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clinical investigations in critical care

Protocol Weaning of Mechanical Ventilation in Medical and Surgical Patients by Respiratory Care Practitioners and Nurses*

Effect on Weaning Time and Incidence of Ventilator-Associated Pneumonia

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Study objectives: (1) To determine the effect of a single ventilator management protocol (VMP) used in medical and surgical ICUs on the duration of mechanical ventilation. (2) To determine the effect of a VMP on the incidence of ventilator-associated pneumonia (VAP).

Design: Prospective, randomized, controlled study.

Setting: University medical center.

Patients: Three hundred eighty-five patients receiving mechanical ventilation between June 1997 and May 1998.

Interventions: A respiratory care practitioner- and registered nurse-driven VMP.

Results: Intervention and control groups were comparable with respect to age, sex, severity of illness and injury, and duration of respiratory failure at the time of randomization. The duration of mechanical ventilation for patients was decreased from a median of 124 h for the control group to 68 h in the VMP group (p = 0.0001). Thirty-one total instances of VAP were noted. Twelve patients in the surgical control group had VAP, compared with 5 in the surgical VMP group (p = 0.061). The impact of the VMP on VAP frequency was less for medical patients. Mortality and ventilator discontinuation failure rates were similar between control and VMP groups. *Conclusions:* A VMP designed for multidisciplinary use was effective in reducing duration of mechanical with a

ventilatory support without any adverse effects on patient outcome. The VMP was also associated with a decrease in incidence of VAP in trauma patients. These results, in conjunction with prior studies, suggest that VMPs are highly effective means of improving care, even in university ICUs.

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Key words: artificial respiration; clinical protocols; ICU; pneumonia; time factors; ventilator weaning **Abbreviations:** APACHE = acute physiology and chronic health evaluation; FIO_2 = fraction of inspired oxygen; MD = physiciandirected; MICU = medical ICU; PEEP = positive end-expiratory pressure; PS = pressure support; RCP = respiratory care practitioner; RN = registered nurse; SBT = spontaneous breathing trial; VAP = ventilator-associated pneumonia; VMP = ventilator management protocol

M echanical ventilatory support is commonly required for critically ill patients. Although it is often lifesaving, it is invasive, expensive, and associ-

ated with a variety of potentially serious complications. Reducing the time a patient spends receiving mechanical ventilatory support is a worthy approach to both improving patient care and reducing its related costs.

A number of studies have demonstrated that standardized approaches to liberation from mechanical ventilatory support can shorten the duration of mechanical ventilatory support.^{1–6} Limitations of previous studies included the use of historical controls^{2,4} and lack of a single, universally applied protocol.^{2,3} No trial has documented the effectiveness of a single protocol for use in medical and

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surgical ICUs in a prospective, randomized, controlled fashion. The potential beneficial effect of a weaning protocol, although significant in some studies,^{3,5} may be diluted by enrollment of patients at ICU admission, some of whom will have prolonged or terminal respiratory failure.

A potential corollary benefit of reducing duration of mechanical ventilation is a reduction in ventilatorassociated complications. The risk of ventilator-associated pneumonia (VAP) appears to be related to duration of mechanical ventilation.^{7,8} We hypothesized that the incidence rate of VAP would be reduced by an effective ventilator management protocol (VMP).

The purpose of our study was to examine the efficacy of a single VMP in both medical and surgical ICUs. The VMP was created during multidisciplinary planning and required no additional support staff for its implementation, in contrast to other efforts.⁹ Because the focus of the study was on ventilator discontinuation, patients were randomized only after meeting objective physiologic criteria indicating a readiness to commence weaning. Standard ventilator management practice was compared with the VMP in a randomized, controlled fashion. In addition, we prospectively examined the effect of the VMP on the incidence of clinically defined VAP in our study population.

MATERIALS AND METHODS

Patients

A total of 335 consecutive patients who were receiving mechanical ventilation were enrolled from the University of California, Davis, Medical Center medical ICU (MICU) and trauma services between June 1997 and May 1998. The MICU service is led by board-certified critical care medicine physicians supervising a fellow, resident physicians, and students. The trauma service is led by trauma/critical care surgical staff supervising trauma fellow(s), resident physicians, and students. MICU and trauma patients located within three particular ICUs were eligible. Respiratory care practitioners (RCPs) were not assigned to one particular ICU, but rather rotated through all adult ICUs. Staffing of RCPs to ventilators in the adult ICUs was generally 1:7. Staffing of registered nurses (RNs) to patients in these ICUs was between 1:1 and 1:2. RCPs and RNs were instructed on trial and VMP procedures before the study, and an interim educational meeting was held for the RCPs approximately halfway through subject enrollment.

