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FLEX: A NEW COMPUTERIZED SYSTEM FOR MECHANICAL VENTILATION

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ABSTRACT. Objective. To describe and evaluate a new weaning and decision support system for mechanical ventilation. **Background.** FLEX is a computerized weaning and decision support system for mechanical ventilation that unlike previous rule-based systems derives many of its rules on the basis of the conditions of individual patients. This system can be used in a wide range of ventilatory modes as well as automatic control of weaning. It incorporates the features of the patented ventilatory mode known as Adaptive Support Ventilation (ASV) along with other new features for control of weaning, and control of patient's oxygenation by adjustment of PEEP and the fraction of inspired oxygen. **Methods.** Ventilator data was collected for 10 patients in medical/surgical ICU at baseline and about 24 hours later. Required data fields for each patient for these two time points were also entered into the FLEX program. Comparison of clinical data and FLEX recommendations were made with regard to minute ventilation, alarms, weaning institution and other variables. **Results.** At baseline, 7 patients were being treated with AC, the remainder with IMV/PS. There was good agreement between the measured and recommended minute ventilations; variances were seen in some patients being treated with permissive hypercapnea and those with evidence of high oxygen needs or other metabolic derangements. At 24 hours, there was improved correlation between measured minute ventilation and that recommended by FLEX, suggesting that clinical adjustments were in-line with Flex recommendations over time. Furthermore, FLEX made recommendations with regard to FIO_2 and PEEP that would potentially diminish the risk of oxygen toxicity, hypoxemia, and barotrauma in selected patients. FLEX has also been implemented as a closed loop system in an initial set up. **Conclusion.** A new weaning and decision support system for mechanical ventilation is presented. The recommendations made by the system were found to be in line with clinical determinations. Further refinements in the FLEX predictions can be easily made by including inputs which represent permissive hypercapnea or increased metabolic demand for selected patients.

KEY WORDS. mechanical ventilation, decision support system, automatic control, weaning..

INTRODUCTION

Choosing the right ventilatory settings in the hospital intensive care unit is a complex and demanding task for most medical personnel. In order to assure optimal settings, the many features and variety of output settings of advanced mechanical ventilators need to be clearly understood as well as the progress of the patient's underlying illness and his/her response to therapy. There have been many

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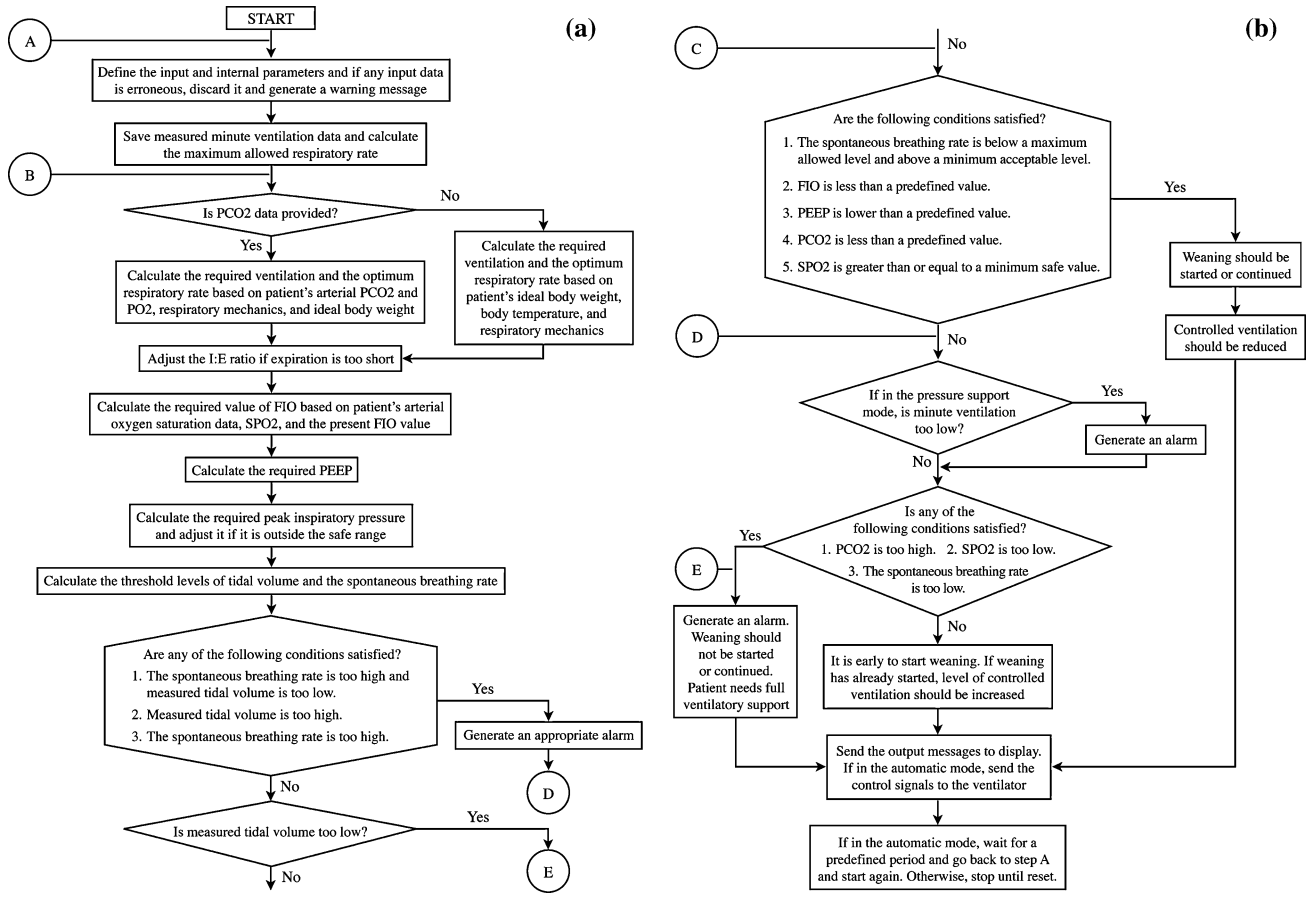

