

# Patient-Ventilator Synchrony and Tidal Volume Variability using NAVA and Pressure Support Mechanical Ventilation Modes

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**Abstract:** Neurally Adjusted Ventilatory Assist (NAVA) is a new ventilatory mode in which ventilator settings are adjusted based on the electrical activity detected in the diaphragm (Eadi). This mode offers significant advantages in mechanical ventilation over standard pressure support (PS) modes, since ventilator input is determined directly from patient ventilatory demand. A comparative study of 22 patients undergoing mechanical ventilation in both PS and NAVA modes was conducted, and it was concluded that for a given variability in Eadi, there is greater variability in tidal volume and correlation between the tidal volume and the diaphragmatic electrical activity with NAVA compared to PS. These results are consistent with the improved patient-ventilator synchrony reported in the literature.

**Keywords:** Mechanical Ventilation, NAVA, Patient-Ventilator Interaction, Tidal Volume Variability.

## 1. INTRODUCTION

One of the most important factors determining the success of mechanical ventilation is patient tolerance to the technique, which is intimately linked to the interaction between the patient and the ventilator. During pressure support (PS), which is the most widely used mode of mechanical ventilation, the optimal combination of the patient's spontaneous breathing activity and the ventilator's set parameters can prove very difficult to achieve, (Vignaux et al., 2009). This issue is very important because if the patient and the ventilator engage in a tug-of-war between conflicting goals, rather than sharing the respiratory workload, the work of breathing will paradoxically increase, leading to the prolonged need for mechanical ventilation, (Tobin et al., 2001; Kondili et al., 2003), or in the case of non-invasive ventilation (NIV), to the failure of NIV in avoiding intubation (Carlucci et al., 2001). In NIV, PS is further complicated by leaks at the patient-ventilator interface which interfere with the flow and pressure signals used to set the ventilator.

The respiratory centre of the brain controls the characteristics of each breath by the propagation of action potentials along the phrenic nerve to excite diaphragm muscle cells. This signal results in contraction of the muscles in the diaphragm, descent of the diaphragm dome, and a decrease in airway pressure, causing an inflow of air into the lungs.

Neurally Adjusted Ventilator Assist (NAVA) is a relatively new mode of mechanical ventilation, which relies on the detection of the electrical activity in the diaphragm (*Eadi*) to determine ventilator pressure settings, (Sinderby et al., 1999).

NAVA is an improvement over existing PS systems, because respiratory activity is measured from a much more proximal site relative to the actual nervous system command (diaphragm excitation rather than airway flow signal), as seen in Fig. 1.

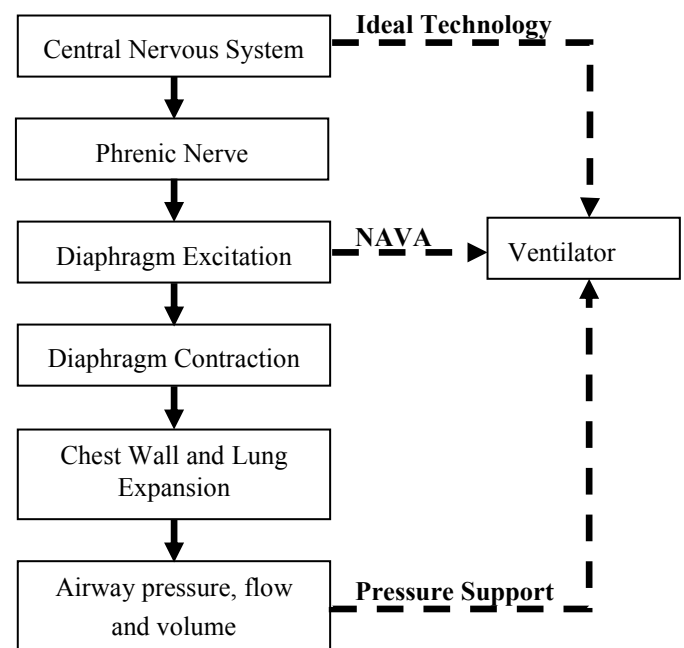


Fig. 1. Transduction chain from the brain to the airway opening (adapted from Sinderby et al., 1999)

