulse transit time (PTT) tracing comprising 13 breaths. The inspiratory $P_{oes}$ and PTT swings were calculated as the difference between the peak and trough for each breath. Note that the vertical axis on the PTT tracing has been inverted, so that a downward deflection on the PTT tracing corresponds to a lengthening of PTT (fall in blood pressure (BP)) and an upward deflection, a shortening of PTT (rise in BP).

**Fig. 2.** – Pulse transit time (PTT) undersampling error. Nine cardiac cycles are represented with a black dot (and dotted line) representing each pulse. Two breaths are represented: intra-oesophageal pressure ($P_{oes}$) by the thick line and PTT by the thin line (inspiration downwards). a) The $P_{oes}$ tracing has the saw-tooth pattern typical of the patients in this study. Note that during the first breath a pulse coincides with the nadir in the $P_{oes}$ tracing and, therefore, the PTT swing is an accurate representation of the $P_{oes}$ swing; however, in the second breath, the pulse does not coincide with the nadir in the $P_{oes}$ tracing and, therefore, the PTT swing underestimates the swing in $P_{oes}$. b) The $P_{oes}$ tracing has the square-wave pattern more typical of awake subjects breathing slowly in time to a metronome against added inspiratory threshold resistance. This pattern of inspiratory effort will greatly reduce the undersampling effect on PTT values.
swings of a certain value will generate a limited range of PTT swings. For this reason, respiratory swings were grouped together according to Poes in sampling bins of 5 cmH₂O (ranging 0 to -65 cmH₂O), and the mean and standard error of the corresponding PTT swings within each bin were calculated. Any Poes bin which contained fewer than five breaths was discarded.

Results

Optimal nCPAP ranged 9.6–16.0 cmH₂O. The range of Poes swings obtained varied considerably between patients and, thus, the number of sampling bins available per patient is also variable (range 3–12).

Figure 3 shows two Poes and PTT tracings from the same patient (patient No. 4). In figure 3a, nCPAP is 3 cmH₂O; and in figure 3b, nCPAP is 16 cmH₂O. Clear differences in the size of the inspiratory swings can be seen on both the Poes and PTT tracings. In addition, on the PTT tracing (fig. 3a), the recurrent arousals at the end of each apnoea can be seen by the repeated drops in PTT (due to rises in blood pressure).

Figure 4 shows the mean and standard error of the PTT swings for each Poes sampling bin in each patient. The regression line for each patient (using the binned data) has also been plotted. The slopes, intercept and r-values for each patient are shown in table 1. All the r-values are above 0.87, and the mean r=0.94.

![Graph showing Poes and PTT tracings](image)

Fig. 3. – Two 4 min sections of the intra-oesophageal pressure (Poes) and pulse transit time (PTT) tracings on the same patient (patient No. 4).

a) Nasal continuous positive airway pressure (nCPAP) is subtherapeutic at 3 cmH₂O, the apnoeas can clearly be seen with large swings in both Poes and PTT throughout. In addition, on the PTT tracing, the arousal at the end of each apnoea can also be inferred by the periodic falls in PTT (corresponding to the blood pressure rise).

b) nCPAP is abolishing apnoeas at 16 cmH₂O; oscillations in Poes and PTT are small, and there are no arousals visible on the PTT trace.
mean PTT swing ms

Patient No. 4

Patient No. 5

Patient No. 6

Patient No. 7

Patient No. 8

Fig. 4. – Individual plots of swings in pulse transit time (ms) against the swings in intra-oesophageal pressure (Poes) (averaged within each 5 cmH2O sampling bin) for each patient. The SEMs and regression lines have also been plotted. n: total number of breaths; r: correlation coefficient of binned data.

Table 1. – Regression values for each patient of pulse transit time (ms) oscillations against intra-oesophageal pressure (Poes) oscillations

<table>
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<th>Patient No.</th>
<th>Slope ms·cmH2O⁻¹</th>
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<th>r-value</th>
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Discussion

This study has shown an excellent correlation between the size of the inspiratory swings in PTT and the size of the inspiratory swings in oesophageal pressure in patients with obstructive sleep apnoea. Measurement of the inspiratory change in PTT may, therefore, be a useful part of a respiratory sleep study, since it is able to provide quantitative information about inspiratory effort in patients with sleep-related breathing disorders.