Fig. 1. Flow chart of the system algorithm.

attempts to improve mechanical ventilation treatment in recent years. These have included the development of new user friendly modes as well as design of intelligent decision support or weaning control systems for assisting clinicians. Most decision support systems developed to date are rule based. These systems are based on various treatment protocols and use fixed rules chosen on the basis of patient's illness to come up with treatment recommendations [1–7] or use fixed rules for control of weaning [8–11]. There are also several decision support systems that are based on physiological or statistical models [12–14].

Although model-based systems can be more informative to the physician, they generally require many patient parameters that are not readily available at bedside. One of the main objectives in the design of the system described in this article has been to develop a new decision support system which is responsive to different patients' requirements without requiring too many patient parameters. Unlike most previous systems, this one is designed for use in a wide range of ventilatory modes, including weaning. The system does not simulate the oxygen and carbon dioxide transport models of the patient, and, consequently, it does not require many parameters that would have otherwise been needed. Yet many of the system rules are not fixed and are based on physiological hypotheses that have been successfully tested in the past.

This system is designed to work with an additional monitoring module and can be used to automatically control weaning.

A brief overview of this system without inclusion of technical details has been provided elsewhere [15]. In this article the system will be described in more detail and comparison of some of the results with clinical data will be presented.

METHODS

System description

A flow chart of the system algorithm is shown in Figure 1. At the beginning of the program, all the inputs and the internal parameters are defined. The input data are compared to predefined ranges and if found erroneous,

are discarded, and in the automatic mode, are replaced by default values. Then the maximum allowed respiratory rate is calculated as:

$$\text{Fmax} = 1/\text{Tmin} = 1/(5 * \text{RES} * \text{COMP}) \quad (1)$$

where RES is airway resistance in cm H_2O/lit/sec and COMP is the respiratory dynamic compliance in lit/cmH_2O.

Next, minute ventilation is calculated from the measured tidal volume and respiratory rate and the program checks whether patient's PCO_2 data is provided at step B. This data can be supplied in different ways. In the advisory mode, PCO_2 can be either the arterial partial pressure of carbon dioxide ($\mathbf{P}_{aCO_2}$) measured by blood gas analysis, or the end-tidal carbon dioxide pressure ($\mathbf{P}_{etCO_2}$). In the automatic mode $\mathbf{P}_{etCO_2}$ is applied to a monitoring module and provided to the system automatically. If PCO_2 data is given, the program goes through an algorithm that computes the required alveolar ventilation of the patient based on his/her arterial partial pressures of CO_2 and O_2. In this calculation, PCO_2 is first compared to a low threshold value (e.g., 30 mmHg). If it is lower than the threshold value, the net effect of PCO_2 on ventilation is set to zero. Otherwise, the net effect of PCO_2 on ventilation is calculated as:

$$\text{VAC} = K_2 * (PCO_2 + K_1) - K_3 \quad (2)$$

where K_1 is the difference between $\mathbf{P}_{aCO_2}$ and $\mathbf{P}_{etCO_2}$ if the input to the system comes from an end-tidal CO_2 analyzer. The value of K_1 can also be used to set a desired level of PCO_2. For example, if the goal $\mathbf{P}_{aCO_2}$ should be kept in the low 30's, K_1 is appropriately a positive number. Conversely, if permissive hypercapnia is desired for the patient, K_1 is appropriately a negative number. K_2 and K_3 are other constants of the equation with typical values of 0.405 and 14.88 respectively.

