RELATIONSHIP OF INFECTIOUS COMPLICATIONS TO OUTCOMES OF WEANING FROM PROLONGED MECHANICAL VENTILATION

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INTRODUCTION

Forty percent of patients who enter an ICU in North America require mechanical ventilatory support to treat respiratory failure;[1] only 5-20% require prolonged mechanical ventilation (PMV).[2,3] Transfer out of the ICU is driven primarily by cost and bed scarcity. Infection in the ICU, often with antibiotic-resistant organisms, has been shown to adversely affect numerous ICU outcomes. When ventilator-dependent patients are transferred to post-ICU care for continued weaning efforts, the risk of complications continues. There is preliminary data from a multicenter study reporting the most prevalent complications at long-term acute-care (LTAC) hospitals are infectious.[4] The current study was undertaken at Barlow Respiratory Hospital (BRH) to measure the effect of infectious complications on selected outcomes in an active post-ICU weaning program.

METHODS

Setting: 49-bed long term acute care (LTAC) hospital, a regional weaning center (RWC).
Study Design: Observational, quality assurance Ventilation Outcomes Study (VOS)[5] with concurrent data collection. No interventions. The study was a secondary analysis of data collected in an IRB approved study.
Study Population: All adult ventilator-dependent patients receiving invasive mechanical ventilation admitted for weaning.
Exclusion Criteria: Ventilator-dependent patients not admitted for weaning: admitted specifically for end-of-life care or terminal weaning, home ventilator training, chronically ventilated patient admitted for treatment of intercurrent medical problem, not a weaning candidate as documented by the physician on admission, prior inclusion in the study. Patients < 18 years of age.
Enrollment Period: March 1, 2002 – February 28, 2003

Data collection: Initial datasets were collected at BRH admission; all available information in the patient's transfer documents and BRH medical record was used to determine premorbid, demographic, and transferring hospital course data. Infectious and other complications treated at BRH were abstracted from progress notes, discharge summaries, and ICD-9 coding. Weaning outcomes were scored at BRH discharge. *Statistical analyses:* The Wilcoxon rank sum test was used to investigate the differences in length of stay and time to wean between patients treated and not treated separately for infection. The Yates-corrected chi-square test was used to investigate: 1) the associations between death and infection, 2) the association between death and the number of treated infections (single vs. multiple), 3) the association between death and isolation for two drug-resistant bacteria, and 4) the association between diabetes and the number of treated infections. Univariate and stepwise analyses were used to investigate the associations between types of infection and: a) sepsis with shock, b) sepsis without shock, and c) septic shock death.

All analyses were conducted at the 0.05 significance level and utilized SAS (Cary, NC: Version 8.02) and STATA (College Station, TX: Version 8.1).

Table 1 Patient Demographics, Status on BRH Admission, Hospital Course, and Weaning Outcomes

Parameter	n = 186
Age, years	74 [22-98]
Female gender	53%
History of smoking	60%
• Pack-years	54 ± 31
Prior episode of mechanical ventilation	19%
Pre-existing diagnosis of diabetes mellitus	28%
Tracheotomized	89%
Urinary catheter	92%
Tube feeding	93%
Stage 2 or higher pressure ulceration	44%
APACHE®III APS	38 [4-98]
Prior LOS in transferring ICU (days)	32 [1-216]
Prior mechanical ventilation time (days)	31[1-215]
BRH LOS (days)	35 [3-167]
Time to wean (days)	19 [3-127]
Weaned	49%
Ventilator-dependent	22%
Died	29%

Table 2 Infections Treated at BRH

Number of Infections Treated per Patient	Frequency	%
0	48	25.8
1	32	17.2
≥2	106	57.0
Type of infection:		
Urinary tract infection	85	45.7
Pneumonia or tracheobronchitis	76	40.9
Clostridium *difficile* colitis	74	39.8
Sepsis with shock	29	15.6
Line sepsis	28	15.1
Sepsis without shock	13	7.0
Aspiration pneumonia	10	5.4

Four of the five most common complications at BRH were infectious. Infections present on admission, and nosocomial infections, were treated in 70% of all PMV patients.

Table 3 Association of Diabetes Mellitus and Number of Treated Infections*

	Treated for 1 infection		Treated for ≥2 infections	
	OR (95% CI)	p	OR (95% CI)	p
Pre-existing diabetes mellitus (DM)				
No (n=134)	1.00		1.00	
Yes (n=52)	1.25 (0.49, 3.20)	0.64	1.94 (0.88-4.28)	0.09
Pre-existing DM treated at BRH				
No (n=8)	1.00		1.00	
Yes (n=44)	7.14 (0.53, 95.38)	0.08	9.64 (1.24, 75.01)	0.01
All patients treated for DM at BRH				
No (n=116)	1.00		1.00	
Yes (n=70)	1.94 (0.78, 4.80)	0.14	3.84 (1.72, 8.59)	<0.01

**Chi-square test*

Diabetes mellitus, known to impair immune function in the chronically critically ill,[6] is a comorbidity associated with the risk of multiple infections in patients with a secure diagnosis of same at BRH. In a report by Esau and Charlebois,[7] patients with diabetes and PMV were less likely to wean, and more likely to require full or partial chronic mechanical ventilation than non-diabetic patients.