Because NAVA uses a direct expression of respiratory center activity to control the ventilator, it should theoretically allow near-perfect synchronization between the patient and the ventilator, and a more natural and variable form of breathing. Therefore, it is hypothesized that tidal volume ( $V_t$ ) under NAVA would show better correlation with  $E_{adi}$  compared with PS. In addition, tidal volume is expected to exhibit greater variability due to the variability in the  $E_{adi}$  input to the ventilator. This has a potential clinical outcome as a greater variability has been linked to a better oxygenation (Mutch et al., 2000b). This research aims to confirm these hypotheses by characterizing respiratory variability with different techniques such as coefficient of variation, Poincaré plots and cumulative distribution functions (CDF).

## 2. METHODOLOGY

### 2.1 Clinical Method

A comparative study of patient-ventilator interaction was performed for 22 patients during standard PS with clinician determined ventilator settings; and NAVA, with NAVA gain set to ensure the same peak airway pressure as the total pressure obtained in PS. A 20 minute continuous recording was performed in each ventilator mode (equating to approximately 300-400 breaths from each patient in each mode), and  $E_{adi}$  and flow traces were recorded at a frequency of 100Hz. The raw traces were transformed using FFT to remove frequencies greater than 1Hz, to reduce noise. A section of a typical filtered trace is shown in Fig. 2.

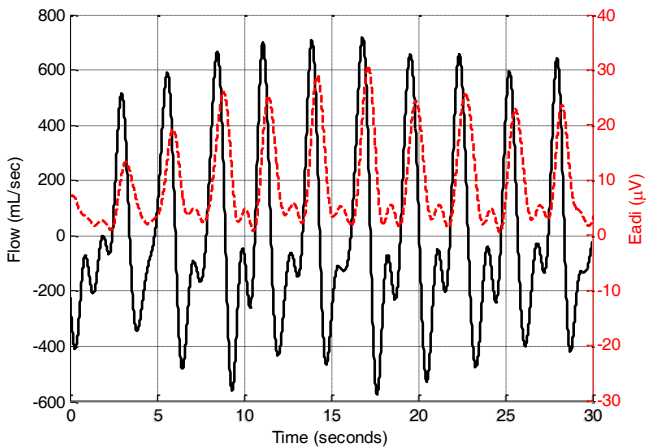


Fig. 2. Typical Flow (solid line) and  $E_{adi}$  (dashed line) traces.

The patient's inspiratory effort is determined from the integral of the  $E_{adi}$  signal of each breath. To the authors' knowledge, it has not previously been investigated if the maximum  $E_{adi}$  value of each breath also correlates directly with the patient's inspiratory effort. This possible correlation is explored in this study.

### 2.2 Signal Pre-processing

The servo-tracker from the ventilator reports the tidal volumes and maximum  $E_{adi}$  values for each breath. Fig. 3 shows a section of a typical patient's  $E_{adi}$  trace, with the raw signal shown (solid) along with the integrated  $E_{adi}$  signal (dots) and servo-tracker  $E_{adi}$  (crosses). However it is observed that although the magnitudes are largely accurate, the timing of each breath does not match. In addition, it is the integral of  $E_{adi}$  which gives the power/energy of the signal, and corresponds to the magnitude of the patient's inspiratory effort, and not the maximum  $E_{adi}$  value. Since breath-to-breath comparisons and variability are required, complete datasets were used, and the  $E_{adi}$  and  $V_t$  values were extracted by integrating the respective signals over each breath identified. The approach allows not only the correct timing for each breath, but also provides the integral of the  $E_{adi}$  signal as opposed to the maximum value. If good correlation is observed between the maximum and integrated  $E_{adi}$  signals, this would allow maximum  $E_{adi}$  values to be used in future investigations, which would simplify the analyses.