After calculation of the net effect of CO_2 on alveolar ventilation, the net effect of O_2 on alveolar ventilation is calculated as:

$$\text{VAO} = 4.72 * 10^{-9} * (104 - P_{aO_2})^{4.9} \quad (3)$$

where P_{aO_2} is the patient's arterial partial pressure of oxygen in mmHg which can be estimated from the arterial oxygen saturation data from a pulse oximeter (SPO_2) as:

$$P_{aO_2} = \frac{-\text{In}\left[1 - (SPO_2)^{0.5}\right]}{0.046} + \text{C3} \quad (4)$$

where C3 is a constant that depends on the patient's blood pH level. It should be noted that VAO which is the net effect of oxygen on alveolar ventilation becomes zero if $P_{aO_2} > 104$ mmHg.

Next, required alveolar ventilation is calculated as:

$$\text{VALV} = (\text{VAO} + \text{VAC}) * \text{VALV(rest)} \quad (5)$$

where VALV is the required alveolar ventilation in lit/min and VALV(rest) is the resting value of alveolar ventilation defined as:

$$\text{VALV(rest)} = 0.0512 * \text{Weight} \quad (6)$$

and Weight is the ideal body weight in Kg. The factor 0.0512 in the above equation is designed for patients with normal basal rates. For patients whose metabolic demands deviate significantly from normal, this factor is adjusted by an appropriate percentage.

Alveolar ventilation is compared with a minimum allowed value at the next step and is raised if necessary, and the patient's dead space is calculated (if not provided) as:

$$\text{VD} = 0.1698 * (\text{VALV}/60) + 0.1587 \quad (7)$$

where VD is dead space in liters.

Next, the program computes the optimum respiratory rate to minimize the respiratory work rate. This is done by using a modified version of an equation derived by Otis et al. [16] as:

$$\text{F1} = 60 \times \left[\frac{-K' \times \text{VD} + \sqrt{(K' \times \text{VD})^2 + 4 \times K' \times \text{RES} \times \Pi^2 \times \left(\frac{\text{VALV}}{60}\right) \times \text{VD}}}{2 \times \text{RES} \times \Pi^2 \times \text{VD}}\right] \quad (8)$$

where F1 is the total optimal respiratory rate in breaths/min and K′ is the respiratory elastance that is 1/COMP.

Next, F1 is adjusted if it is too high or too low and the required ventilation is calculated as:

$$\text{MV} = \text{VALV} + \text{F1} * (\text{VD} + \text{VED}) \quad (9)$$

where MV is the required minute ventilation and VED is the added dead space due to tubes and connections to the ventilator in liters.

The next step is adjustment of the inspiratory to expiratory time ratio (I:E) as shown in the flow chart of Figure 1. This ratio is adjusted only if the expiratory time, TE, is less than 2.5 * RES * COMP.

Returning to step B, if PCO_2 data is not provided, the arterial partial pressure of CO_2 is assumed to be normal (e.g., 39 mmHg), but the algorithm takes a different route to compute the required ventilation. In this case, minute ventilation, MV, is calculated as MV = (6.7/66) * Weight, and for every degree Celsius of body temperature above 37°, MV is increased by 8%. Also, for patients whose metabolic demands are significantly different from normal, MV is further adjusted by an appropriate percentage. The dead space is next calculated as a function of Weight as VD = 0.0026 * Weight, and the respiratory time constant RCEM is defined as RCEM = RES * COMP.

Next, Eq. 8 is solved iteratively to find the optimal rate of respiration F1 to minimize the respiratory work rate. In this iterative process, VALV is replaced by (MV-F1 * VD). After computing F1, the I:E ratio is adjusted if the expiratory time is less than 2.5 * RCEM as was described before.

After completion of this part of the program, the required value of fraction of inspired oxygen (FIO) is calculated. This calculation is based on patient's arterial oxygen saturation data, SPO_2, and the present FIO value supplied by the ventilator. This data is provided by a monitoring module if the system is used to control the ventilator automatically, or it can be manually input to the system via the computer keyboard in the advisory mode.

Fraction of inspired oxygen (FIO) is computed through a procedure in which SPO_2 is compared successively to several threshold values. First, SPO_2 is compared to a high level (e.g. 95%). If it is greater than or equal to this value and FIO is not greater than 0.25 (i.e. 25%), no change is done to FIO. But if SPO_2 is high and FIO is greater than 0.25, the FIO level is decreased as:

$$\mathrm{FIO(new)} = 0.25 + (\mathrm{FIO(old)} - 0.25) * 0.65 \qquad (10)$$

However, if SPO_2 (as a fraction) is lower than 0.95, then it is compared to a second threshold value. If SPO_2 is between 0.94 and 0.95, FIO is decreased (if it is higher than 0.3) as:

$$\mathrm{FIO(new)} = 0.3 + (\mathrm{FIO(old)} - 0.3) * 0.65 \qquad (11)$$

If SPO_2 is lower than 0.94, it is compared to a third threshold value. If it is in the 0.92 to 0.94 range, then if FIO is lower than 0.4, it is raised to this level. But if SPO_2 is lower than the third threshold value (e.g., 0.92), it is compared to a fourth threshold value. If it is in the range of 0.91–0.92, then FIO is raised to 0.45 if it is lower than this value. However, if SPO_2 is still found to be lower than the 4th threshold value (e.g., 0.91), then FIO is raised to a high value such as 0.7 if it is lower than this value and then PEEP is incremented by 2 cm H_2O if at least a fixed period of time (e.g., 10 min) has passed since the last adjustment in PEEP.

