Interpretive Oximetry: Future Directions for Diagnostic Applications of the SpO_2 Time-Series

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The potential morbidity of unrecognized airway instability in hospitalized patients receiving sedation (1–3) and/or narcotics (4–6) has been recently highlighted. Upper airway instability is closely linked to visceral fat (7) and body mass index. Regrettably, the number of patients with a high body mass index has been progressively rising in the US over the past two decades. One study (8) found the incidence of obesity in a US intensive care unit to exceed 60%. For these reasons, more widespread use of portable monitors to detect obstructive apneas during the postoperative monitoring of subpopulations at risk for airway instability has been advocated. However, traditional application of apnea monitoring uses a basic alarm threshold associated with a range of preset criteria defining the occurrence of a single apnea event. Since desaturations associated with a self-limiting apnea are not prolonged, the post operative application of simple threshold based apnea monitors which apply oximetry as a primary modality is limited by the need to minimize the occurrence of false alarms based on transient deflections related to artifact or motion. Such devices are also limited by the requirement of multiple patient interfaces such as chest bands or airflow monitors to differentiate artifact from an apnea-related desaturation.

Alternatively, a range of abbreviated polysomnography technologies, of the type commonly applied in sleep labs, is sometimes moved to the bedside for the evaluation of upper airway instability. However, the software utilized in such systems applies a simplistic set of 25 year old arbitrary counting rules to infer the presence of airway instability (9). These rules generally include counting all apneas or hypopneas which exceed 10 seconds, adding them together, and then inferring the presence of clinically significant airway instability based on the occurrence of a simple minimum summation (such as 10 per hour). Such simplistic summation technology is difficult to interpret in the management of complex postoperative patients in real-time since it renders an arbitrary summation output, which oversimplifies the pathophysiology of airway instability and lacks sufficient mathematical power to grade the severity of the complex and dynamic variations in the timed datasets of monitored airway instability.

Fortunately, several recent studies have led to a much broader understanding of the pathophysiology of upper airway instability during sleep and deep sedation. Recently, it has been shown that as upper airway instability increases, sleeping patients develop a predictable and unique pattern of duplicative waveform cycles (10). In particular, as airway instability worsens, dynamic interactions between the mechanical stability of upper airway, respiratory control, and the arousal threshold, produce a duplicative pulmonary arrhythmia, which is characterized by cyclic reentry based collapse of the upper airway alternating with brief episodes of hyperventilation derived from arousal-based recovery. This produces a dynamic and duplicative Spo_2 time-series pattern of clustered desaturation transients having distinct morphologic similarities in the time domain. This sentinel pattern can be recognized and characterized in real-time by an interpretive microprocessor system when monitored by high fidelity pulse oximetry (11).

Perhaps one of the most important recent findings pertaining to pulse oximetry has been the recognition that the Spo_2 waveform outputs proceeds through predictable stages as the upper airway instability increases. As elegantly shown by Younes et al (10), while patients with very mild instability often have isolated and scattered apneas, patients with more severe upper airway instability will develop a unique pulmonary arrhythmia associated with cyclic pathophysiologic reentry of upper airway obstruction (see Fig. 1). Within this self-propagating arrhythmia, each reentering airway obstruction is reversed by an intervening and precipitous episode of hyperventilation based recovery (see arrows, Fig. 1). This produces a duplicative and cyclic output of clustered variations along the Spo_2 timed data set. This process of cyclic reversal

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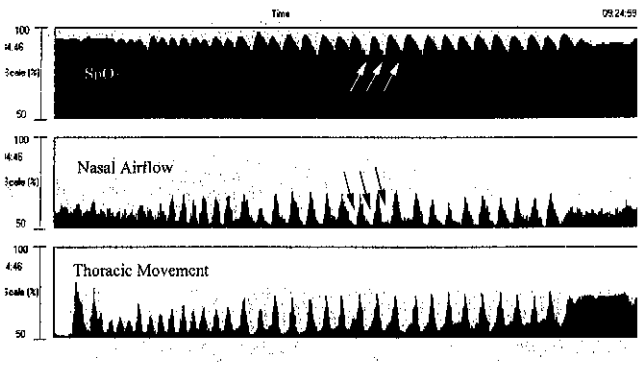

Figure 1. Pattern of timed SpO2 waveform demonstrating the non-sustained paroxysmal pulmonary arrhythmia typical of rapid cycling reentry of upper airway obstruction. Note the duplicative output and explosive ventilation during brief intervals of recovery (arrows).

might be termed "survival by repetitive rescue" because it is the brief intervening and recurring arousals, which "rescues" the patient from each obstructive apnea. Although rescue generally occurs precipitously at the nadir of each desaturation the specific relationships between the depth of sedation, the arousal threshold, and the magnitude and morphology of desaturation events within a cluster of obstructive apneas has not been studied. However, the remarkable dependency on the arousal threshold for repetitive rescue may explain the increased sensitivity of these patients to narcotics and sedatives (1,2,5) and provides further impetus for monitoring these patterns along the Spo_2 time series in postoperative patients receiving large doses of narcotics or sedatives (4,5).

