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Detecting Asynchrony and Risk of Aspiration (DARS)

**Richard Branson, Chris Blakeman, Dina Gomaa, Michael Goodman
University of Cincinnati Sponsored Research Services**

**Dario Rodriguez
711 HPW/RHBA**

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711TH HUMAN PERFORMANCE WING,
AIRMAN SYSTEMS DIRECTORATE,
WRIGHT-PATTERSON AIR FORCE BASE, OH 45433
AIR FORCE MATERIEL COMMAND
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JAMES B. LEHMAN
Research Program Manager
Product Development Branch
Airman Biosciences Division

//signature//

MATTHEW J. DALTON, DR-III
En Route Care Product Area Lead
Product Development Branch
Airman Biosciences Division

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| 14. ABSTRACT: Introduction Asynchrony is the modern term for describing the patient 'fighting' or 'bucking' the ventilator. This study is looking at the impact of transport on asynchrony during transport, and if there is an association between asynchrony and the development of ventilator associated pneumonia (VAP). In preparation for mechanically ventilated patient movement, medications for sedation, pain and anxiety are often increased to improve patient comfort and safety. These drugs can both improve and worsen asynchrony. Methods Consent was obtained from a legally authorized representative (LAR). A respiratory monitor was placed inline the ventilator circuit to monitor pressure and flow signals for at least 20 minutes before transport, during transport, and at least 20 minutes after transport. vital signs, ventilator settings, and endotracheal tube cuff pressure were measured before and after transport and recorded. Sputum samples were obtained before and after transport. Results The primary exposure in this study was transportation, and primary outcomes (vital signs) were compared at three timepoints: before, during, and after transport. In this pilot study p-values for significance were 0.10. Statistical significance of differences between timepoints was tested using repeated measures generalized linear models clustered within subject. P-values presented are for the global null hypothesis (all timepoints equal.). Conclusion Data from the first 22 subjects does not show an increase or decrease in asynchrony during transport. We have demonstrated that the data can be effectively analyzed and reported. These results indicate that more data is needed, we will continue to enroll subjects. | | | | | |
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1.0. SUMMARY/DISCLAIMER

The following final technical report provides results regarding a clinical trial that explored the impact of transport on asynchrony during transport, and if there is an association between asynchrony and the development of ventilator associated pneumonia. The University of Cincinnati Institutional Review Board and the United States Air Force Human Research Protection Office approved the clinical trial. The final report will include information covering the methods, results for each research activity.

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2.0. BACKGROUND

Asynchrony is the modern term for describing the patient 'fighting' or 'bucking' the ventilator. An asynchrony index greater than (>) 10 percent (%) is associated with prolonged mechanical ventilation and poor outcome. We are studying the impact of transport on asynchrony, and if there is an association between asynchrony and the development VAP. Studies of asynchrony are complicated by manual detection methods, requiring laborious review of graphic displays of pressure and flow waveforms (11). More recently, Blanch and others have developed systems for automated detection of asynchrony. These systems rely on artificial intelligence to accurately measure asynchrony in the Intensive Care Unit (ICU) (12). The system requires the analysis of pressure and flow waveforms which are routinely displayed, but not commonly saved. While Blanch et al have shown that asynchrony events occur in 'clusters' associated with patient condition and procedures and that sedation level impacts asynchrony index (13), no studies have evaluated asynchrony associated with transport. VAP has been independently associated with transport of the patient from the ICU (14). However, the factors influencing VAP during transport have not been clearly elucidated. Bercault and co-workers suggest that changes in patient position and ventilation may lead to silent aspiration around Endotracheal Tube (ETT) cuffs (15). They identified the supine position required for most diagnostic procedures, manipulation of ventilator circuits (condensate drainage into the ETT) and lack of suctioning equipment as potential factors. This is supported by the large trial demonstrating an increase in VAP associated with the supine position (16). Detecting silent aspiration around the ETT cuff is difficult, but the use of markers suggestive of gastrointestinal fluids (amylase, pepsin) in the tracheal secretions has been described (17- 20) This method has been used to compare the efficacy of different ETT cuff shapes and materials. We plan to measure pepsin & amylase before and after transport as a surrogate for silent aspiration. The results of the study will define the impact of transport on patient ventilator asynchrony both during transport and prior to and following the event. We have observed that in preparation for patient movement,

medications for sedation, pain and anxiety are often increased to improve patient comfort and safety. These drugs can both improve and worsen asynchrony. Our study will be the first to use pepsin and amylase in tracheobronchial secretions to provide evidence of silent aspiration as a potential cause of VAP following patient movement.