After computation of the required FIO and PEEP, the RATIO of PEEP to FIO (as a percentage) is defined and compared to a range between a low and a high value (e.g., 0.12–0.24). If RATIO is not within the specified range, PEEP is adjusted. It should be noted that PEEP is only increased if sufficient time has elapsed since the last adjustment in PEEP.

Next, the calculated tidal volume (MV/F1) is compared to a safe range and adjusted if necessary and then the required peak inspiratory pressure is calculated as:

$$\mathrm{Ppeak} = (\mathrm{Vt}/\mathrm{COMP}) + \mathrm{PEEP} \qquad (12)$$

where Ppeak is the required peak inspiratory pressure in cm H_2O and Vt is the calculated required tidal volume in liters.

Ppeak is then compared to a minimum pressure which is PEEP + 5 cm H_2O and a maximum value which is 8 cm H_2O below the maximum pressure alarm limit set on the ventilator. If Ppeak in not in the safe range, its value is adjusted.

In the next step of the algorithm, the acceptable ranges of tidal volume and spontaneous breathing rate are defined. These values are needed to determine whether the patient's spontaneous breathing effort is adequate for weaning. In the pressure support mode, the measured spontaneous tidal volume range is between 70% and 160% of the required tidal volume for the patient. The minimum acceptable breathing rate is 45% of the optimal rate in the assist mode and 75% of that rate in the pressure support mode. The maximum breathing rate is defined at 180% of the optimal rate. These ranges may be modified for different patients and since they always depend on the calculated required ventilation and optimal breathing rate of each patient, the rules applied for weaning will depend on the conditions of individual patients.

In the following step of the algorithm, the program generates appropriate alarms and passes to step D which will be described later if any of the following conditions is detected:

(a) The spontaneous breathing rate is too high and tidal volume is too low.
(b) The spontaneous breathing rate is too high.
(c) Measured tidal volume is too high.

If none of the above conditions is present, measured tidal volume is checked to see whether it is too low, and if it is, control passes to step E which will be described later.

However, if none of the above adverse conditions is present, the program proceeds to the next step at C where the next set of weaning conditions are checked. Those conditions are:

(a) The spontaneous breathing rate is within the acceptable range
(b) Required FIO is not too high (e.g., lower than 0.5)
(c) Required PEEP is not too high (e.g., below 6 cm H_2O)
(d) Arterial partial pressure of CO_2 is not too high (e.g., less than 53 mmHg)
(e) Arterial oxygen saturation is greater than or equal to a minimum value (e.g., 0.91)

If the above conditions are satisfied, then weaning should be started or continued with lowered level of controlled ventilation. It should be noted at this point that not all the conditions listed above are necessarily checked for all patients. For example, in more stable patients, it may be sufficient to check only the first condition before proceeding to weaning. If weaning is started or continued at this point, the level of controlled ventilation is reduced by a certain percentage (e.g., 20%). In the next step, all the optimal calculated values and messages are sent to display. If the system is used in the advisory mode, the program stops and waits until reset again. Otherwise, if the system is used in the automatic mode, the outputs are sent to the ventilator and the program waits for a predefined period of time (e.g., 15–30 min) and then goes back to step A and starts all over again.

Back to step C, if the weaning conditions are not satisfied, program passes to step D. At step D, it is checked whether measured minute ventilation is too low and if it is, possibility of apnea is detected, and an alarm is generated. Next, the program checks the following conditions:

(a) Is arterial partial pressure of CO_2 too high?
(b) Is arterial oxygen saturation too low?
(c) Is the spontaneous breathing rate too low?

If the answer to any of these questions is yes, then the system generates an alarm that patient needs full ventilatory support at step E. Otherwise, it is determined that weaning should not be started but if it has begun, the level of controlled ventilation should be increased to the previous higher value. It should be noted that if measured tidal volume is too high, the program increases the controlled level of ventilation if the measured minute ventilation is found to be low at step D. Then the program continues by sending the outputs to display and if in the automatic mode, the required outputs are sent to the ventilator.

Next, if in the advisory mode, the program stops until reset, and if it is in the automatic mode, it waits for a predefined period of time and then goes back to step A.

During the weaning procedure, reduction of the controlled level of ventilation can be done in different ways. One way is to reduce the minute ventilation provided by the ventilator by a certain percentage (e.g., 20%) as compared to the calculated required amount of ventilation. Or in the ventilatory support mode, the level of pressure support provided by the ventilator can be reduced by a certain percentage (e.g., 15%–20%) as compared to the required peak inspiratory pressure calculated by the program. Regardless of the amount of the reduction in the controlled level of ventilation, the outputs controlling the PEEP and FIO levels are always adjusted in accordance with the required calculated values in the automatic mode and are not subjected to any reduction whether the patient is being weaned or not.

