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Automatic selection of tidal volume, respiratory frequency and minute ventilation in intubated ICU patients as startup procedure for closed-loop controlled ventilation

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Abstract

Objective: Before a patient can be connected to a mechanical ventilator, the controls of the apparatus need to be set up appropriately. Today, this is done by the intensive care professional. With the advent of closed loop controlled mechanical ventilation, methods will be needed to select appropriate startup settings automatically. The objective of our study was to test such a computerized method which could eventually be used as a start-up procedure (first 5–10 minutes of ventilation) for closed-loop controlled ventilation.
Design: Prospective Study.
Settings: ICU's in two adult and one children's hospital.
Patients: 25 critically ill adult patients (age ≥ 15 y) and 17 critically ill children selected at random were studied.
Interventions: To simulate 'initial connection', the patients were disconnected from their ventilator and transiently connected to a modified Hamilton AMADEUS ventilator for maximally one minute. During that time they were ventilated with a fixed and standardized breath pattern (Test Breaths) based on pressure controlled synchronized intermittent mandatory ventilation (PCSIMV).
Measurements and main results: Measurements of airway flow, airway pressure and instantaneous CO_2 concentration using a mainstream CO_2 analyzer were made at the mouth during application of the Test-Breaths. Test-Breaths were analyzed in terms of tidal volume, expiratory time constant and series dead space. Using this data an initial ventilation pattern consisting of respiratory frequency and tidal volume was calculated. This ventilation pattern was compared to the one measured prior to the onset of the study using a two-tailed paired t-test. Additionally, it was compared to a conventional method for setting up ventilators. The computer-proposed ventilation pattern did not differ significantly from the actual pattern ($p > 0.05$), while the conventional method did. However the scatter was large and in 6 cases deviations in the minute ventilation of more than 50% were observed.
Conclusions: The analysis of standardized Test Breaths allows automatic determination of an initial ventilation pattern for intubated ICU patients. While this pattern does not seem to be superior to the one chosen by the conventional method, it is derived fully automatically and without need for manual patient data entry such as weight or height. This makes the method potentially useful as a startup procedure for closed-loop controlled ventilation.

Introduction

Mechanical ventilation of patients is performed in three consecutive phases which are roughly comparable to flying an aircraft: taking off, flying and landing.

For mechanical ventilation this would mean connecting the patient to the machine and initiating ventilation, maintaining ventilation adequate for the underlying disease, and finally discontinuing mechanical support in order to reinstitute normal spontaneous breathing. In phase two and three (maintenance phase and weaning) machine settings and adjustments are usually guided by rational decisions based on arterial blood gas analysis, and pulmonary and chest wall mechanics.

In phase one, when the patient is initially connected to the machine, one has to preset ventilator parameters without exactly knowing how much ventilation the patient needs. Physicians and respiratory therapists usually rely on rough estimates or on clinical experience [1].

Automatic maintenance of mechanical ventilation by means of closed loop control has been done successfully in the past and was reported in a number of studies [2–12]. However, little or no attention has been paid to the problem of automatically selecting the initial ventilator settings for a given patient. If closed loop control of ventilation is to become a useful clinical tool, it clearly ought to start from the very moment the patient is connected to the machine. In other words, clinically useful closed loop controlled ventilation must start with computer-proposed ventilator settings. This paper describes the proposed method and its feasibility for use in intubated patients.

Patients and methods

Procedure

Twenty-five critically ill adult patients (age ≥ 15 y) and 17 critically ill children selected at random from the Cantonal Hospital Chur, the Zurich City Hospital 'Triemli' and the University Children's Hospital Zurich were investigated (Table 1). The protocol was approved by the ethical committees of the participating hospitals. All patients had been intubated and connected to either a Hamilton VEOLAR ventilator or a Siemens 900C ventilator prior to the investigation. Inclusion criteria were hemodynamic and respiratory stability. Patients were considered as hemodynamically stable if they were not under circulatory shock and no vasoactive drugs were administered. Patients were considered as repiratory stable if no considerable changes in the patient's need for respiratory support were observed over the last few hours preceeding our measurements. In pediatric patients who were intubated with cuffless tubes, tightness was tested with a pressure of 30 cmH2O. If the pressure did not fall more than a few cmH2O after waiting for several seconds the absence of a leak was assumed. No distinction was made between orally or nasally intubated patients or those with tracheostomies. Patients in all ventilatory modes were entered into the study. This included synchronized intermittent mandatory ventilation (SIMV), controlled mechanical ventilation (CMV), pressure controlled ventilation (PCV), pressure support ventilation (PSV) and pressure controlled ventilation with continuous flow (IMV).

For the investigation, the patients were disconnected from the ventilator and transiently connected to a modified Hamilton AMADEUS ventilator for approximately one minute. The AMADEUS was programmed to apply specific Test-Breaths. The Test-Breaths were analyzed and the results used to calculate the initial ventilator settings. The patients were then reconnected to the previous machine.