3.0. METHODS

Patients requiring mechanical ventilation who will require transport for diagnostic or therapeutic procedures in radiology will be evaluated for enrollment. Informed consent will be obtained from the legally authorized representative (LAR) prior to transport, a respiratory monitor (non-invasive) will be placed in line with the ventilator circuit to monitor the pressure and flow signals needed for the detection of asynchrony. This will take place 1 hour before transport. Data will be extracted from the EMR (Electronic Medical Record) regarding demographic data, ventilator settings, injuries, and the dosage of all drugs for treatment of pain and anxiety. Patients will have a sample of their tracheal secretions collected prior to transport during normal airway care. These samples will be sent to the Surgical Research Unit trauma research laboratory for analysis of pepsin and amylase. During transport, airway pressure and flow signals will be recorded to the respiratory monitor. One member of the research team will accompany the clinical team on transport. Any concerns with the research equipment will be recorded. The dosages of drugs for pain and anxiety during the transport will be recorded. Upon return to the SICU (Surgical Intensive Care Unit), a period of observation of one hour will be recorded while the patient is on the ICU ventilator. Pressure and flow waveforms will be stored. Drug dosages will be recorded during the post-transport phase. Following return to the SICU, patients will again collect a sample of tracheal secretions during standard airway care for analysis of pepsin and amylase. Asynchrony index, the number of asynchronous breaths divided by total number of respiratory cycles x 100. An asynchrony index of > 10% is associated with prolonged ventilation and poor outcomes. The collected samples will be destroyed once they have been analyzed for the study.

4.0. RESULTS

The primary exposure in this study was transportation, and primary outcomes (vital signs) were compared at three timepoints: before, during, and after transport. These outcomes were systolic and diastolic blood pressure (SBP and DBP), mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR) oxygen saturation (SpO₂) and ETT cuff pressure. In this pilot study p-values for significance were 0.10. Statistical significance of differences between timepoints was tested using repeated measures generalized linear models clustered within subject. P-values presented are for the global null hypothesis (all timepoints equal.)

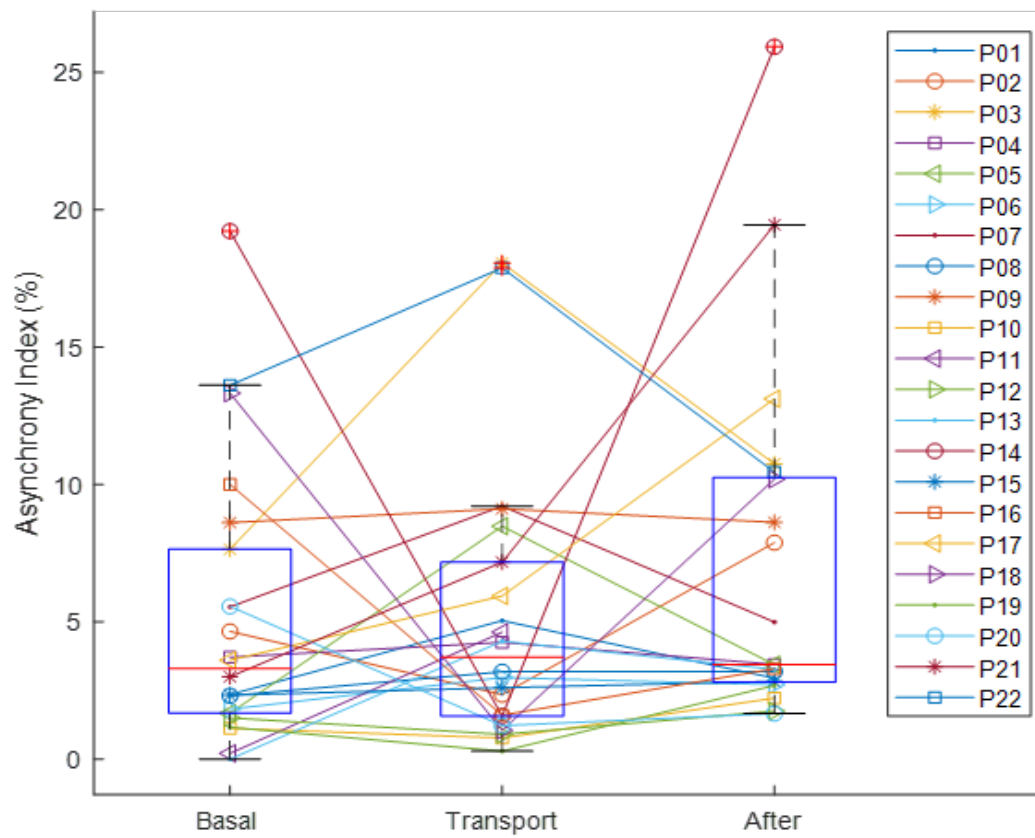
Raw data presented in Tables 1 and 2 were initially averaged per subject per timepoint, and then further summarized as described in the tables. However, data were not averaged before computing p-values.