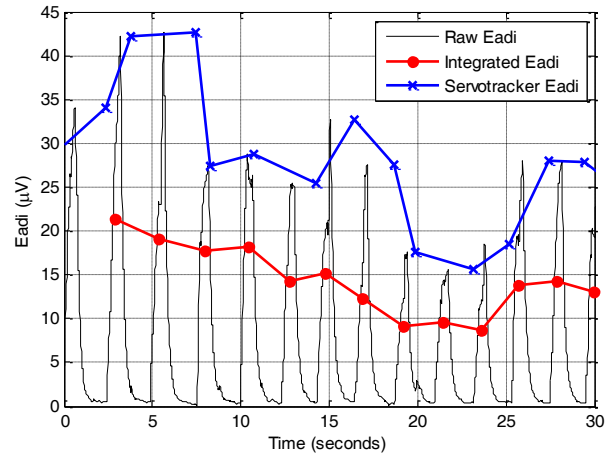


Fig. 3. Servotracker  $E_{adi}$  and integrated  $E_{adi}$  Signal.

A breath is determined by the flow signal, and is defined to commence when the flow signal becomes positive, and terminate when the flow signal becomes negative. The flow signal is integrated to obtain the tidal volume, and tidal volumes less than 50mL are discarded as artifacts. The  $E_{adi}$  signal is integrated between the same two time points to obtain the corresponding  $E_{adi}$  value.

Correlations are reported between the integrated flow ( $V_t$ ) and integrated  $E_{adi}$  signals; and between the maximum  $E_{adi}$  value and the integrated  $E_{adi}$  value. Power spectrums also illustrate the synchrony between  $V_t$  and  $E_{adi}$ .

Variability is shown in 3 ways:

1. Coefficient of Variation (CV = standard deviation/mean) in tidal volume over all breaths for each patient in each ventilator mode;
2. Poincaré plots of tidal volume show breath-to-breath variability. The tidal volume of the  $i^{\text{th}}$  breath is plotted against the tidal volume of the  $(i+1)^{\text{th}}$  breath;

- Cumulative distribution plots showing percent of  $V_t$  and  $Eadi$  signals within a pre-determined “variability band” for each patient. Areas are calculated between  $Eadi$  and  $V_t$  for the 5th-95<sup>th</sup> percentiles illustrate degree of synchrony between  $Eadi$  and  $V_t$ .

The CV gives a normalized measure of variation, appropriate when it cannot be assumed that different groups have the same mean. However, it is more relevant to a normal distribution, and can be skewed by outliers. In addition, this measure considers  $V_t$  independently, and disregards the influence of variability in  $Eadi$ . The poincaré plots again investigate  $V_t$  independently, but illustrate variability from one breath to the next, as opposed to variability over the 20 minute recording. Cumulative distribution plots are effective in quantifying the spread of data, and are useful in eliminating the effect of outliers. In addition, such plots allow comparison between the variability in  $V_t$  and  $Eadi$ .

### 3. RESULTS

#### 3.1 Synchronization

The integral of the  $Eadi$  signal is used for determining the electrical activity for each breath, and is in direct relationship with the patient’s inspiratory effort. It has not previously been investigated if the maximum  $Eadi$  value of each breath also correlates directly with the patient’s inspiratory effort. In this study, the maximum  $Eadi$  value was correlated with the integrated  $Eadi$  value for each patient across all breaths. Population statistics for the correlation coefficient across all patients are shown in Table 1.

**Table 1. Correlation between maximum and integrated  $Eadi$  (LQ = Lower Quartile; MED = Median; UQ = Upper Quartile)**

	LQ	MED	UQ
PS	0.96	0.97	0.98
NAVA	0.93	0.97	0.99

Under PS, the correlation coefficient was  $0.96 \pm 0.03$ , and under NAVA,  $0.95 \pm 0.04$  over all 22 patients (mean  $\pm$  standard deviation), showing excellent correlation between maximum and integrated  $Eadi$  values, and supporting the premise that the maximum  $Eadi$  value at each breath could be used to represent  $Eadi$  in future work.

Correlations between the integrated  $Eadi$  and flow signals are shown in Table 2 for both NAVA and PS. Under PS, the correlation coefficient was  $0.31 \pm 0.40$ , and under NAVA,  $0.73 \pm 0.23$  over all 22 patients (mean  $\pm$  standard deviation). A two-sample Kolmogorov-Smirnov goodness-of-fit hypothesis test shows that the NAVA and PS correlation datasets are significantly different with a p-value of  $2.75 \times 10^{-5}$ .