Despite the clear need for early recognition of upper airway instability inpatients receiving narcotics or deep sedation, these distinct patterns have not been widely recognized in this clinical environment. These patterns have been missed because they have been largely hidden by the long Spo_2 averaging intervals, applied with hospital-based pulse oximetry (12). Furthermore, unlike the storage of electrocardiographic data, which is provided at a high rate so that the cardiac arrhythmia patterns can be readily recognized, the sampling frequency of stored Spo_2 datasets is often insufficient to reproduce the waveform for retrospective review with sufficient resolution to identify the waveform patterns of the pulmonary arrhythmias (13).

Figure 1 shows a typical Spo_2 time series pattern produced by the reentry based pulmonary arrhythmia induced by upper airway instability. Note that, adjusting for the delay, this same general cluster pattern is present in a contemporaneous time series of airflow amplitude and chest wall movement. As evident from the pattern, the pathophysiologic process driving the generation of this waveform is duplicative. As illustrated in Figure 2, this type of pulmonary arrhythmia

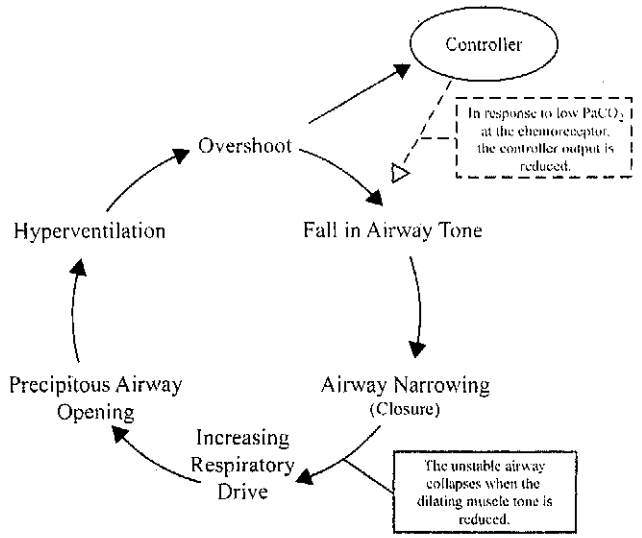

Figure 2. Pulmonary arrhythmia developing in association with marked narrowing or collapse of an unstable upper airway due to insufficient upper airway muscle tone. Hypocarbia transient induces a fall in respiratory controller output causing a fall in muscle tone, which, in the presence of mechanical instability, causes the airway to collapse again, so that the entire cycle reenters.

develops in association with marked narrowing or collapse of an unstable upper airway due to insufficient upper airway muscle tone. A progressive rise in $PAco_2$ and fall in Spo_2, and an increasing but ineffective respiratory effort against the closed airway follow this collapse. Provided the patient is not too deeply sedated, when the arousal threshold is breached, the patient will experience a general arousal response (but may not awaken). At this time, the increased respiratory drive associated with the elevated $PAco_2$ at the chemoreceptor site is further magnified by the superimposed stimulation of the occurrence of the arousal itself, causing a marked increase in afferent output to the muscles of the upper airway and the diaphragm. This combined effect induces precipitous airway opening and explosive ventilation causing a ventilation overshoot (14). These precipitous episodes of hyperventilation, which rapidly reverse each consecutive apnea, are readily seen along the airflow plot of Figure 1. The overshoot results in a hypocarbia transient and, as again illustrated in Figure 2, this transient induces a fall in respiratory controller output causing a fall in muscle tone, which, in the presence of mechanical instability, causes the airway to collapse again, so that the entire cycle reenters. As is typical of pathophysiologic reentry, the above repeating sequence often develops precipitously and may become sustained producing a process of cyclic reentry of airway closure. This generates the clusters of duplicative desaturation and resaturation cycles.

As is true of a cardiac arrhythmia, reliable real-time recognition of a pulmonary arrhythmia induced by

upper airway instability is dependent on the sufficiency of waveform fidelity (12,13) and upon consideration of the physiologic, and the potential pathophysiologic, factors affecting cluster waveform morphology. Figures 1 and 3 illustrate typical monomorphic patterns of reentry of airway closure. Within the self-propagating and duplicative obstructive cycles, each desaturation generally has a lower absolute slope value then its associated resaturation producing an angulated morphology, which is also duplicative (9). While the general morphologies of waveform clusters induced by uncomplicated airway instability are predictable, the more detailed features of the clusters are dependent on the degree of airway closure, and on a range of other clinical factors, which affect the desaturation slope and the recovery interval between desaturations. Factors that affect the slope of desaturation include: cardiac output, through its effect on mixed venous oxygen saturation (15); alveolar volume and oxygen partial pressure at the onset of airway closure; and the recovery interval between consecutive apneas within a cluster (16). Although the monomorphic patterns of desaturation shown in Figure 3 are typical of uncomplicated obstructive reentry, patients with superimposed hypoventilation may demonstrate more polymorphic and complex patterns of clustered desaturations.