Randomization

Eligible patients were identified by twice-daily RCP screening in the participating ICUs. Entry criteria were the following: (1) PaO₂/fraction of inspired oxygen (FIO₂) \geq 200; (2) static compliance \geq 25 mL/cm H₂O; (3) minute volume \leq 15 L/min (\leq 200 mL/kg/min); and (4) lack of failure of ventilator discontinuation within the past 24 h. Pregnant patients, patients < 18 years old, mentally disabled patients, and prisoners were excluded. A prospective, randomized cohort design was used. Once qualification for study entry was established, the patients were randomly assigned to either the physician-directed (MD) or the VMP group. Randomization was by opaque, sealed, numbered envelopes stratified for MICU and trauma services and for ICU. The UC Davis Human Subjects Review Committee approved the study, and the informed consent requirement was waived.

Study Protocol

Physicians caring for patients randomized to the experimental (VMP) groups were notified, and a verbal order was requested for study entry. VMP group patients were then screened for the appropriateness of an immediate spontaneous breathing trial (SBT). Patients receiving ventilation > 72 h before study entry did not meet criteria for an immediate SBT, and the protocol directed the incremental decrease of each subject's FIO₂, positive end-expiratory pressure (PEEP), intermittent mandatory ventilation rate, and pressure support (PS) level, as tolerated, in a prioritized fashion.

Patients were then screened for SBTs twice daily. To pass the SBT screen, patients had to have the following: (1) a Glascow coma score ≥ 10 or a tracheostomy, (2) a mean arterial pressure of ≥ 60 mm Hg without vasopressor agents (dopamine was allowed in doses $\leq 5 \ \mu g/kg$ body weight/min), and (3) an adequate cough not limited by pain. Physician approval for SBTs was not required. A 30-min SBT was used and was performed on flow-by mode, $PS \le 8 \text{ cm } H_2O$ with $PEEP \le 8 \text{ cm } H_2O$, or T piece, at the discretion of the RCP. The SBT was terminated for oxygen saturations < 92%, respiratory rate > 30 breaths/min, spontaneous tidal volumes < 5 mL/kg body weight, or respiratory distress. Physicians were asked at the end of successful SBTs to approve discontinuation of mechanical ventilation. If an SBT was not tolerated, the patients were returned to their prior settings and were rescreened every 6 h between 7:00 AM and 7:00 PM for a repeat SBT, to a maximum of two SBTs each day.

Incremental reduction of FIO_2 , PEEP, intermittent mandatory ventilation, and PS was allowed 24 h/d for VMP patients. Patients in the VMP group were not allowed to undergo SBT (and therefore subsequent ventilator discontinuation) between 7:00 PM and 7:00 AM unless they met criteria for an immediate SBT on study entry (Fig 1).

Patients randomized to the control group were managed as per standard ICU practice. Physicians' orders were required for all ventilator changes and weaning assessments. Algorithmic orders were allowed. No specific information on the VMP was provided to any participating physician. Physicians caring for patients randomized to the experimental (VMP) group were instructed not to interfere with the ventilator management by the RCP unless the patient was in respiratory distress or was unstable. Physicians on the trauma service referred to a printed, standardized approach to ventilator management that had been in use before our study. There was no structured approach to weaning patients on the MICU service.

Definitions

All definitions were selected *a priori*. APACHE (acute physiology and chronic health evaluation) II, injury severity, and Glascow coma scores were calculated in the usual manner.^{10,11} VAP was clinically defined as initiation of antibiotics for clinical suspicion of VAP in association with two of the following: (1) positive endotracheal tube aspirate or bronchoscopy cultures; (2) fever or rising peripheral leukocyte count; and (3) pulmonary opacities consistent with pneumonia without objective evidence



FIGURE 1. VMP (see text for details). ABG = arterial blood gas; MAP = mean arterial pressure; RR = respiratory rate; Sao_2 = arterial oxygen saturation; VT = tidal volume; GCS = Glascow coma scale; IMV = intermittent mandatory ventilation.

of left atrial hypertension. The objective criteria for ventilator discontinuation readiness were defined as (1) passage of the SBT screen, and (2) successful completion of a 30-min SBT performed on flow-by mode, PS $\leq 8~{\rm cm}~{\rm H_2O}$ on PEEP $\leq 8~{\rm cm}~{\rm H_2O}$, or T piece (see above). Successful discontinuation of mechanical ventilation was defined as continuous independence from ventilator support for a 24-h period.