**Table 2. Correlation between integrated  $Eadi$  and flow signals (LQ = Lower Quartile; MED = Median; UQ = Upper Quartile)**

	LQ	MED	UQ
PS	0.18	0.41	0.60
NAVA	0.73	0.79	0.89

As expected, the correlation is much greater for NAVA than PS, indicating that the patient and ventilator are much better synchronized under NAVA than PS.

Power spectrums for  $V_t$  and  $Eadi$  under PS and NAVA are shown in Fig. 4 for a section of the frequency domain for a typical patient, and further illustrate the better correlation observed under NAVA. This result is expected, since NAVA reacts in real-time to the electrical signal from the diaphragm, and adjusts the delivered pressure accordingly. Therefore, the frequency of changes in pressure and thus  $V_t$ , should be in synchrony with changes in  $Eadi$  in comparison to PS, which is not influenced by  $Eadi$ . Lastly, this result illustrates that NAVA promotes breathing exactly when and how (as seen by the magnitude of the  $V_t$ ) the body demands.

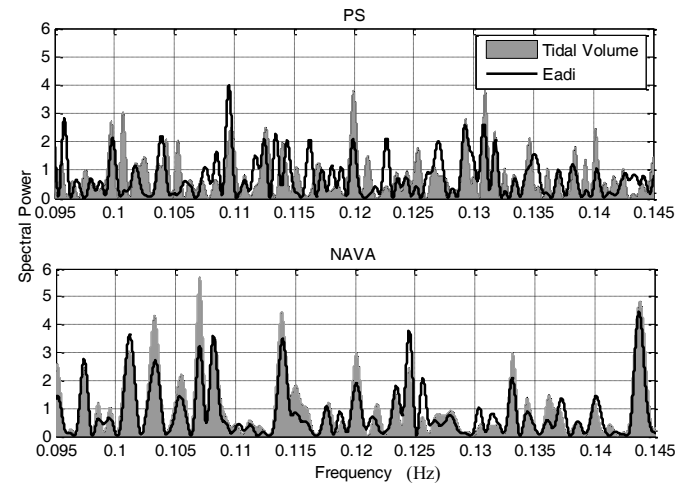


Fig. 4. FFT for a selected frequency range for a typical patient.

#### 3.2 Variability

The coefficient of variation in tidal volume is shown in Table 3. Under PS, the coefficient of variation was  $0.13 \pm 0.08$ , and under NAVA,  $0.28 \pm 0.20$  over all 22 patients (mean  $\pm$  standard deviation). Using a two-sample Kolmogorov-Smirnov goodness-of-fit hypothesis test, the PS and NAVA CV datasets were found to be significantly different with a p-value of 0.0015, with the NAVA data set being more variable.

**Table 3. Coefficient of Variation (CV) in  $V_t$  (LQ = Lower Quartile; MED = Median; UQ = Upper Quartile)**

	LQ	MED	UQ
PS	0.07	0.10	0.17
NAVA	0.15	0.20	0.32

Poincaré plots of the  $i^{\text{th}}$  versus  $(i+1)^{\text{th}}$  breath further illustrate the greater variability observed under NAVA. A typical patient is shown in Fig. 5.