The Test-Breaths were based on pressure controlled synchronized intermittent mandatory ventilation (PCSIMV). The mode is similar to SIMV with the exception that the mandatory breaths are pressure controlled and not volume controlled. In addition, the spontaneous breaths are augmented by pressure support ventilation. The exact specifications are shown in Table 2. The levels of pressure control and pressure support were each set to 15 cmH_2O above PEEP. The SIMV frequency was set to 6/min and 15/min for adults and children, respectively. If a patient was entirely passive, he received 6 or 15 breaths per minute at a pressure level

Table 1. Patient Description.

patient	Height [cm]	Weight [kg]	Age [y]	FIO2	PEEP [cmH2O]	Clinical information
1	113	20.5	4	0.26	4	Severe head injury *
2	170	65.0	70	0.30	2	COPD. **
3	165	70.0	82	0.49	8	Respiratory failure following bowel paralysis
4	175	65.0	82	0.40	5	Respiratory failure
5	160	60.0	39	0.40	5	Severe head injury and thoraic trauma *
6	180	80.0	37	0.30	3	Severe head injury; tracheostomized *
7	58	5.8	0.3	0.35	5	Tetralogy of Fallot; corrective surgery
8	160	45.0	26	0.30	3	Severe head injury; tracheostomized *
9	79	9.4	1.0	0.35	2	Tetralogy of Fallot; corrective surgery
10	180	68.0	18	0.30	3	Severe head injury *
11	168	53.0	76	0.34	3	Stenosis after thoracotomy; neuromuscular failure
12	170	75.0	76	0.30	5	Ruptured aortic aneurism
13	170	68.0	34	0.30	4	Necrotizing pancreatitis
14	170	70.0	81	0.38	5	Polytrauma; tracheotomized
15	120	20.5	8	0.33	6	Severe head injury *
16	120	24.0	6	0.40	6	Status epilepticus
17	170	50.0	15	0.30	3	Severe head injury *
18	70	7.7	0.6	0.60	8	Pneumonia
19	134	31.0	7	0.28	5	Severe head injury *
20	65	5.1	1.0	0.80	8	ARDS
21	80	9.5	2	0.40	5	Pulmonary stenosis, corrective surgery
22	176	80.0	52	0.30	3	Severe head injury *
23	175	65.0	23	0.30	5	Insulin overdose; hypox, brain damage
24	180	80.0	55	0.30	5	Intoxication
25	183	89.0	51	0.40	5	Coronary bypass
26	158	42.0	39	0.30	4	Thoracotomy for lobectomy
27	175	92.0	74	0.40	4	Septic shock
28	175	80.0	47	0.30	3	Intracerebral hemorrhage
29	145	50.0	67	0.40	6	Pneumonia, kyphoskoliosis
30	176	80.0	34	0.40	3	Severe head injury
31	165	58.0	49	0.30	5	Polytrauma
32	161	70.0	61	0.50	3	Brain tumor
33	63	6.2	0.5	0.30	2	Tetralogy of Fallot, palliative surgery
34	170	70.0	69	0.30	3	Pelvic fracture; coagulation disorder
35	182	84.0	27	0.50	10	Pancreatitis with ARDS
36	93	12.5	2	0.33	4	Epiglottitis
37	85	11.4	1.7	0.40	5	Epiglottitis
38	65	6.1	0.6	0.30	3	Pulmonary stenosis, corrective surgery
39	125	26.0	8	0.45	4	Severe head injury,*
40	89	10.0	3	0.40	4	Tetralogy of Fallot, corrective surgery
41	76	7.8	0.7	0.35	4	Tetralogy of Fallot, corrective surgery
42	59	4.7	0.2	0.35	5	Coarctation of aorta, corrective surgery
Mean ± SD	137 ± 44	46 ± 30	32 ± 30	0.37 ± 0.10	4.5 ± 1.7	

Description of the patients, mean ± standard deviation. Asterisk denotes intentional hyperventilation, two asterisks (**) indicate intentional hypoventilation.

Table 2. Specifications of the Test-Breath pattern.

Ventilation mode	PCSIMV
Frequency	6/min (10–15/min for children)
PCV-level above PEEP	15 cmH2O
Pressure Support above PEEP (Δp)	15 cmH2O
Insufflation time for PCV cycle (TI)	1 s
Trigger Sensitivity	– 3 cmH2O
F_{IO2}	not specified
PEEP	not specified

Specifications of the Test-Breath pattern (Test-Breath) used to obtain information from the patient. PCSIMV is a pressure controlled mode, consisting of PCV cycles and voluntary spontaneous breaths, augmented by pressure support.

of 15 cmH_2O above PEEP and an inspiratory time of 1 second. The tidal volume depends on the patient's pulmonary impedance, i.e. airways resistance and total compliance. If, on the other hand, a patient was partly or fully spontaneously breathing, the machine provided pressure support at a level of 15 cmH_2O with interspersed mandatory breaths. Since the mandatory breaths were pressure controlled, the resulting inspiratory peak flow will depend on the breathing activities of the patient and the pulmonary impedance. The same, of course, was true for the spontaneous breaths. Figure 1 shows the PCSIMV breath pattern for a passive and spontaneously breathing patient. It was anticipated that this method would create reasonable volumes in all patients irrespective of the mode of ventilation. Test runs on a mechanical lung model and a pilot study done in 62 healthy volunteers breathing through a mouthpiece confirmed this.