Using the system

FLEX can be used both as an advisory tool and as an automatic controller for weaning. If used as an advisory tool, the required inputs can be either provided automatically via a monitoring module, or keyed in manually by the clinician.

If the system is used as an advisor, it is reset and started by the clinician when the patient's status is reviewed and ventilatory parameters need to be adjusted. Each time the system is started, the clinician can create a new file for a new patient or follow up on an existing patient. The clinician can also view the previous data for a patient, which is accumulated and memorized by the system over time and presented graphically to the clinician. When patient data is needed to be entered, a window is opened which is shown in Figure 2. The needed input data for a patient are:

(a) The patient information such as ID number, name, address, etc.
(b) The patient's ideal body weight in Kg and his/her body temperature in degree Celsius.
(c) The patient's blood gas information, PCO_2 and SPO_2. The PCO_2 data may be the arterial partial pressure of CO_2 measured by using blood gas analysis (P_{aCO_2}), or the end-tidal pressure of CO_2 (P_{etCO_2}) measured by using exhaled gas analysis. If PCO_2 input is zero,

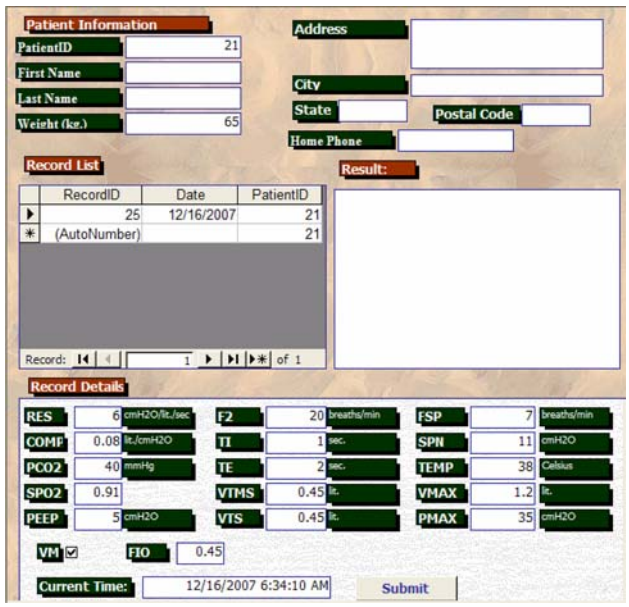

Fig. 2. A patient's record window.

P_{aCO_2} is assumed to be in the normal range. The SPO_2 data is provided by using a pulse oximeter.

(d) The respiratory mechanics data (i.e., airway resistance, RES, and dynamic compliance, COMP).

(e) Ventilatory parameters such as the set tidal volume (VTS), total respiratory rate (F2), positive end-expiratory pressure (PEEP), the inspiratory to expiratory time ratio (TI:TE), the fraction of inspired oxygen (FIO which is the same as FIO_2), and the ventilatory mode (VM). For example VM is zero in the volume control/assist mode and is equal to 1 in the pressure control/assist mode.

(f) Measured ventilatory parameters that are the spontaneous breathing rate (FSP), the measured peak inspiratory pressure (SPN), and the measured tidal volume (VTMS) which is the spontaneous tidal volume for spontaneously breathing patients (if SPN is not measured, it is calculated by the program).

(g) Maximum alarm limits for tidal volume (VMAX) and pressure (PMAX) set on the ventilator.

After submission of the input data, the system computes the optimal required values of ventilation, respiratory rate, peak inspiratory pressure, FIO, PEEP, and any necessary adjustment in the inspiratory to expiratory time ratio. The computations are designed to regulate patient's blood gases within a normal range and to prevent the untoward effects of hypoxia, hyperoxia, hypocapnia, hypercapnia, and oxygen toxicity. It should be noted that depending on the mode of ventilation, some of the input data may become redundant. For example, if the patient is breathing spontaneously in pressure support mode, VTS and VTMS will be the same and similarly F2 and FSP will be the same. However, the system is designed to be flexible for use in a wide range of ventilatory modes rather than being limited to a specific ventilation modality.

FLEX also checks the spontaneous effort of the patient. As it was described in the previous section, weaning is not recommended if the spontaneous effort is weak or there is some indication of an adverse condition. In that case if weaning has already started and the patient is not alarmingly hypoxic or hypercapnic, the system recommends increasing controlled level of ventilation as long as the spontaneous breathing rate is not too low. However, if PCO_2 is too high or SPO_2 is too low, or the spontaneous breathing rate falls below an acceptable minimum, the system recommends cessation of weaning and return to full ventilatory support (e.g., assist control).