There is not an exact relationship between PTT swings and Poes swings on a breath-by-breath basis, due to the fact that a new PTT value can only be calculated with each cardiac cycle and the difference between the heart rate and the respiratory rate is not great enough to prevent undersampling of PTT (fig. 2a). In fact, plotting PTT swings against Poes swings on a breath-by-breath basis yields much poorer correlations. Therefore, we would suggest that PTT can provide breath-by-breath data but that PTT should be used to assess the degree of inspiratory effort by averaging over a number of breaths, or possibly over a whole night to give the average inspiratory effort for the sleep study.

Examination of the regression lines shows that the intercept values (y-axis) are quite variable (range 1.2–10.1 ms, mean 6.0 (SD 2.9) ms). The positive intercept would
suggest that even when there is no swing in $P_{\text{oes}}$ there is a change in PTT. In an earlier study looking at the relationship between PTT swings and inspiratory effort using a face-mask with inspiratory threshold valves and measuring pressure swings at the mouth [14], the vertical intercept was also positive. This was attributed to the variable inspiratory effort required to overcome the elastic recoil of the lungs and the airways resistance, exacerbated by overbreathing in response to the face-mask. Thus, we would not expect to see the same phenomena comparing PTT swings with pressure changes within the oesophagus. In fact, the mean intercept value is lower in the current study (6.0 ms compared to 12.6 ms in the earlier study) but it is not clear why the intercept value should still be positive. PTT, as we measure it, is composed of two periods, the pre-ejection cardiac period (PEP) + the PTT from the aortic valve to the finger. There may be other influences on either or both of these periods, which occur in time with respiratory output from the brain stem (e.g. changes in autonomic tone or blood pressure), that are responsible for the small oscillations in PTT which seem to occur even when there is no inspiratory effort. Further work is required to investigate possible causes and their variation between subjects.

The slopes of the regression lines in the current study are shallower than those in the earlier study, where increased inspiratory efforts were produced by using added threshold inspiratory resistance valves ($0.39 \text{ms} \cdot \text{cmH}_2\text{O}^{-1}$ compared to $0.57 \text{ms} \cdot \text{cmH}_2\text{O}^{-1}$). In the earlier study, a metronome was used to produce slow, regular inspiration and expiration of 2.5 s each, producing a respiratory rate of 12 breaths·min$^{-1}$. This will tend to produce a square-wave breathing pattern rather than the saw-tooth pattern seen in the patient group in this study (fig. 2b). Square-wave breathing will be less susceptible to the undersampling problem of PTT than the saw-tooth pattern; thus, it is not surprising that the regression lines are less steep in the current study.

Other potential errors from using swings in PTT to represent swings in oesophageal pressure could occur if the PEP responded differently to falls in intrathoracic pressure between individuals. For example, a ventricle with poor myocardial contractility might take longer to reach the extra pressure necessary to open the aortic valve during a fall in intrathoracic pressure than a fully vigorous left ventricle. This would alter the slope of ΔPTT against Δ$P_{\text{oes}}$, and this potential problem is currently under investigation. The true PTT portion of our measurement might be influenced by the elasticity and compliance of the arterial tree, although this might be expected to alter absolute PTT more than the oscillations engendered by breathing. Ultimately, the usefulness of this technique as a diagnostic tool in the investigation of sleep-related breathing disorders requires a validation against conventional sleep study techniques, and such a study is also in progress [16].

In conclusion, measuring inspiratory swings in PTT can provide quantitative information about inspiratory effort in patients with obstructive sleep apnoea provided breaths are averaged rather than inspected on a breath-by-breath basis. Monitoring PTT may, therefore, be an alternative to the measurement of oesophageal pressure in respiratory sleep studies, particularly so since it can also provide a measure of sleep fragmentation [17], and can be logged by fully portable systems.

References