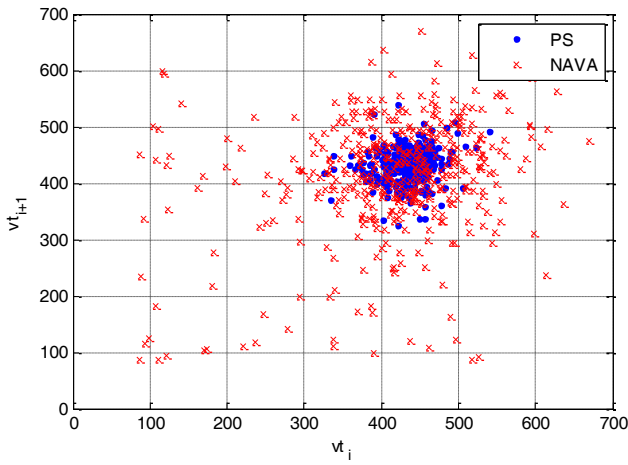


Fig. 5. Poincaré plot for a typical patient

The poincaré plots and CV values described thus far give the variability in tidal volume as an isolated metric. Over all patients, there is no significant difference in the variability in  $Eadi$  between PS and NAVA ([LQ, MED, UQ] = [0.36, 0.49, 0.81], and [0.33, 0.44, 0.88] for PS and NAVA, respectively, with a two-sample Kolmogorov-Smirnov p-value of 0.82). However, for a given patient over a given time period, the variability in output ( $Vt$ ) should be dependent on the variability of input ( $Eadi$ ).

For each patient under both PS and NAVA, the  $Vt$  and  $Eadi$  values were normalised to their median value, and cumulative distribution plots were generated as seen in Fig. 6. The  $Eadi$  signals are very close, but  $Vt$  is far more variable for NAVA.

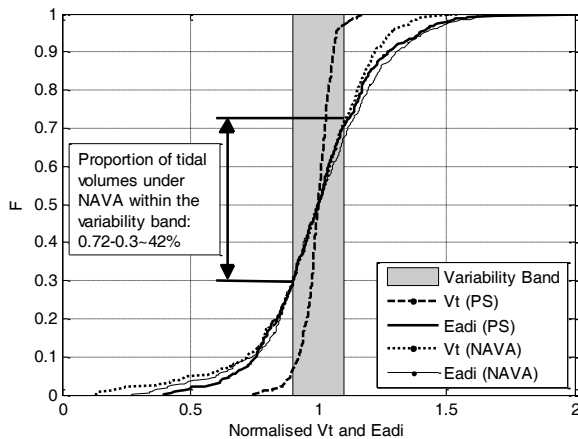


Fig. 6. CDF plot for a typical patient showing range of  $Eadi$  and  $Vt$  under PS and NAVA.

A variability band of  $\pm 10\%$  of the median was defined, such that the proportion of  $Vt$  and  $Eadi$  values for a specific patient falling outside the band could be used as a measure of variability. It can be seen in Fig. 6 that the variability in  $Eadi$  is very similar between PS and NAVA for this patient (59%

and 63% outside the variability band for PS and NAVA, respectively). The variability in tidal volume is comparable for NAVA, with 58% falling outside the variability band. However, the variability in tidal volume is much smaller for PS, with only 9% falling outside the band. The non-parametric population statistics of this type of analysis are shown in Table 4.

**Table 4. %  $Vt$  and  $Eadi$  outside Variability band (LQ = Lower Quartile; MED = Median; UQ = Upper Quartile)**

Mode	Metric	LQ	MED	UQ
PS	$Eadi$	62.12	73.59	87.57
	$Vt$	6.45	26.70	39.83
	$Vt/Eadi^*$	0.12	0.31	0.57
NAVA	$Eadi$	59.49	64.30	76.94
	$Vt$	39.27	49.34	68.81
	$Vt/Eadi^*$	0.61	0.85	0.98

\*NAVA and PS significantly different with p-value of  $1.16 \times 10^{-4}$  using two-sample Kolmogorov-Smirnov goodness-of-fit hypothesis test.

These results show that for a given patient-specific variability in  $Eadi$ , a much larger variability in tidal volume is observed under NAVA than PS. When a Fisher exact test is performed on the number of breaths with  $Vt$  and  $Eadi$  inside and outside the variability band, and a cumulative distribution function is plotted of the p-values, Fig. 7 is obtained.