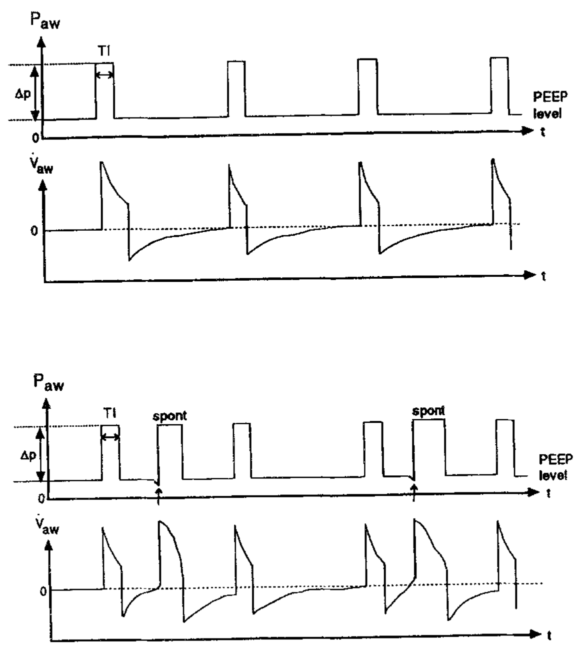

Fig. 1. Pressure Controlled Synchronized Intermittent Mandatory Ventilation (PCSIMV). Top: Idealized pressure (Paw) and Flow (V'aw) vs. time curves as obtained with test breaths in entirely passive subjects. Duration of inspiration (TI) is given by the ventilator and is the same for all breaths. No breaths are generated by the patient. Bottom: Same curves as obtained with test breaths in a spontaneously breathing patient. Note additional breaths with varying inspiratory times triggered by the patient (arrows). Inspiratory flow is positive. Inspiratory pressure above PEEP (Δp) is the same for ventilator triggered and patient triggered breaths.

Measurements

Tidal volume (V_T-actual), respiratory frequency (f-actual) and the mean of inspired and expired minute ventilation, subsequently termed minute ventilation (MV-actual) were recorded before connecting the patients to the modified AMADEUS ventilator and served as control data. In case of the mixed ventilation modes V_T-actual was calculated as the mean minute ventilation divided by the mean respiratory rate immediately prior to the study.

Measurements during the application of the Test-Breaths includes airway flow, airway pressure and instantaneous concentration of CO_2 in the exhaled air. For this purpose a heated Jaeger baby-pneumotachograph and a Novametrix 1260 mainstream CO_2 analyzer were placed between the ventilator Y-piece and endotracheal tube with the pneumotachograph being nearer to the Y-piece. All data were low-pass filtered using a second-order bessel filter

Table 3. Results of 39 patients for whom the computer-proposed method was successful.