Outcomes

The total duration of mechanical ventilation and the incidence of VAP were defined as primary outcomes *a priori*. Secondary outcomes were the duration of mechanical ventilation from study entry to discontinuation of ventilator support, the duration of mechanical ventilation from initiation of mechanical support to meeting ventilator discontinuation criteria (Fig 2), the ventilator discontinuation failure rate, and death.

Data Analysis

Standard methods of exploratory data analyses were used to calculate summary statistics and to explore the distribution of each explanatory variable (Minitab Statistical Software, Release 11; Minilab Inc.; State College, PA). Univariate relationships between experimental group assignments and outcomes (achieving ventilator independence or meeting objective criteria for ventilator discontinuation) were examined using either a χ^2 or a Wilcoxon rank sum statistic. Kaplan-Meier survival curves were



FIGURE 2. Time-line detail of outcomes as related to clinical progress. MV = mechanical ventilation.

generated for each group, and a log rank statistic was used to test the null hypothesis that group assignment does not affect the time to meet an end point. Cox proportional hazards analysis was used to compare time to each end point after adjustment for covariates, including age, APACHE II, sex, duration of respiratory failure before study entry, and admission diagnoses (SAS Statistical Software, Version 7; SAS Institute; Cary, NC). Using a two-sided test and assuming a type 1 error of 0.05, the study was expected to have 80% power to detect a 1.5-day difference between groups with respect to the time to ventilator discontinuation. We also estimated a similar degree of power to detect a 1.5% absolute change in incidence rate of VAP.

Results

Demographic Variables

A total of 335 patients were enrolled in the study. Seventeen patients otherwise eligible were not enrolled. These patients had brief periods of mechanical ventilation, averaging 2 ventilator days only. Data

from a total of 82 patients were right censored for completion of the survival analysis per previously determined exclusion criteria. Patient data were censored for deterioration in clinical status, defined as repeated increases in mechanical support, study violations by physicians assuming ventilator management of experimental group subjects, death, transfer to other facilities, and refusal of physicians, patients, or patient's families to participate further. There were no differences in the proportions of patients censored within the combined treatment and control groups and MICU and trauma subgroups. Two hundred fifty-three patients were evaluated from study entry to ventilator discontinuation, with 124 patients (49%) receiving MD weaning and 129 patients (51%) receiving VMP weaning. There were no notable differences in age, sex, APACHE II or injury severity scores, or duration of respiratory failure

Characteristics	Medicine		Surgery	
	MD $(n = 88)$	VMP (n = 82)	MD $(n = 81)$	VMP (n = 84)
Age, yr	56.6 ± 16.0	54.5 ± 17.1	41.0 ± 17.6	41.5 ± 18.3
Sex, % male	59	63	68	75
APACHE II	22.8 ± 7.5	20.6 ± 7.4	15.4 ± 5.6	15.5 ± 6.5
Injury severity score			20.1 ± 13.3	18.7 ± 14.0
Diagnosis, No.†				
Postoperative trauma (38.8)			67	63
Nonoperative trauma (8.4)			9	16
Pneumonia (7.5)	14	11	1	
Neurologic emergency (7.5)	9	15	1	
Poisoning (6.6)	9	12		
GI bleed/liver (5.4)	7	11		
COPD/asthma (4.8)	10	6		
Respiratory failure (4.5)	11	3	1	
Metabolic/renal (2.1)	5	2		
CHF (2.1)	5	2		
Respiratory failure duration before study entry, h	75.6 ± 131.1	56.7 ± 103.1	37.0 ± 47.6	51.0 ± 111.0
Right censored, No.‡	32	22	13	15

Table 1-Patient Characteristics at Time of Randomization*

*Data are presented as mean \pm SD unless otherwise indicated. CHF = congestive heart failure.