If the patient's spontaneous effort is acceptable, the system checks other patient variables such as PCO_2, SPO_2, FIO, and PEEP, and if they are found within acceptable ranges, initiation or continuation of weaning with reduced level of controlled ventilation is recommended.

FLEX also checks for a number of other safety measures as described in the previous section and comes back with recommendations and warning messages as appropriate. An example of the system's output for a patient is shown below.

WEANING IS SUGGESTED, CONSIDER REDUCING CONTROLLED VENT.
Total Required Minute VENTILATION = 7.6144
TOTAL FREQUENCY 14.1078
PEEP = 5.4
FIO_2 = 0.45
VTS = 0.5397
TOTAL INSPIRATORY PRESSURE = 12.1466
TE = 2.8353
TI = 1.4177
PLEASE COME BACK.

The system can be used in the advisory mode as often as necessary. The patient data is accumulated over time and PCO_2, SPO_2, and PEEP data can also be displayed graphically.

If in the automatic weaning mode, the system receives its required input data through a monitoring module automatically. Signals for the reduced or increased levels of controlled ventilation as well as the required FIO and PEEP are provided to the ventilator while the messages are displayed on the computer for the clinician.

The open loop advisory system has been tested by comparing the system recommendations with clinical

data. A sample of those results will be provided in the next section. The closed-loop weaning system has been implemented by running the algorithm on a microprocessor with a monitoring module providing the input data from a ventilator, a pulse oximeter, and an end-tidal CO_2 analyzer to the microprocessor automatically. The processor executed the algorithm and provided the outputs to a ventilator which was a Siemens Servo Ventilator 300A in the initial set up. The microprocessor communicated with a laptop computer through an RS232 communication port.

EVALUATIONS

Patient characteristics

FLEX was tested on a wide variety of patients with differing diagnoses, including those undergoing permissive hypercapnia, a strategy designed to improve weaning and avoid ventilator associated complications in patients with certain diagnoses. The 10 patients data sets that were evaluated with FLEX consisted of all adults (age 64 ± 3 years, 7 males, 3 females, weight 71 ± 5 kg, mean $\pm$ SEM). At the start of treatment (i.e., time 0), 7 patients were on AC mode ventilation, and 3 were on IMV/PS mode. Two of the ten patients had their ventilation goal set for permissive hypercapnea. Four of the ten patients required an $FIO_2 > 0.5$.

The patients' characteristics including their P_{aCO_2}, and SPO_2 data at time 0 (baseline) and at 24 hours later are provided in Table 1. The initial approach in this study was to evaluate FLEX at the traditional daily (24 hour) point, with the plan to evaluate at more frequent time points in the future. The protocol for data collection and analysis was reviewed and approved by the University of California Irvine Institutional Review Board.

Results

Tables 2 and 3 show comparisons of clinical data with FLEX recommendations at baseline (time 0) and 24 hours after baseline measurement, respectively.

At the start of treatment at time 0, the set minute ventilation for the 10 patients was 7.86 ± 0.47 l/min. The measured minute ventilation was 10.36 ± 0.76 l/min. At 24 hours, set ventilation was 6.53 ± 1.20 l/min and the measured minute ventilation was 10.05 ± 0.88 l/min. Thus, in general, over 24 hours, there was decreased minute ventilation requirements and decreased set minute ventilation for this patient population.

At time 0, there were no recommendations to wean by FLEX for any of the 10 patients. Likewise, at 24 hours, FLEX did not recommend weaning for any of the 10 patients. However, in the previous 24 hours, a decreased level of support was instituted for three of the 10 patients. Two patients were converted form IMV to CPAP mode, and one was converted from AC to IMV mode. The two

Table 1. Patient characteristics (time 0 is at baseline, and time 24 is 24 hours after time 0)

Patient	Sex	Weight (kg)	Age	Diagnosis	SPO_2 at time 0	SPO_2 at time 24	P_{aCO_2} at time 0 (mmHg)	P_{aCO_2} at time 24 (mmHg)
A	M	72	53	Pneumonia, respiratory failure	0.95	0.95	50	48
B	M	87	72	Pneumonia, lung cancer	0.95	0.98	60	64
C	F	100	68	Pneumonia, asthma, renal failure	0.98	1	38	43
D	M	59	71	Myocardial infarction, aspiration pneumonia	1	1	34	34
E	F	70	68	Trauma, liver laceration and fractures, nosocomial pneumonia	0.97	0.97	42	45
F	F	48	69	Thrombotic stroke, myocardial infarction, CHF	1	1	41	39
G	M	62	51	Cholangiocarcinoma, gastric outlet obstruction, severe sepsis	0.95	1	62	51
H	M	59	78	Altered level of consciousness, drug OD	1	0.96	57	58
I	M	88	52	Cardiomyopathy, CHF	0.97	0.97	48	39
J	M	65	58	Myocardial infarction, CHF with cardiogenic shock	0.92	0.99	41	42

Table 2. Comparison of clinical data with FLEX recommendations for 10 patients at baseline (time 0)