Patient	Median values from Test-Breath			Computer-proposed Ventilation psttern			Deviation of computer-proposed from actual breath pattern			House Rule Breath pattern			Deviation of House Rule Breath pattern from actual breath pattern			Actual breath pattern			
	V_{ds} [ml]	RC [s]	V_T [ml]	V_T^c [ml]	f^c [/min]	MV^c [l/min]	ΔV_T^c [ml]	Δf^c [/min]	ΔMV^c [l/min]	V_T^H [ml]	f^H [/min]	MV^H [l/min]	ΔV_T^H [ml]	Δf^H [/min]	ΔMV^H [l/min]	V_T [ml]	f [/min]	MV [l/min]	VentMode
1	23	0.71	61	123	20.9	2.6	27	−6.1	0.0	246	15	3.7	150	−12	1.1	96	27	2.6	IMV
2	123	0.97	549	665	13.1	8.7	296	−2.9	2.8	780	10	7.8	411	−6	1.9	369	16	5.9	PSV
3	125	0.94	542	676	13.3	9.0	67	2.3	2.3	840	10	8.4	231	−1	1.7	609	11	6.7	SIMV
4	156	0.91	709	843	13.4	11.3	143	5.4	5.7	780	10	7.8	80	2	2.2	700	8	5.6	SIMV
5	75	0.83	375	402	16.0	6.4	−298	6.0	−.6	720	10	7.2	20	0	.2	700	10	7.0	SIMV
6	133	0.85	689	719	13.8	9.9	−31	3.8	2.4	960	10	9.6	210	0	2.1	750	10	7.5	CMV
7	14	0.45	34	77	25.8	2.0	17	5.8	.8	70	20	1.4	10	0	.2	60*	20	1.2*	IMV
8	74	0.80	499	399	16.3	6.5	199	−8.7	1.5	540	10	5.4	340	−15	.4	200	25	5.0	PSV
9	8	0.26	43	45	32.5	1.5	−45	12.5	−.3	113	20	2.3	23	0	.5	90	20	1.8	IMV
10	70	0.71	527	376	17.4	6.6	−424	7.4	−1.5	816	10	8.2	16	0	.2	800	10	8.0	SIMV
11	89	0.47	294	480	18.5	8.9	270	−10.5	2.8	636	10	6.4	426	−19	.3	210	29	6.1	PSV
12	127	1.05	706	687	12.7	8.7	223	−1.3	2.2	900	10	9.0	436	−4	2.5	464	14	6.5	PSV
13	71	0.76	512	385	16.8	6.5	−67	−8.2	−4.8	816	10	8.2	364	−15	−3.1	452	25	11.3	PSV
14	109	0.93	610	588	13.3	7.8	121	−1.7	.8	840	10	8.4	373	−5	1.4	467	15	7.0	SIMV
15	48	0.58	239	258	20.7	5.3	58	−3.3	.5	246	15	3.7	46	−9	−1.1	200	24	4.8	IMV
16	46	0.39	207	249	24.3	6.1	−1	12.3	3.1	288	15	4.3	38	3	1.3	250	12	3.0	PCV
17	75	1.82	545	403	11.5	4.6	−197	1.5	−1.4	600	10	6.0	0	0	0.0	600	10	6.0	CMV
18	15	0.29	47	79	30.5	2.4	4	10.5	.9	92	20	1.8	17	0	.3	75	20	1.5	IMV
19	37	0.63	290	202	20.8	4.2	−127	6.8	−.4	372	10	3.7	43	−4	−0.9	329	14	4.6	CMV
20	5	0.36	37	28	29.0	0.8	−52	14.0	−.4	61	20	1.2	−19	5	0.0	80	15	1.2	PCV
21	30	0.35	95	160	27.0	4.3	27	15.0	2.7	114	20	2.3	−19	8	.7	133	12	1.6	PCV
22	159	1.29	789	858	11.7	10.0	8	−.3	−.2	960	10	9.6	110	−2	−.6	850	12	10.2	SIMV
23	90	0.84	579	484	14.7	7.1	134	−9.3	−1.3	780	10	7.8	430	−14	−.6	350	24	8.4	PSV
24	72	1.12	615	387	14.3	5.5	77	−5.7	−.7	960	10	9.6	650	−10	3.4	310	20	6.2	PSV
25	128	1.03	660	689	12.8	8.8	−211	2.8	−.2	1068	10	10.7	168	0	1.7	900	10	9.0	CMV
26	81	0.57	339	438	17.9	7.9	−66	7.9	2.8	504	10	5.0	0	0	0.0	504	10	5.0	PSV
27	76	0.36	293	408	21.9	8.9	72	−3.1	.5	1104	10	11.0	768	−15	2.6	336	25	8.4	SIMV
28	80	0.57	749	432	18.1	7.8	93	−4.9	0.0	960	10	9.6	621	−13	1.8	339	23	7.8	PSV
29	55	0.38	232	299	23.6	7.1	−10	1.6	.3	600	10	6.0	291	−12	−.8	309	22	6.8	SIMV
30	124	0.82	743	669	14.0	9.4	252	−4.0	1.9	960	10	9.6	543	−8	2.1	417	18	7.5	PSV
31	80	0.55	473	429	18.3	7.9	−24	3.3	1.1	696	10	7.0	243	−5	.2	453	15	6.8	PSV
32	113	1.31	766	613	11.6	7.1	176	−7.4	−1.2	840	10	8.4	403	−9	.1	437	19	8.3	PSV
33	7	0.36	18	38	28.8	1.1	−42	3.8	−.9	74	20	1.5	−6	−5	−.5	80*	25	2.0*	IMV
34	81	0.81	576	437	15.6	6.8	−49	1.6	0.0	840	10	8.4	354	−4	1.6	486	14	6.8	PSV
35	97	0.53	468	525	16.8	8.8	60	−3.1	−.5	1008	10	10.1	543	−10	.8	465	20	9.3	SIMV
36	22	0.37	98	120	27.1	3.3	−110	15.1	.5	150	15	2.3	−80	3	−.5	230	12	2.8	IMV
37	23	0.51	92	123	23.9	2.9	10	−6.1	−.5	137	15	2.1	24	−15	−1.3	113	30	3.4	IMV
38	21	0.46	48	111	25.1	2.8	41	−7.9	.5	73	20	1.5	3	−13	−.8	70	33	2.3	IMV
39	40	0.45	243	218	23.6	5.1	−161	9.6	−.2	312	10	6.2	−67	−4	−2.2	379	14	5.3	CMV
Mean	72	0.70	394	388	19.2	6.2	12	1.4	0.5	586	12.4	6.2	210	−5.3	0.5	376	17.8	5.7	
SD	44	0.33	255	235	6.0	2.8	150	7.4	1.8	347	4.0	3.1	229	6.7	1.4	235	6.6	2.7	

Lung function indices obtained by Test-Breaths are listed as well as computer-proposed ventilation pattern (V_T^c, f^c, MV^c) and suggested ventilation pattern according to 'House Rules' (V_T^H, f^H, MV^H). Additionally the differences between the computer-proposed and actual breath pattern (ΔV_T^c, Δf^c, ΔMV^c) and the differences between the breath pattern according to the House Rules and the actual breath pattern (ΔV_T^H, Δf^H, ΔMV^H) are listed. Finally actual breath pattern and ventilation mode are listed (CMV: 5 patients, SIMV: 9, IMV: 9, PCV: 13, PSV: 3). * Estimated value, neither MV nor V_T was measured.