†The numbers in parentheses are the percentage of all study patients in each diagnostic category.

\$See text for explanation.

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 Table 2—Primary Outcomes*

Outcomes	MD	VMP	p Value
Duration of mechanical ventilation, m	nedian h		
(interquartile range)			
Medicine $(n = 170)$	232 (63-435)	78 (38–168)	0.0003
Surgery $(n = 165)$	111 (52–181)	64 (30–156)	NS
Combined $(n = 335)$	124 (54–334)	68 (33–164)	0.0001
VAP, No. of patients in treatment arm	ns (%)		
Medicine $(n = 170)$	8 (9)	6 (7)	0.674
Surgery $(n = 165)$	12 (15)	5 (6)	0.061
Combined $(n = 335)$	20 (12)	11 (7)	0.100

*NS = not significant.

before study entry between MD and VMP-directed groups (Table 1). Admission diagnoses were similarly distributed within MICU and trauma patient groups, and numbers of patients with asthma, COPD, pneumonias, and postrespiratory arrests were similar between treatment and control groups.

Duration of Mechanical Ventilation

On the MICU service, the median duration of mechanical ventilation was 232 h in the MD weaning group and 78 h in the VMP group (p = 0.0003, Wilcoxon test; Table 2). Kaplan-Meier survival plots of the probability of continued ventilatory support are shown in Figure 3. Time point analysis suggested the most salutary effect of the VMP on MICU

service mechanical ventilator duration was between the subjects' study entry and their meeting ventilator discontinuation criteria (median, 87 h in MD group and 18 h in VMP-directed group; p < 0.0001, Wilcoxon test). Multivariate analysis demonstrated the odds of attaining ventilator independence were statistically better in the VMP group than in the MD group (risk ratio, 1.67; p = 0.009).

On the trauma service, Kaplan-Meier survival plots of the probability of continued ventilatory support suggested that a difference in mechanical ventilation duration between MD and VMP-directed groups was only present in the first 96 h (Fig 4). The median duration of mechanical ventilation for patients discontinued from ventilatory support in the



FIGURE 3. Probability of continued ventilatory support in MICU patients.

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first 96 h was 52 h in the MD weaning group (n = 44, 25% censored) and 33 h in the VMP group (n = 53, 13.2% censored; p = 0.067, Wilcoxon test). Time point analysis suggested the beneficial effect of the VMP on trauma service patients was primarily on the duration of mechanical ventilation after the subjects met ventilator discontinuation criteria until the time of ventilator discontinuation (median, 22 h in MD group and 6 h in VMP-directed group; p = 0.012, Wilcoxon test). Multivariate analysis also showed that VMP management (risk ratio, 1.65; p = 0.006) led to more rapid ventilator discontinuation after subjects met ventilator discontinuation criteria.

Combined group analysis indicated that duration of mechanical ventilation was decreased from a median of 124 h for all MD patients to 68 h in the VMP group (p = 0.0001; Table 2). Multivariate analysis demonstrated that VMP management (risk ratio, 1.41; p = 0.0076) led to a reduced duration of mechanical ventilation.

VAP

The overall rate of VAP in our selected study population was 0.71/1,000 h of mechanical ventilation. Thirty-one total instances of VAP were noted, 14 from the MICU service and 17 from the trauma service (Table 2). On the trauma service, 12 subjects in the MD group had VAP, compared with 5 in the VMP-directed group (p = 0.061, χ^2). The impact of the VMP on VAP frequency was less for all patients combined (p = 0.100, χ^2) because of reduced VMP effect on VAP in the MICU patients. Binary logistic regression suggested a protective effect of the VMP for VAP on the trauma service (risk ratio, 0.39; p = 0.119).

To examine the value of our clinical VAP definition for predicting changes in clinical outcomes, the relationship of VAP to mortality and ventilator discontinuation failure was examined. One of the MICU patients with clinically diagnosed VAP died during the study, but no trauma patients with VAP died (p = 0.84, χ^2). Three MICU patients and 5 trauma patients with VAP had ventilator discontinuation failures, compared with only 23 of 301 patients without VAP (p = 0.0008, χ^2). Thus, a clinical diagnosis of VAP was more common among patients with ventilator discontinuation failures, although not among those that died.