| Measure | Before transport | During transport | After transport | P for difference |
|--|------------------|------------------|-----------------|------------------|
| SBP mmHg | 122 94, 158 | 128 102, 173 | 124 100, 161 | 0.75 |
| DBP mmHg | 62 49, 88 | 67 49, 86 | 63 44, 88 | 0.13 |
| MAP mm Hg | 82 66, 105 | 84 69, 105 | 82 68, 103 | 0.76 |
| HR bpm | 92 71, 120 | 91 67, 116 | 94 65, 119 | 0.24 |
| RR breaths/min | 20 11, 35 | 21 12, 31 | 23 12, 33 | 0.23 |
| SpO ₂ % | 97 94, 100 | 97 93, 100 | 96 92, 100 | 0.14 |
| ETT cuff pressure cm H ₂ O | 30 24, 40 | -- | 25 14, 40 | 0.0002 |

All measures are mean (5th, 95th percentile), averaged first by subject at each timepoint. P-values are type 3 tests of fixed effects from repeat-measure generalized linear model, clustered by subject, testing the global null (all timepoints equal.) Model of ETT cuff pressure excludes the missing timepoint.

Statistical Results

No measure varied significantly between timepoints except ETT cuff pressure (p=0.0002, Table 1). Mean within-subject changes in vital signs during transport, compared to before, all averaged an absolute value of less than 10% (Table 2) while after transport all averaged an absolute value within 5% of 'before' except for ETT cuff pressure (28% lower after transport). With the exception of ETT cuff pressure none of these differences were deemed clinically significant. Data from the first 22 patients does not show an increase or decrease in asynchrony during transport. We have demonstrated that the data can be effectively analyzed and reported. We provided the group from Spain with a Zoll ventilator to assist with identification of asynchrony. Zoll has been working with BetterCare to establish the software into the ventilator to recognize the presence of asynchrony and provide context sensitive help to the caregivers on how to ameliorate the problems. This is one of the goals of the study. Data from the first 22 transports are shown in Figure 1.



| | Basal | Transport | After |
|-------------|-------------------|---------------|------------------|
| Median (RI) | 3.33 (1.67– 7.64) | 3.72 (2-7.17) | 3.44 (2.8-10.25) |

Figure 1: Data from the first 22 transports

However, some individuals did experience clinically relevant changes in vital signs: for example, 5th and 95th percentiles for SBP change were -22% and +43% during transport, and -34 and +16% after transport.

| Table 2: Within-subject change in measures between timepoints | | |
|---|--------------------------------------|-------------------------------------|
| Measure | Percent change: during vs. before | Percent change: after vs. before |
| SBP mmHg | 6.3 -22, 43 | 1.3 -34, 16 |
| DBP mmHg | 9.4 -16, 43 | 0.60 -17, 19 |
| MAP mmHg | 3.8 -13, 27 | -0.61 -28, 17 |
| HR bpm | 1.9 -13, 15 | 1.6 -13, 15 |
| RR breaths/min | 9.1 -13, 52 | 5.5 -13, 25 |
| SpO ₂ % | 0.13 -3.3, 3.1 | -1.3 -5.4, 3.0 |
| ETT cuff pressure cm H ₂ O | -- | -28 -85, 0 |
| All measures are mean (5 th , 95 th percentile), averaged first by subject at each timepoint. | | |

5.0. DISCUSSION

Over part 1 of the study 110 subjects were screened for enrollment. Twenty-seven subjects (27) signed informed consent (legally authorized representative, surrogate) and 22 subjects were studied. Six subjects were consented but never required transport from the ICU. During transport vital signs and ventilator settings were continuously monitored. Ventilator waveforms were exported to a excel spreadsheet and shared with BetterCare (Spain) for independent analysis.

These findings regarding cuff pressure are potentially important. Transport from the ICU has been determined as an independent risk factor for development of ventilator associated pneumonia. The etiology of this findings has never been elucidated. This data suggests that changes in patient position during transport and imaging may result in alteration in ETT position and a fall in cuff pressure allowing secretions above the cuff to seep into the lower airway. Further analysis of the presence of pepsin or amylase in tracheal secretions may provide additional confirmation of this pathology.

Patients requiring mechanical ventilation for critical illness often have variable vital signs associated with pain, agitation, and level of sedation. Further enrollments should identify individuals at risk for sustained, clinically relevant changes in vital signs during transportation and take steps to mitigate these changes.

6.0. CONCLUSION

Data from the first 22 subjects does not show an increase or decrease in asynchrony during transport. We have demonstrated that the data can be effectively analyzed and reported. These results indicate that more data is needed, we will continue to enroll subjects.

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

| | |
|------------------|-----------------------------------|
| - | Minus |
| % | Percent |
| + | Plus |
| > | Greater Than |
| DBP | diastolic blood pressure |
| ETT | endotracheal tube |
| HPW | Human Performance Wing |
| HR | heart rate |
| ICU | Intensive Care Unit |
| LAR | legally authorized representative |
| MAP | mean arterial pressure |
| RR | respiratory rate |
| SBP | systolic blood pressure |
| SICU | Surgical Intensive Care Unit |
| SpO ₂ | Oxygen Saturation |
| VAP | Ventilator Associated Pneumonia |