



# Lower inter-breath interval complexity is associated with extubation failure in mechanically ventilated patients during spontaneous breathing trials

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## Abstract

**Objective:** To determine if higher complexity of respiratory periods as measured with nonlinear analysis techniques will identify intubated patients who will successfully separate from mechanical ventilation after 30 minute spontaneous breathing trials (SBT).

**Methods:** Respiratory waveforms from SBT of patients in Surgical and Burn ICUs were recorded for analysis. The decision to extubate was made by attending physician. Extubated patients were observed for 48 hours; reintubation or non-invasive positive pressure ventilation (NIPPV) was marked as failure. Analysis of waveform data by complexity software was performed *post-hoc* and metrics compared between successful extubation versus respiratory embarrassment within 48 hours of extubation.

**Results:** 32 subjects (24 burn, 8 trauma/surgical admissions; mean age 40 +/- 17; 26 men and 6 women) who were intubated >24 hours were extubated after SBT. Twenty-four successfully separated from mechanical ventilation and 8 failed. Age, gender and mechanism of injury did not influence outcome. All complexity statistics except Approximate Entropy (ApEn) and Signal Stationarity (StatAV) were different between groups. Results from complexity analysis are summarized below (SampEn = Sample entropy; SOD = similarity of distribution; Symbolic Distribution Entropy = DisNEn; Bit-per-word Entropy = BPWEn).

**Conclusion:** In intubated patients, the respiratory periods in those who successfully separated from mechanical ventilation were more irregular than those who failed. This implies a higher regulatory complexity of respiration. As collective measures of regulatory complexity, these statistics may then be useful markers in predicting outcome of SBT.

## Introduction

The inability to tolerate separation from mechanical ventilation or the need for re-intubation occurs in as many as 20% of mechanically ventilated patients. Multiple studies have shown that a diverse collection of variables used to predict successful separation from mechanical ventilation perform poorly and add little to the physician's clinical judgment. Recently, attention has focused on the use of breathing variability as a weaning predictor. Data from healthy human volunteers as well as two recent weaning studies support this hypothesis although contrasted findings have been reported.

The purpose of this study was to measure the regularity of breathing patterns of intubated patients undergoing spontaneous breathing trials (SBTs) using a comprehensive analysis of respiratory waveforms. We hypothesize that patients who successfully separate from mechanical ventilation will have a more irregular breathing pattern than those who fail extubation as measured by methodologically different nonlinear metrics. A comparative assessment of the utility of these measures as applied to respiratory domain is provided below.

## Methods

### Subjects and Protocol

Subjects were prospectively recruited from one Level I trauma center with separate burn and surgical/trauma ICUs during a 9-month period. Criteria for inclusion into this study were mechanical ventilation with an endotracheal tube for >24 hours and the ICU attending physician's judgment that the patient was ready for SBT and possible extubation. All SBT were performed with 5 cm H<sub>2</sub>O of both positive end-expiratory pressure (PEEP) and pressure support (PS) for 30 minutes. The decision to extubate was made by attending physician. Separation from mechanical ventilation was considered a failure if the subject required any ventilatory support within 48 hours of extubation.

### Waveform Analysis

Respiratory flow and pressure waveforms were continuously monitored on the Draeger Evita XLVentilator (Dräger Medical, Lubeck, Germany).

Two-hundred-breath datasets were imported into WinCPRS software (Absolute Aliens Oy, Turku, Finland). The software generated the instantaneous inter-breath interval (IBI) time series.

The following waveform analysis techniques were applied: ApEn, SampEn, SOD, DisNEn, BPWEn and StatAv.

### Statistical Analysis

T-test or Mann-Whitney U test as appropriate was used for continuous variables and Fisher's exact test was used for categorical variables using SAS v 9.1, (SAS Institute, Cary, NC).

## Results

Thirty-three subjects in this study completed an SBT and were extubated. A total of 24 subjects successfully separated from mechanical ventilation. There were eight failures with one failure rescued with NIPPV. The mean duration for time to failure was 22.4 hours (a range of 0.96 to 47.25 hours). The characteristics of the two groups, along with RR, duration of IBI, NIF and RSBI calculated during SBT, are provided in *Group Characteristics* table.

Nonlinear results are provided in table form below. As measured by SampEn the IBI in the success group was more irregular than in the failure group, in which the subjects had a lower SampEn and thus a more regular IBI distribution. ApEn, however, was not different between groups. SOD was lower in the success group, implying a more dissimilar signal distribution; and higher in the failure group, pointing to a more regular signal amplitude distribution. The stationarity value (StatAv), which measures baseline shifts in the signal, was not different among groups). BPWEn and DisNEn changed in concordance with SampEn and denoted lower signal irregularity in the failure group.

### Group Characteristics

	Pass (N=24)	Fail (N=8)	p
AGE	37 ± 17	49 ± 15	0.08
APACHE II score	13 ± 4	9 ± 3	0.02
RR Mean	30.86 ± 30.12	26.15 ± 8.37	0.78
NIF	-33 ± 10	-35 ± 11	0.60
RSBI	47 ± 29	40 ± 27	0.78
VENT (days)	4.71 ± 3.63	4.30 ± 3.95	0.75
Sex (%F)	13%	38%	0.15
MECH (%Surg/Burn)	21%/79%	38%/63%	0.38

Mean ± standard deviation; APACHE II, Acute Physiology and Chronic Health Evaluation II

RSBI, Rapid Shallow Breathing Index

NIF, Negative Inspiratory Force

### Non-linear results

	Pass (N=24)	Fail (N=8)	p
SampEn	1.87 ± 0.27	1.36 ± 0.39	0.00
ApEn	0.97 ± 0.06	0.93 ± 0.11	0.36
RRISOD	0.17 ± 0.03	0.24 ± 0.05	0.01
DisNEn	0.82 ± 0.06	0.75 ± 0.06	0.01
BPWEn	4.94 ± 0.38	4.51 ± 0.34	0.01
StatAv	0.33 ± 0.13	0.29 ± 0.10	0.88

Mean ± standard deviation

## Conclusions

- The primary finding of this study is that in intubated patients undergoing SBT, the IBIs in those who failed to separate from mechanical ventilation were more regular than in those who were successfully extubated.

- RR, NIF and RSBI did not differ between groups and all subjects who were extubated had weaning parameters predictive of success.

- As collective measures of regulatory complexity, these statistics may then be useful markers in predicting outcome of SBT.

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