Secondary Outcomes

The duration of mechanical ventilation from initiation of mechanical support to meeting ventilator discontinuation criteria was significantly reduced for the MICU patients and all patients combined on the VMP (Table 3). The duration of mechanical ventilation from study entry to discontinuation of ventilator support was significantly reduced by use of the VMP for MICU, trauma, and both groups combined.

There was no difference in ventilator discontinuation failure rates between all MD and VMP-directed patients (p = 0.28, χ^2). The ventilator discontinuation failure rate was greater for the VMP-directed as compared with the MD MICU patients (10.8% vs 4.8%, p = 0.185, χ^2 test), but still within the range of expected ventilator discontinuation failure rates.^{3–5,12}

All-cause mortality for intent-to-treat patients was not different for patients managed by physicians as compared with those managed by VMP (p = 0.146, χ^2). Study subjects were selected on the basis of adequate pulmonary physiology, thus explaining the rather low observed mortality rates.

Other Results

The decision to perform tracheotomy or transfer to long-term acute care facilities was left to the discretion of the managing physicians. In the MICU group, 19 patients underwent tracheotomy; 13 of these were physician managed and 6 were VMP managed. In the trauma service group, 15 patients underwent tracheotomy; 8 of these were physician managed and 7 were VMP managed. Five MICU group patients were discharged to a long-term acutecare facility. Four of these patients were physician managed, and only one patient was VMP managed. No trauma service patients were discharged to a long-term acute-care facility.

DISCUSSION

Standardization of patient management through the use of protocols and guidelines is increasingly being adopted as a means to monitor and improve quality of care and reduce costs.¹³ Our prospective, randomized trial demonstrates the feasibility and effectiveness of a single, easily implemented VMP in shortening the duration of mechanical ventilation for MICU and surgical ICU patients. This protocol required no additional staff and minimal specific training of RNs and RCPs. A physician order was required during the VMP only for ventilator discontinuation once patients met objective ventilator discontinuation criteria. The median duration of mechanical ventilation was reduced by 2.33 days without affecting ventilator discontinuation failure rates.

A low probability value was noted for the comparison of all-cause mortality of patients managed by physicians with those managed by VMP (p = 0.146). This might indicate a trend toward increased mortality for the patients randomized to the weaning



FIGURE 4. Probability of continued ventilatory support in trauma patients.

protocol. More severely ill study patients were excluded by the entry criteria of the protocol, and as a result, our overall mortality was low and the study was not powered to differentiate small changes in mortality from chance occurrence. More importantly, no patients died as a direct result of the weaning protocol, and it would seem unlikely that a weaning protocol comparable to or better than physician management would adversely affect mortality.

The subjects' disease process and the duration of respiratory failure before study entry affect the total duration of mechanical ventilation. A VMP will not influence the resolution of the patient's respiratory failure. Examining the time frame from protocol entry to ventilator discontinuation allows a focused look at the effect of a weaning protocol. Although our primary study end point was total duration of mechanical ventilation, the duration of mechanical ventilation from study entry to ventilator discontinuation is arguably the most important measure of the effect of the VMP on the weaning process. We found a highly statistically significant improvement in this variable for both medical and surgical patients in the VMP group.

Physician practice impacted on the effectiveness of the VMP. On the trauma service, a standardized MD approach to ventilator management was in place during the study. Control patients were managed with SBTs that were lengthened and/or performed more frequently, as tolerated. However, the decision to extubate the patient was not standardized, but was left to the physicians' subjective impression of patient readiness. The duration of mechanical ventilation from study entry to meeting mechanical ventilator discontinuation criteria (the "weaning time") was not significantly affected by the VMP in the trauma population, but the duration of ventilation from meeting ventilation discontinuation criteria to ventilator discontinuation was. In fact, a 70% reduction in duration of mechanical ventilation after VMP patients met ventilator discontinuation criteria was observed. There was no difference in ventilator discontinuation failure rate between trauma VMP and control groups, suggesting that the ventilator discontinuation criteria of the VMP was as specific as the subjective impressions of the trauma physicians. Thus, the use of subjective criteria for determining ventilator discontinuation readiness led to unnecessary prolongation of mechanical ventilation in the MD trauma control group. It is likely that weaning time and total duration of mechanical ventilation were not significantly reduced by the VMP because a standardized, although less formal, weaning protocol was already in place. In contrast, in the MICU, in which there was no structured approach to weaning in place for the control group, the VMP outperformed physicians for each segment of the weaning process.