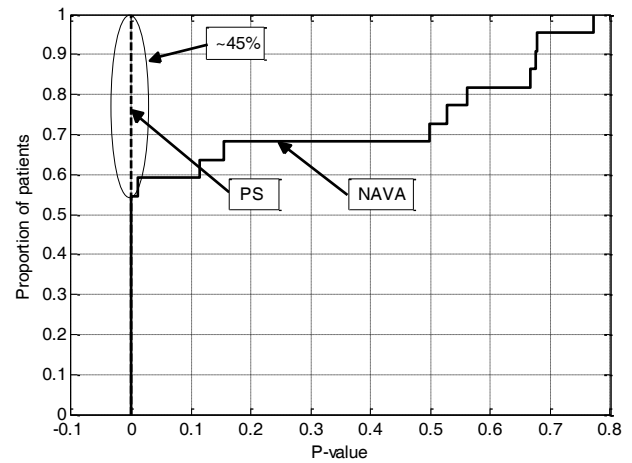


Fig. 7. CDF of Fisher exact P-values of  $Vt$  and  $Eadi$  values inside and outside the variability band.

Fig.7 shows that for all patients under PS, the ratio of breaths inside and outside the variability band is unrelated between  $Vt$  and  $Eadi$  ( $p=0$  for all patients). With NAVA, 45% patients have no significant difference ( $p>0.05$ ) between  $Vt$  and  $Eadi$  proportions, indicating that the proportion of breaths with  $Vt$  and  $Eadi$  inside and outside the variability band is related. Therefore, it is these 45% of patients who could have benefited from the NAVA ventilation mode as opposed to the PS mode.

When the percent  $Vt$  outside the variability band is plotted against the percent  $Eadi$  outside the band, Fig. 8 is obtained, where the solid line is the line  $y=x$  (100% match of

variability). Each individual patient is marked on the plot with a number such that each individual patient's position under NAVA and PS can be compared.

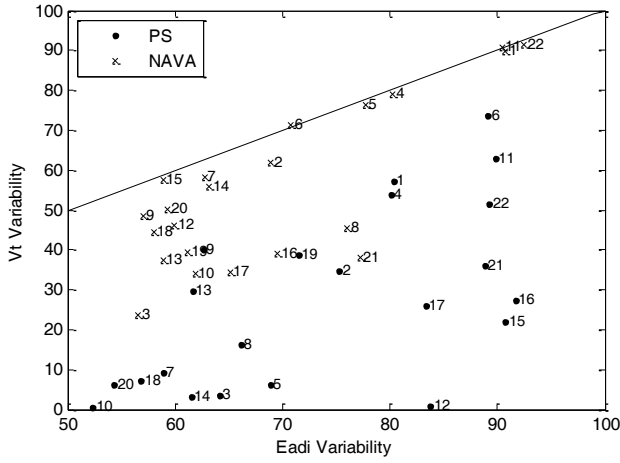


Fig. 8. Variability in  $V_t$  as a function of variability in  $E_{adi}$ .

Fig. 8 shows that for a given variability in  $E_{adi}$ ,  $V_t$  will have higher variability under NAVA. Note that the 45% of patients who would have benefitted from NAVA (from Fig. 7) are those lying closest the  $y=x$  line in Fig. 8. It is considered that it is likely to be best for the patient for the variability in  $E_{adi}$  and  $V_t$  to be similar (ie closer to the  $y=x$  line in Fig. 8), as this outcome would indicate the best correlation between the body's demand ( $E_{adi}$ ) and supply ( $V_t$ ). Future work will examine if higher variability in  $V_t$  correlates with better patient outcomes and greater likelihood of successfully disconnecting the patient from the ventilator.

Fig. 6 can also be used to calculate the area between  $E_{adi}$  and  $V_t$  CDF profiles for each patient in each ventilator mode, as shown in Fig. 9. The population statistics shown in Table 5 illustrate that variability in  $V_t$  is much closer to variability in  $E_{adi}$  under NAVA, by having smaller areas of difference between these normalized curves. Using a two-sample Kolmogorov-Smirnov goodness-of-fit hypothesis test, the PS and NAVA differences in  $E_{adi}$  and  $V_t$  ( $A1+A2$  in Fig. 9) were found to be significantly different with a p-value of 0.00016.