One of the most striking variables, which affect the morphology of these waveform clusters, is the recovery interval between apneas. The factors, which define the duration of the recovery intervals, are poorly understood and comprise an area of intense research. In addition, the affect of sedation or narcotics on the recovery interval duration has not been studied. Factors, which further increase airway instability, such as further weight gain or airway edema may contribute to reduction in the recovery interval since collapse may require less of a fall in the afferent output during the hypocarbia transient associated with post apnea hyperventilation overshoot thereby terminating recovery prematurely. In addition, an increase in the rate of alveolar CO_2 exchange during the recovery may increase the rate of overshoot and potentially reduce recovery time between consecutive apneas.

Since oxygen uptake is critically time dependent, factors reducing the recovery interval have the potential to induce regional and global oxygen debt, which may be cumulative within a prolonged cluster of closely spaced apneas (11) and which may alter the morphology of the cluster. When recovery intervals between prolonged apneas within a cluster are very short, there may be insufficient time for return of the venous oxygen saturation to normal, even though the arterial saturation has normalized. During rapidly cycling and prolonged apneas, consecutive waves of oxygen depletion move from arterial to venous systems. In the presence of very short recovery intervals,

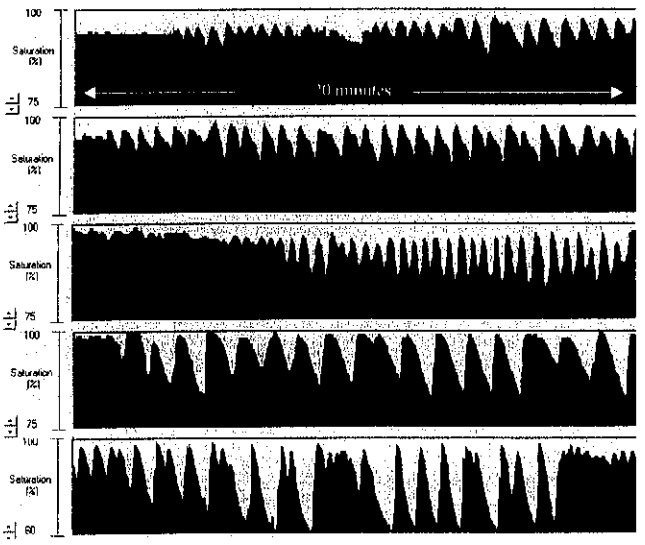

Figure 3. Oximetry recordings of the reentry based arrhythmia of upper airway instability in five patients with obstructive sleep apnea. Note the characteristic paroxysmal and duplicative cluster patterns induced by cyclic reentry of upper airway collapse.

the preceding depletion wave impacts the subsequent wave to alter the configuration of the subsequent desaturation waveform such that the initial portion of the subsequent desaturation is increased (16). This produces a biphasic wave of desaturation with the first more rapid phase being related to venous oxygen depletion and the second slower phase to oxygen consumption.

Since, as illustrated in the above example, recovery intervals may be insufficient to allow repletion of global body oxygen stores even with normal vascular flow, apnea clusters having prolonged apneas and short recovery intervals have the potential to cause significant regional ischemia in the presence of coronary disease (17). In this regard, a recent study found that cardiac ischemia during obstructive sleep apnea was most commonly associated with the occurrence of a cluster of three or more closely spaced obstructive apneas and the severity of the apnea related desaturation (18). For these reasons, as with cardiac arrhythmias, characterization of specific waveform morphologies, and in particular the determination of the intervals and relationships of repeating Spo_2 waveform events, represent important diagnostic components of the Spo_2 data set analysis (19).