Patient	Vent. mode	Set vent. (l/m)	Total breath. rate (b/m)	Set FIO	Set PEEP (cm H_2O)	Meas. vent. (l/m)	Meas. spont. breath. rate (b/m)	FLEX rec. vent. (l/m)	FLEX rec. breath. rate (b/m)	FLEX rec. FIO	FLEX rec. PEEP (cm H_2O)	FLEX wean. rec.	Set vent./meas. vent.	Meas. vent./FLEX rec. vent.	Set vent./FLEX rec. vent.
A	A/C	6	10	0.4	5	6.4	0	7.54	14	0.35	5	No	0.93	0.85	0.8
B	A/C	7.8	15	0.8	10	10.6	0	10.87	28	0.61	10	No	0.73	0.98	0.72
C	A/C	10.4	19	0.7	15	15.6	3	11.71	28	0.54	13	No	0.66	1.33	0.89
D	IMV	9	13	0.3	6	9.4	1	9.11	22	0.28	6	No	0.96	1.03	0.99
E	IMV	7	22	0.3	5	11.1	12	11.97	28	0.28	5	No	0.63	0.93	0.56
F	A/C	6	16	0.3	5	8.9	0	7.69	20	0.28	5	No	0.67	1.16	0.78
G	A/C	9.6	16	0.8	8	11.8	0	6.29	17	0.61	8	No	0.81	1.88	1.53
H	A/C	7.2	18	0.4	5	10.6	6	6	18	0.35	5	No	0.68	1.76	1.2
I	A/C	8.4	13	0.3	5	10.4	1	7.62	20	0.28	5	No	0.81	1.36	1.1
J	IMV	7.2	18	0.8	7	8.8	6	6.5	17	0.8	9.6	No	0.82	1.35	1.11

Table 3. Comparison of clinical data with FLEX recommendations 24 hours after baseline measurement

Patient	Init. vent. mode	Vent. mode at 24 hours	Set vent. (l/m)	Total breath. rate (b/m)	Set FIO	Set PEEP (cm H_2O)	Meas. vent. (l/m)	Meas. spont. breath. rate (b/m)	FLEX rec. vent. (l/m)	FLEX rec. breath. rate (b/m)	FLEX rec. FIO	FLEX rec. PEEP (cm H_2O)	FLEX wean. rec.	Set vent./meas. vent.	Meas. vent./FLEX rec. vent.	Set vent./FLEX rec. vent.
A	A/C	A/C	6	11	0.4	5	7.06	0	7.31	14	0.35	5	No	0.85	0.97	0.82
B	A/C	A/C	10.5	15	0.8	10	11.3	0	10.79	27	0.61	10	No	0.92	1.04	0.97
C	A/C	A/C	10.4	16	0.6	15	11.1	3	11.6	27	0.51	12	No	0.93	0.96	0.9
D	IMV	CPAP	0	26	0.3	6	11	26	9.18	14	0.28	6	No	0	1.2	0
E	IMV	CPAP	0	33	0.3	5	11	33	12.79	27	0.28	5	No	0	0.86	0
F	A/C	IMV	6	12	0.3	5	6.5	1	6.03	17	0.28	5	No	0.92	1.08	0.99
G	A/C	A/C	9.6	19	0.8	8	14.9	0	6.29	18	0.61	8	No	0.64	2.37	1.52
H	A/C	A/C	7.2	15	0.4	5	9.6	6	5.38	15	0.35	5	No	0.75	1.78	1.34
I	A/C	A/C	8.4	12	0.3	5	8.8	1	7.68	21	0.28	5	No	0.95	1.15	1.09
J	IMV	IMV	7.2	13	0.65	5	7	6	6.6	15	0.51	6	No	1.02	1.06	1.09

patients who were downgraded to CPAP mode developed tachypnea, suggesting that FLEX accurately recommended against weaning in these patients and would have prevented the poor outcome.

With regard to FIO_2 recommendations, the FIO_2 at time 0 was set at 0.50 ± 0.07 for the 10 patients. FLEX recommended an FIO_2 of 0.44 ± 0.06 at time 0, substantially less. Likewise, at 24 hours the set FIO_2 was 0.49 ± 0.07, and FLEX recommended an FIO_2 of 0.41 ± 0.04. This suggests that FLEX would help the clinical decision making to minimize the use of higher FIO_2, perhaps decreasing the risk of oxygen toxicity.

In general, there were few differences between the set PEEP and FLEX recommended PEEP in the 10 patients at time 0 and time 24 hours. However, FLEX did recommend an increase in PEEP for a patient with FIO_2 of 0.8 and recommended a decrease in PEEP for a patient with FIO_2 of 0.7. This suggested that FLEX could augment weaning by combined recommendations for both PEEP and FIO_2 to minimize risk for both oxygen toxicity and barotraumas.