Table 4. Mean absolute deviation of the proposed breathing pattern from the actual breathing pattern and mean relative deviation as a percentage of the mean of the proposed and actual value.

	Difference ± SD	Relative difference ± SD [% of mean]
$V_T^c - V_T$-actual	12 ± 150 ml	0 ± 41
f^c – f-actual	1.4 ± 7.4 l/min	9 ± 38
MV^c – MV-actual	0.5 ± 1.8 l/min	9 ± 32
$V_T^H - V_T$-actual	210 ± 229 ml*†	35 ± 40
f^H – f-actual	5.3 ± 6.7 /min*†	– 32 ± 38
MV^H – MV-actual	0.5 ± 1.4 l/min*†	5 ± 25

Statistical analysis was done on absolute values using a paired two-group two-tailed t-test. A regression analysis was done on differences for dependency on the mean of actual and proposed values. Superscript C denotes computer-proposed values, superscript H denotes values determined by House Rules. Relative difference is obtained by dividing actual difference by the mean of actual value and proposed value. * = significant difference ($p < 0.05$). † = significant dependency of the absolute difference on the mean of both values ($p < 0.05$).

with a 3-dB cutoff frequency of 25 Hz and read into an IBM-PC/AT compatible microcomputer at a sampling rate of 60 Hz using an AD converter DT2801 (Data Translation Inc, Marlboro, MA 01752–1192, USA). The signals were corrected for gas viscosity changes and CO_2 analyzer delay [13]. From the flow and CO_2 signal a CO_2 vs. volume curve was constructed to determine series dead-space [14]. Endtidal CO_2 was not used as a parameter. Calibration of the sensors was done prior to each measurement.

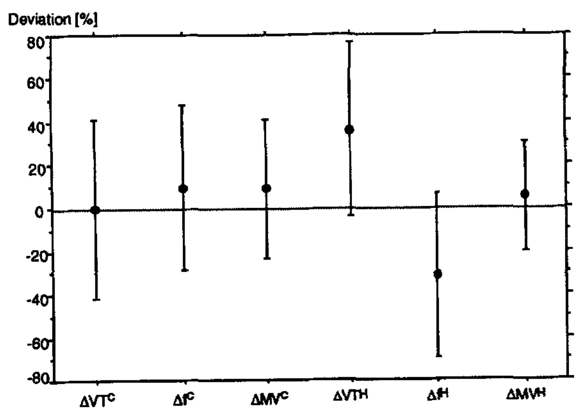

Fig. 2. Deviation of the computer-proposed breath pattern from the actual breath pattern as a percentage of the mean of both values (ΔV_T^c, Δf^c, ΔMV^c), as well as deviation of the breath pattern proposed by the House Rules from the actual breath pattern as a percentage of the mean of both values (ΔV_T^H, Δf^H, ΔMV^H). Error bars depict one standard deviation. Computer-proposed ventilation pattern did not differ significantly from actual breath pattern ($p > 0.05$). Ventilation pattern according to House Rules differred significantly from actual breath pattern.

Of the series of Test-Breaths, breaths number 2 to 6 were analyzed in terms of tidal volume (V_T), expiratory time constant (RC) and series dead space (V_{dS}). The mathematical formula to calculate RC is given in the appendix, no distinction was made between spontaneous and mechanical breaths for the analysis. The median of V_T, RC and V_{dS} was taken for all further calculations. The Test-Breath procedure was considered successful only if V_T was greater than twice V_{dS} and less than 10 times V_{dS}.

A pilot study in 8 intubated patients was conducted to test the procedure and measuring techniques including software debugging.

Computer-proposed initial V_T, f and MV from the Test-Breaths

The data obtained during the application of the Test-Breaths were used to derive ventilator settings for MV, V_T and f: Computer-proposed tidal volumes (V_T^C), respiratory frequencies (f^C) and minute ventilation (MV^C) were computed from median values of V_{dS} and RC. V_{dS}, a measure for the volume of the conducting airways, was used as a measure for patient size. The calculation of V_T^C was based on it according to the formula given in the appendix. f^C was calculated on the basis of the expiratory time constant RC and V_{dS} using a 'minimal work of breathing' approach [15, 16]. Finally, MV^C was calculated as $f^C*V_T^C$. The exact formulae are given in the appendix. For comparison, the initial ventilation pattern was also determined by means of a set of 'House Rules'. These rules are commonly used in the participating hospitals to select the initial ventilation pattern of patients and were applied in this study to derive V_T^H, f^H and MV^H. Details are given in the appendix.

The difference between the computer-proposed ventilation parameters V_T^C, f^C, MV^C and those of the actual breath pattern V_T-actual, f-actual and MV-actual were assessed by means of a paired two-group two-tailed t-test. Additionally a regression analysis was done to determine whether the difference of the compared values depended on their mean [17]. The ventilation pattern proposed by the House Rules was submitted to the same statistical analysis as the computer-proposed ventilation pattern. All statistical tests were made with StatView 4.0 (Abacus Concepts, Berkeley, CA, USA).