Recently, microprocessor-based pulmonary arrhythmia pattern recognition (applied to time data sets of both airflow and Spo_2) has been approached by both object based pattern recognition and transform-based processing. Since a cyclic duplicative pattern also develops along the pulse waveform in response to the rapidly cycling apnea, several studies have examined the utility of frequency domain analysis to recognize these additional periodic components generated by the reentering

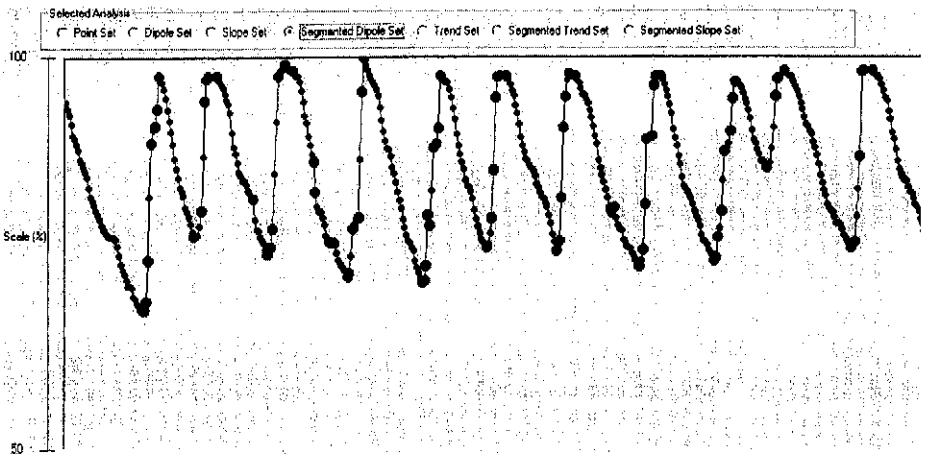

Figure 4. An example of object oriented pattern recognition and analysis of the SpO2 data set in the time domain. This patient exhibits a typical SpO2 reentry cluster (shown here transformed into basic dipole fragments for analysis by the processor). Each of these fragment objects as well as larger more complex objects derived from them are stored in a relational database for analysis, comparison, and pattern recognition. Note: this patient demonstrates a reentry arrhythmia pattern consistent with a high degree of upper airway instability with very short recovery intervals (bounded by vertical rectangles) and a low "recovery to duration" ratio of about 0.3.

clusters of the pulmonary arrhythmia (20). However, as noted above, the waveform hallmark of airway instability is a particular timed sequence of clustered, precipitous, and generally unidirectional changes in the Spo_2 timed data set, which occurs in association with the development of the duplicative pulmonary arrhythmia. For this reason, the analysis, recognition, and quantification of the pulmonary arrhythmia pattern along the Spo_2 waveform is readily approached in the time domain and this provides the opportunity to output all of the time dependent characteristics of the pulmonary arrhythmia, as, for example, cluster duration and the mean apnea duration to recovery interval ratio within a given paroxysmal apnea cluster. While more basic transform or rules-based methods can detect the occurrence of the pulmonary arrhythmia associated with airway instability, both the detection of the waveform patterns and the analysis of the timed relationships between and along recognized waveform events are considered important. As with conventional electrocardiographic arrhythmia detection, pattern recognition in the time domain provides the ability to provide recognition along with comprehensive interval determination and morphology analysis. Ultimately, these two methods of Spo_2 signal processing may be found to be synergistic for diagnostic purposes.

Figure 4 illustrates an example of a process of digital pattern recognition in the time domain for the real-time recognition of airway instability. Using this object-oriented waveform processing method, the Spo_2 timed data is first fragmented (transformed) into basic timed domain objects called dipoles. Each of these objects is stored in the relational database. The larger, more complex objects inherit the characteristics of the basic objects and are built from the basic objects. When applied, such a pattern recognition process proceeds in several phases. In the first phase, desaturation and resaturation objects are identified. In the second phase, coupled desaturation-resaturation objects are identified. In the third phase, different pulmonary arrhythmia patterns are identified, and in the fourth phase the temporal and spatial relationships between and within the different objects are calculated and compared.

In summary, in an arousal capable patient, moderate to severe upper airway instability causes the development of a pulmonary arrhythmia characterized by pathophysiologic reentry of airway obstruction alternating with rescue by a brief arousal response. This reentry process renders a range of recognizable patterns of clustered and duplicative desaturation-resaturation transients separated by brief events of recovery. The morphology of these clusters depends on complex relationship between residual oxygen stores, dynamic gas exchange, and the degree of mechanical upper airway instability. The resulting waveforms can be analyzed in the time domain such that specific temporal and spatial relationships of the waveform events can be identified and compared. For this reason, future high fidelity interpretive pulse oximeters, which incorporate digital pulmonary arrhythmia recognition technology, may represent an important advance for the real-time monitoring of upper airway instability during sleep and sedation in the hospital and for the evaluation of sleep-disordered breathing in the home.

The evolution of the clinical application of the pulse oximeter appears to be proceeding in a manner analogous to that of the electrocardiogram more than 25 years ago. As the signal fidelity of pulse oximeters has

improved, important new Spo_2 time series patterns have emerged. It is anticipated that, in the future, a new class of high fidelity interpretive oximeters will be developed to engage these emerging patterns thereby extending the functionality of pulse oximetry to provide a new generation of diagnostic devices.

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