With regard to measured and recommended minute ventilation, the measured ventilation was on the average 26% higher than that recommended by FLEX at time 0. When two patients were excluded from the analysis who were designated for permissive hypercapnea (patients G and H), this difference decreased to 12%. This exclusion was justified in that these higher numbers would have been expected for patients with permissive hypercapnea. Thus, the predictive minute ventilation value for FLEX is well within the expected variability for this parameter (20%), supporting its utility.

At time 24 hours, the measured ventilation was on the average 24% higher than the recommended. When excluding the 2 permissive hypercapnea patients, this number decreased to 4%, much smaller than the previous 12%. This suggests that the clinical approach and the FLEX recommendations were in line with each other if looked at over time. This further demonstrates the potential utility of the FLEX program in assisting in weaning.

Furthermore, it can be seen from Table 1, that in patients A and B who were not designated for permissive hypercapnia, the measured P_{aCO_2} values were high at 50 and 60 mmHg at time 0, and were at 48 and 64 mmHg at time 24 respectively. Referring to Table 2 results, it can be seen that at time 0, FLEX recommended ventilation values for these patients that were 25% and 39% higher than the set values respectively. This indicates that applying the higher ventilation values recommended by FLEX would have led to lower P_{aCO_2} values at time 24 and correction of hypercapnia that persisted due to insufficient ventilation. Once again, this comparison demonstrates the potential utility of FLEX in better management of respiratory patients.

DISCUSSION AND CONCLUSION

The trend of enhancing mechanical ventilation is toward automation. There are already two major closed-loop techniques for automatic control of the main outputs of the ventilator in use worldwide that have been generally accepted. Those are SmartCare marketed by Drager Inc. [10, 17] and Adaptive Support Ventilation (ASV) marketed by Hamilton Medical which is a mode of a patented technology under license of US Patent No. 4,986,268 [18]. However, despite the accelerating trend towards automation, the majority of advanced ventilators are still mainly open-loop devices whose outputs need to be properly set by clinicians.

FLEX is a new system for mechanical ventilation that can be used both as an open-loop advisory tool and also as an automatic controller for weaning. The system is designed for use in a wide range of ventilatory modes. It provides many required ventilatory parameters regardless of whether all such data is needed. In other words, some of the computed parameters of the system may not be needed to be set on the machine depending on the mode of ventilation. FLEX is also designed to be user friendly and its input data is limited to those that are essential and can be obtained at patient's bedside relatively easily.

FLEX incorporates the features of ASV closed-loop system which was originally described in 1991 [18]. It also includes other closed-loop characteristics [19–20], and many additional new features for control of patient's oxygenation and weaning. FLEX incorporates the principle of MMV technology [21] and uses many closed-loop features to expedite weaning in a safe and optimal manner.

In the closed-loop mode, one of the potential advantages of FLEX is to automate the weaning process and allow for more frequent weaning evaluations (up to almost continuous), without having to increase the time commitment of dedicated personnel. The closed-loop version of FLEX is designed with a module which receives patient and ventilator data automatically. The patient data that the module receives include SPO_2 from a pulse oximeter, and the end-tidal PCO_2 from a gas analyzer. The FLEX algorithm in this mode is executed by a microprocessor that communicates with the module and provides the output data automatically to the ventilator via a digital to analog converter board. The microprocessor also communicates with the physician's personal computer and sends warnings and other messages to display as needed. The closed-loop version of FLEX has

been tested in an initial set up using a Siemens Servo Ventilator 300A.

The open-loop advisory version of FLEX has been tested in many retrospective clinical comparisons. The sample results presented in this article show that FLEX recommendations were in line with clinical determinations. When used to retrospectively analyze data from 10 patients with respiratory failure on mechanical ventilation in this study, FLEX showed much clinical potential. It was able to predict failure of weaning in two patients via a recommendation not to wean in these patients. It recommended an average decrease in FIO_2 for the 10 patients, which could help prevent oxygen toxicity. It recommended a level of PEEP and FIO_2, which in combination, could help avoid both oxygen toxicity and barotraumas, the two main harbingers in the use of mechanical ventilation. When patients who were designated for permissive hypercapnea were excluded from the analysis, the actual and FLEX recommended minute ventilations were very similar. Furthermore, at 24 hours, the similarities in the actual and FLEX recommended minute ventilation were even closer, suggesting the correct predictive role for FLEX over time. This was further confirmed by considering the P_{aCO_2} data of patients. FLEX recommended values for ventilation were more in line with the requirements of two patients who were not designated for permissive hypercapnia, and applying the FLEX recommended values would have most likely led to correction of hypercapnia of those patients.

In conclusion, the results of this preliminary study show that FLEX has the potential to be used as an effective tool in the management and weaning of patients on mechanical ventilation. A new patent application has also been filed on this system. However, more detailed clinical evaluations of the open-loop as well as the closed-loop weaning version of FLEX are needed to fully assess the effectiveness of the system in the treatment of mechanically ventilated patients with different underlying illnesses.

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