Results

42 patients were subjected to the Test-Breath procedure. The Test-Breaths were tolerated by all 42 patients. In 41 patients the Test-Breaths yielded a measurable V_{ds}. In one patient (Number 42; 4.7 kg; 0.2 years old) V_{ds} could not be measured. In 2 children the V_T was smaller than $2*V_{ds}$ but larger than $1.5*_{Vds}$ (patients 40–41). Only the results of the patients whose V_T was larger than $2*V_{ds}$ were subjected to further analysis (patients 1–39; Table 3). This included all patients older than 3 years.

The computer-proposed ventilation pattern and the ventilation pattern proposed by the House Rules were compared with the actual breath pattern and are given in Table 3. Table 4 and Figure 2 show the results of the statistical analysis. The computer-proposed ventilation pattern did not differ significantly from the actual breath pattern. The difference between V_T^C, f^C and MV^C and the corresponding V_T-actual, f-actual and MV-actual did not depend on the mean of these values ($p > 0.05$). For 33 of the 39 patients the difference between the computer-proposed and the actual minute ventilation was between – 50% and + 50% of the mean of both values. In contrast, the tidal volume, respiratory frequency, and the resulting minute ventilation proposed by the House Rules differed significantly ($p < 0.05$) from the actual volume and respiratory frequency. Still, for 38 of the 39 patients MV^H-MV-actual was between – 50% and + 50% of the mean of both values. In this case the difference between V_T^H, f^H and MV^H, and the corresponding V_T-actual, f-actual and MV-actual was dependent on the mean of these values.

Discussion

We tested a computerized non-invasive bedside method to propose initial ventilator settings in critically ill patients for eventual use as a start-up procedure for closed-loop controlled ventilation. For this purpose we applied a standardized breath pattern based on pressure controlled SIMV. The procedure was tolerated well by all patients. In 100% of the patients older than 3 years a meaningful proposition for the patient's ventilation pattern based on the Test-Breaths could be made. In 75% (9 out of 12) of the children under the age of 3 the method was successful as well. Please note that neither the computer-proposed breath pattern nor the breath pattern according to the House Rules were actually tested on the patients. What was done was a theoretical comparison between the actual breath pattern and the two other breath patterns, no pattern being used as a reference standard. Therefore no judgement of the patient's actual breath pattern was made and no arterial blood gas analysis was performed.

Several investigators have developed control algorithms to automate mechanical ventilation based on expired or arterial P_{CO2} or arterial pH. The first controllers were successfully tested during anesthesia and in patients with normal lungs [2, 3]. Subsequent control algorithms were tested quite successfully on animals. They were based on mean expired CO_2 [4, 5], end tidal CO_2 [6–10], arterial CO_2 [11] or arterial pH [12]. In all studies, the initial settings of tidal volume, minute ventilation and respiratory frequency were made by the investigator. Subsequently, control was turned over to the automatic system.

Little attention was paid to the problem of automatic selection of the initial ventilator settings. To human operators it is a simple task to judge the appropriateness of an initial tidal volume and a respiratory frequency. This is not to say that one can easily find optimal values for said parameters. But it is evident from the body size and clinical signs that a tidal volume of 600 ml is not suitable for, say, a small child. This may sound like a trivial argument, yet it is not with respect to closed-loop controlled ventilation. Being a machine, a ventilator has only limited knowledge about the attached patients. All of this knowledge is derived from measurements of gas flow, pressure, and CO_2 concentration at the airway opening. Unprocessed, this data cannot identify the size, pathology, or degree of muscular activity of the patient. At a given preset pressure level, for example, low tidal volumes are compatible with stiff lungs, high airway resistance, and/or poor synchronization of patient and ventilator. Alternatively, the patient may be simply a small child without pulmonary pathologies. The first problem therefore is to find a breathing pattern that can be used on patients of any size. pathology, and state of spontaneous breathing. The second problem is how an algorithm can distinguish between patients of different size based on measurements of airway flow, pressure and CO_2 concentration. The third problem is how an algorithm can identify the primary mechanical properties of lungs and chest wall. The fourth problem is how to select appropriate values for frequency and tidal volume to ventilate the patient adequately during the initial phase. All these problems are addressed by the method proposed in this paper.

For the Test-Breaths, we used a novel mode of ventilation, pressure controlled SIMV. It was anticipated that the same inspiratory pressure can be applied in infants as well as in adults. The same pressure was applied for the mandatory breaths and the spontanous breaths. The tidal volume achieved with this pressure depends on the total respiratory impedance. Since total respiratory compliance is smaller in children compared to adults, the resulting tidal volumes will also be smaller in children and larger in adults. Another rationale for choosing pressure controlled ventilation was that the peak pressure is predictable, so there is no risk of inadvertent barotrauma. The combination of pressure controlled ventilation with SIMV makes this mode applicable to fully mechanically ventilated as well as to spontaneously breathing patients. The pressure support above PEEP (Δp) was set to 15 cmH_2O for the Test-Breaths. First trials on healthy volunteers were made with a Δp of 20 cmH_2O (no PEEP). Because several volunteers reported discomfort at a Δp of 20 cmH_2O. Δp was set to 10 cmH_2O in the pilot study. In the actual study a Δp of 15 cmH_2O was chosen to compensate for the increased airway resistance due to the endotracheal tube.