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Table 4 Association of Length of Stay and Time to Wean to Treatment of Infection

Infection	LOS (days)	p	Time to Wean* (days)	p
Urinary tract infection				
No (n=101)	27.0 [3-150]	<0.01	14.0 [3-74]	<0.01
Yes (n=85)	49.0 [11-167]		22.0 [8-127]	
Pneumonia or tracheobronchitis				
No (n=110)	28.5 [3-109]	<0.01	17.0 [3-101]	0.03
Yes (n=76)	50.0 [7-167]		22.0 [7-127]	
Clostridium *difficile* colitis				
No (n=112)	27.0 [3-167]	<0.01	15.0 [3-101]	<0.01
Yes (n=74)	47.0 [15-136]		23.5 [7-127]	
Line sepsis				
No (n=158)	32.5 [3-150]	<0.01	18.0 [3-119]	0.03
Yes (n=28)	56.5 [7-167]		38.0 [9-127]	
Aspiration pneumonia				
No (n=176)	35.0 [3-167]	0.05	18.0 [3-127]	0.03
Yes (n=10)	53.5 [14-131]		34.5 [19-119]	

**In the 95 patients who weaned*

Median length of stay and time to wean from mechanical ventilation were significantly longer in patients sustaining any of the five infections above, than in non-infected patients.

Table 5 Association: Death as Outcome, Infection Treatment, and Isolation

Infection (in order of frequency)	Death		
	OR	95% CI	p
Urinary tract	1.15	0.61-2.17	0.67
Pneumonia or tracheobronchitis	2.61	1.36-4.98	<0.01
Clostridium *difficile* colitis	0.95	0.50-1.81	0.87
Line sepsis	3.52	1.54-8.04	<0.01
Aspiration pneumonia	1.05	0.26-4.22	1.00*
Two or more infections treated	3.19	1.27-8.00	0.01
Isolation for MRSA	0.79	0.40-1.56	0.49
Isolation for VRE	1.24	0.30-5.13	0.72*

**Fisher's exact test*

Pulmonary and more serious infections, and more than one infection, would be expected to have a significant impact on mortality, which is the case above.

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Table 6 Association: Infections and Sepsis, and Death Caused by Sepsis*

Infection	Association	OR	95% CI	p
Aspiration pneumonia	Sepsis w/o shock	7.64	1.33-43.78	0.02
Clostridium *difficile* colitis	Sepsis w/o shock	9.09	1.65-50.06	0.01
Pneumonia or tracheobronchitis	Sepsis w/ shock	4.13	1.64-10.40	<0.01
Death	Sepsis w/ shock	30.1	10.5-86.3	<0.01

**Univariate logistic regression for values <0.20 that preceded this stepwise logistic regression analysis is not shown; gender and age adjusted. Only significant associations are shown.*

The association of lower respiratory infection, except that caused by aspiration of gastric contents, with sepsis with shock was significant. This is important because sepsis with shock was itself associated with death in hospital. Both aspiration pneumonia and C. *difficile* colitis were significantly associated with sepsis without shock.

Risk indicators associated with specific infections may be contributing factors in the occurrence of the infection, or the result of it, with the infection actually present on admission. It follows from this that: 1) if the risk indicator is a contributor, and 2) the mechanism resulting in the contribution is known, and 3) that mechanism can be modified with demonstrable good effect, then the risk indicator is clinically significant, as well as statistically significant. An example of a risk indicator fulfilling the three criteria may be diabetes, although infection can unmask diabetes as well. Diabetes may meet criteria numbers one and two, but may not meet number three. If in the ICU tighter glucose control decreases infection,[8] criterion number three above might be met with tighter glucose control in PMV patients post-ICU – if further study proved it so.

SUMMARY AND COMMENTS

Of complications that typically befall ventilator-dependent patients (infectious, cardiovascular, mechanical), common complications treated in patients weaning from mechanical ventilation in the post-ICU setting are infectious. These patients have a host of conditions that may make them particularly susceptible to infections, including: age, multiple organ dysfunction, ICU exposure to broad spectrum antibiotics with resultant antibiotic resistance,[9] impaired mental status, incontinence, indwelling lines (venous catheters, Foley catheters), aspiration, and tracheostomy. In this cohort of 186 post-ICU patients studied at BRH:

- Infection, on admission or nosocomial, was treated in 70% of patients.
- More than one infection was treated in 57% of patients.
- The prior diagnosis and concurrent treatment of diabetes mellitus was associated with sepsis and treatment of multiple episodes of infection.
- Treatment of five types of infection was associated with prolongation of length of stay and time to wean.
- Treatment of lower respiratory infection was associated with sepsis with shock, while treatment of aspiration pneumonia and treatment of C. *difficile* was associated with sepsis without shock.
- Death as an outcome was associated with treatment for lower respiratory infection, line sepsis, sepsis with shock, and multiple infections.
- High incidence of infection and the attendant risk of mortality from infection should mandate a high allocation of resources directed at this complication in hospitals and units weaning patients from PMV in the post-ICU setting.

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