Published studies suggest that physician acceptance is paramount to the success of a VMP. In one

Outcomes	MD	VMP	p Value
Protocol effectiveness, median h (interquartile range)			
Duration of MV from initiation to meeting MV			
discontinuation criteria			
Medicine $(n = 170)$	174 (49–359)	53 (23-136)	0.0001
Surgery $(n = 165)$	55 (27–109)	33 (20-151)	NS
Combined $(n = 335)$	79 (36–234)	42 (21-136)	0.0001
Duration of MV from study entry to ventilator			
discontinuation			
Medicine $(n = 170)$	141 (48–324)	35 (12–124)	0.0001
Surgery $(n = 165)$	69 (23–144)	43 (17-99)	0.0001
Combined $(n = 335)$	97 (31–214)	38 (16-106)	0.093
Complications, No. of patients in treatment arms (%)			
Ventilator discontinuation failures			
Medicine $(n = 170)$	4(5)	8 (11)	0.185
Surgery $(n = 165)$	6 (8)	7(9)	0.825
Combined $(n = 335)$	10 (6)	15 (9)	0.280
Hospital mortality			
Medicine $(n = 170)$	9 (11)	13 (16)	0.275
Surgery $(n = 165)$	1(1)	4 (5)	0.368
Combined $(n = 335)$	10 (6)	17 (10)	0.146

Table 3—Secondar	y Outcomes*
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*MV = mechanical ventilation.

study, physicians used three separate protocols in four ICUs to facilitate acceptance.³ A scheme for identification of patients capable of spontaneous breathing was effective in two MICUs,⁵ but surgical physician acceptance was only 63% during the first year of the large-scale implementation of the protocol.¹² A multidisciplinary, multidepartmental team was used to develop our VMP. The education and leadership provided by physician, RCP, and nursing opinion leaders to their respective counterparts helped ensure the success of implementation of the VMP. A separate analysis of house staff attitudes found that, regardless of department, house staff considered VMPs beneficial to patients, and RNs and RCPs competent to perform weaning. They did not view protocols as detrimental to education or a threat to their autonomy in the ICU.¹⁴

Acceptance of our VMP is suggested by the brief duration of mechanical ventilation after patients met ventilator discontinuation criteria. There was little difference between MICU and trauma subjects in this regard, with > 75% of patients identified as meeting extubation criteria liberated from mechanical ventilation within 24 h, and > 90% by day 3.

Previous estimates of ventilator protocol costbenefit have not included the impact of protocols on ventilator-associated complications. Our study found a difference (p = 0.061) in the incidence of clinically defined VAP between VMP and control trauma patients. The beneficial effect of reducing invasive mechanical ventilatory support on the incidence of VAP has been demonstrated in other studies.^{15,16} The low numbers of VAP observed in this study reduces the certainty of the conclusion that VAP may be reduced by a weaning protocol. The effect of protocol weaning on VAP should be examined in other clinical trials and venues. The less significant effect of the VMP on VAP in the MICU, despite a more dramatic shortening of time receiving mechanical ventilation, may be explained by the preponderance of respiratory admission diagnoses, which may have confounded our clinical definition of VAP.

Our study had other potential limitations. Although it was prospective, randomized, and controlled, it could not be blinded. It is possible that RNs and RCPs may have been more motivated in their weaning of patients on the VMP. Careful monitoring by a protocol manager failed to detect overt bias. A clinical definition of VAP was used rather than a pathologic or invasive sampling method. Although studies have demonstrated the difficulties in clinically predicting the presence of VAP,¹⁷ the impact of invasive airway culture sampling on outcome of VAP remains controversial.¹⁸ In terms of antibiotic and resource utilization, a clinical definition is not only adequate but also relevant.

CONCLUSION

A VMP designed for multidisciplinary use was effective in reducing duration of mechanical ventilatory support without any adverse effects on patient outcome. The VMP was also associated with a decrease in incidence of VAP in trauma patients and with a trend toward a reduction in the incidence of VAP in combined medical and surgical groups. Our protocol was implemented without additional staff and with minimal specific training of RNs and RCPs and was well accepted by physicians. These results, in conjunction with those of prior studies, suggest that VMPs are highly effective means of improving care, even in university ICUs where physicians are present around the clock.

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