The IMV frequency was chosen to allow for spontaneous breathing yet to prevent gross hypoventilation in case of apnea. A frequency of 6/min was arbitrarily chosen with the above criteria in mind. In small and paralyzed children, however, a frequency of 6/min would have caused intolerable hypoxemia. For these patients, an IMV frequency of 10–15/min was selected.

Inspiratory time (T_I) of the mandatory breaths was set to 1 second. With this T_I, an inspiratory pressure of 15 cmH_2O can create a substantial V_T even in obstructive patients. For example, in a patient with a resistance of 25 $cmH_2O/(l/s)$ and a compliance of 40 ml/cmH_2O, the resulting tidal volume will be 15 cmH_2O*40 ml/cmH2O*0.63 = 378 ml [18].

To obtain the computer proposed breath pattern, it was necessary to have an estimate of the patient's weight. Radfords correlation between deadspace and weight was used for that purpose [19]. Radford measured the deadspace using the Bohr equation which gave him the 'respiratory deadspace' (VD_{resp}), an estimate of the physiological deadspace. The series deadspace (V_{dS}) used throughout this study is an estimate of the anatomical deadspace, thus it is smaller than VD_{resp}. However, the difference is small in a healthy subject. Assuming that V_{dS}, being primarily dependent on the patient's morphology, doesn't change much with pathology, one can say that V_{dS} is a viable approximation of the patient's physiologic deadspace in a healthy state.

V_{ds} is, however, influenced by length and diameter of the endotracheal tube. This may lead to some deviations from the true V_{ds}. The principal correlation between V_{ds} and patient size and weight should however be preserved, because small patients use small endotracheal tubes and large patients use large ones. One exception may be tracheostomized patients. 3 tracheostomized patients were included in our study. No significant difference ($p > 0.05$) was observed in the deviations of their computer proposed breath patterns from the actual breath patterns compared to the deviations observed in the rest of the patients. This indicates that V_{ds} should give a crude but reliable indication of body weight for all patients.

f_C is calculated using Otis' equation for minimal work of breathing. In this equation, the respiratory frequency depends on RC, V'_A and a 'deadspace portion' of the tidal volume (V_D) [15]. Because this equation uses RC as an argument, the patient's lung mechanics are taken into account when the respiratory rate is calculated. This should yield an appropriate respiratory frequency for patients with different lung pathologies, such as ARDS or COPD patients.

Otis' work was obviously done with spontaneously breathing subjects in mind. The question therefore arises, whether a breath pattern based on a modified version of Otis' formula is suitable for a paralyzed patient. Indeed, a good reason would be to choose a breathing pattern that encourages the patients to breathe on their own as early as possible. Under this aspect, selecting a breathing pattern intended for a spontaneously breathing subject is a rational choice.

To calculate V'_A, the CO_2 production V'_{CO2} had to be estimated first. V'_{CO2} was assumed to be 6 ml/min/kg for infants and 3 ml/min/kg for adults [20]. In this study it was assumed that V'_{CO2} per kg decreases linearly with increasing body weight from the infant value to the adult value, which was assumed to be valid for all patients with a body weight above 45 kg (see appendix). Without this correction of the assumption of the CO_2 production per weight for small patients, an untolerable risk for hypoventilation would have arisen for these patients. To allow for increased ventilation needs, V'_{CO2} was then increased by 50%. This corresponds to the increase in metabolic activity measured in septic patients [21]. The desired V'_A was then set to 20 times V'_{CO2}. This means that a patient with the estimated CO_2 production has an alveolar CO_2 concentration of 5%. This concentration corresponds to an arterial CO_2 tension of 38 mmHg at sea level in absence of an alveolar deadspace. Taking into account the increased CO_2 production for septic patients in the estimation of V'_{CO2} increases the chance of hyperventilation for nonseptic patients. This is probably tolerable for the initial phase of ventilation since the main effects of hyperventilation are a decrease in arterial CO_2 and an increase in pH. On the other hand, besides changing arterial CO_2 and pH in the opposite direction, severe hypoventilation can also decrease arterial O_2. Whereas changes in arterial CO_2 and pH can be tolerated quite well [22], a decreased arterial O_2 content can have grave consequences.

An alternative to estimating V'_{CO2} would to actually measure V'_{CO2}. The patient has to be in a steady-state condition to allow a measurement of V'_{CO2}. This means that his breathing pattern and his metabolism must not change for a considerable amount of time prior to the measurement. Because the Test-breath pattern almost certainly does not coincide with the patient's previous breathing pattern, steady state cannot be assumed and V'_{CO2} measurement is not possible.

The method used to measure RC yield exact values for a one-compartment lung of a completely passive patient with full exhalation. Most of our patients were at least partially spontaneously breathing. This questions the reliability of the measurement of RC in these cases. Iotti measured RC with our method in 8 spontaneously breathing patients using different levels of pressure support [23]. For comparison, the patients were paralyzed and resistance and compliance measured separately. The two methods correlated with a correlation coefficient of 0.752. The method used in this study tends to overestimate the time constants below 1 s and underestimate those above 1 s. While the correlation coefficient indicates that this method does not allow an accurate measurement of the expiratory time constant, it is sufficient to obtain a rough estimate for the time necessary for a complete expiration.