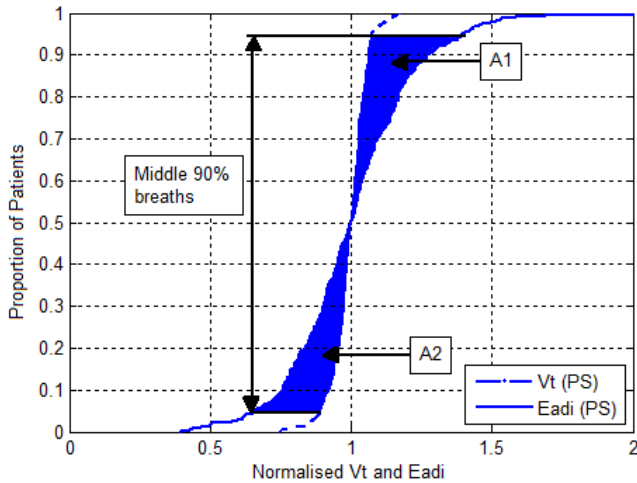


Fig. 9. 90<sup>th</sup> percentile area between  $E_{adi}$  and  $V_t$  CDF profiles.

Table 5. %  $V_t$  and  $E_{adi}$  outside Variability band (LQ = Lower Quartile; MED = Median; UQ = Upper Quartile)

	LQ	MED	UQ
PS	0.08	0.13	0.26
NAVA	0.03	0.05	0.08

It is observed in Fig. 8 that the variability in  $V_t$  is always less than the variability in  $E_{adi}$ , or within 1% of unity, suggesting that the degree of variability observed in  $V_t$  is limited by the variability seen in  $E_{adi}$ . A patient's  $V_t$  or  $E_{adi}$  is described as "variable" if  $x\%$  of its values lie within the variability band. If  $x$  is allowed to vary from 0 to 100, then the proportion of patients with a variable  $V_t$  given a variable  $E_{adi}$ ,  $P(V_t=\text{variable}|E_{adi}=\text{variable})$ , can be plotted, as seen in Fig. 10.

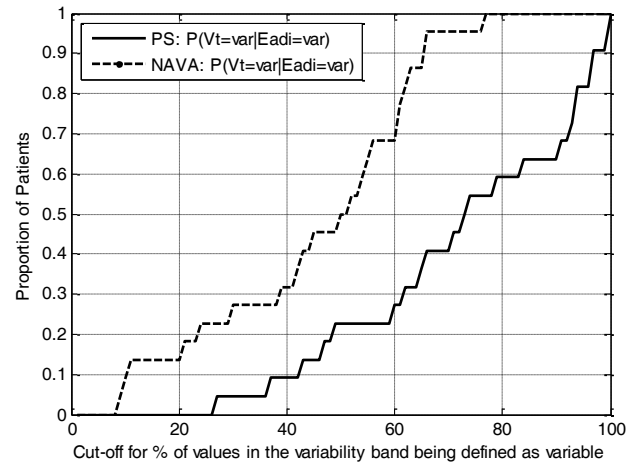


Fig. 10. Proportion of patients with variable  $V_t$  given a variable  $E_{adi}$ .

It is observed that for any reasonable choice of  $x$  between 0 and 100, a greater proportion of patients under NAVA have a variable  $V_t$  given a variable  $E_{adi}$ . This observation is especially relevant when  $E_{adi}$  is highly variable, as evidenced by the x-intercept of 26% with PS, compared to 8% with NAVA.

#### 4. CONCLUSIONS

22 patients underwent a 20 minute period of mechanical ventilation in PS mode followed by 20 minutes in NAVA mode.  $E_{adi}$  and flow signals were analysed, and it was found that significantly better correlation between  $E_{adi}$  and  $V_t$  was achieved in the NAVA ventilation mode, as expected, since in NAVA mode,  $E_{adi}$  determines the pressure settings on the ventilator which then influences flow characteristics.

In addition, it has been shown through a variety of different analyses that for a given variability in  $E_{adi}$ , a higher variability is observed in  $V_t$  under NAVA than PS. There is much speculation in the literature that increased breathing

variability is desirable, and is thought to be responsible for increased success in patient separation from the ventilator (Wysocki et al., 2006); and greater recruitment of atelectatic lung units (Mutch et al., 2000b). Future work will aim to correlate the greater tidal volume variability observed under NAVA with better patient outcomes.

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