It is well known that expiratory and inspiratory time constants can be different. For emptying of the lungs, the expiratory time constant is most important. Adequate inspiration can always be guaranteed by adjusting Paw. Exhalation is mostly passive and can only be guaranteed by a sufficiently low respiratory frequency or a low I:E ratio [18].

We used V_{ds} and RC to derive a suitable initial ventilation pattern, i.e. V_T^c, MV^c, and f^c. The computer-proposed ventilation pattern did not differ significantly from the actual breath pattern on the average, although the differences in some patients were considerable. V_T^c was below 12 ml/kg for 34 of the 39 patients; the maximum was 18 ml/kg. The average V_T^c was lower than the tidal volumes recommended for initial ventilator settings by Kacmarek [1]. Therefore the risk of excessive airway pressure should be low. Still, it cannot be totally excluded, especially in case of patients with a low lung compliance, such as ARDS patients. However, the computer-proposed breathing pattern is envisioned as the startup pattern for closed-loop controlled ventilation and the maximum pressure limit set by the clinician will need to be part of the algorithm. The computer-proposed respiratory rates were between 12 and 33 breaths/min being higher for children than for adults. This coincided with the range of f-actual. For 5 patients the difference between MV^c and MV-actual exceeded 50% of the mean of both values. Assuming normoventilation by the actual breath pattern, this would have meant a gross deviation from normoventilation for some of the investigated patients, if the computer-proposed ventilation pattern had been actually applied. It cannot be said whether such deviations would have negative effects on the patient. After all, the method is intended exclusively for the initial phase of ventilation, and adjustments are necessary after blood gas analysis. Further studies and an actual application of the computer-proposed ventilation pattern are needed to elucidate this question.

The House Rules proposed tidal volumes which were on the average 18% larger than the mean of V_T^H and VT-actual. On the contrary, f^H was 16% smaller than the mean of f^H and f-actual. As a result, MV^H was on the average 2.6% higher than MV-actual. This is even more remarkable when one considers that for 10 patients the MV-actual was above normal because these patients were hyperventilated for therapeutic reasons. Although MV^H probably would have been adequate for most patients, there were large differences between f^H and f-actual, and V_T^H and V_T-actual; this was especially true in the patients who were spontaneously breathing. The patient's weight is a critical parameter in the House Rules. According to Kacmarek the patient's ideal weight should be used [1]. We have used the weight entered on the patient sheet or, if not available, the estimated weight when we conducted the study. This might not be the best method, but it is the one that is usually practiced and we wanted the House Rules to represent the clinical practice.

Compared to the ventilation pattern calculated by the computer, the House Rules proposed on the average a ventilation pattern with the same minute ventilation, but significantly larger tidal volumes and lower respiratory rates. Our data does not allow to say which one of the methods would have resulted in a better ventilation. However, the House Rules need the patient's weight as input, while the computerized method does not need any operator input at all. The authors believe that this is the substantial advantage of the computerized method.

The patients investigated in this study were ventilated in different modes, part of them were spontaneously breathing and part of them were paralyzed. Some patients had healthy lungs, other had lung pathologies of varying severeness. Clearly not only the patients morphology and lung mechanics, but also the above mentioned differences had an influence on the patients breathing pattern. We have lumped together all patients for the statistical analysis ignoring these differences because splitting up the patients into different categories would have resulted in samples too small for a meaningful statistical comparison.

Conclusion

Our study shows that the computerized method can serve as a viable strategy to determine the initial ventilator settings for a wide range of patients. No manual data entry is required for the procedure. Obviously the series deadspace (V_{dS}) can serve as a rough but reliable clue to the patient's morphology independent of his pathological status, provided it is measured under the standard conditions used in this study. The data suggest that the computer-proposed ventilator settings might be suitable to ventilate a patient for a limited time as the startup values for a closed loop controlled ventilation algorithm.

This study demonstrates theoretical feasability. However, further studies are necessary to evaluate the effects on blood gases when the computer-proposed ventilation pattern is actually applied.

Appendix

Calculation of the Lung Function Indices

The calculation of the series dead space (a measure for anatomical dead space) V_{dS} is based on the analysis of the F_{CO2} versus V_E diagram. V_{dS} gives the position of the first marked upswing (phase 2) of the CO_2 curve. The exact formulae are given in [14].

RC, a measure of the expiratory emptying pattern or time constant, is calculated according to the Formula

$$RC = 0.001 * V_E / V'_{Emax} \qquad [1]$$

where RC is in seconds, V_E is the expired volume in ml and V'_{Emax} is the maximal expiratory flow in l/s. This formula gives the exact time constant if the flow decays exponentially with time and expiration is complete. This is the case if the resistance is flow-independent, the total compliance is independent of volume and exhalation is completely passive. In reality, incomplete expiration, flow-dependent resistance and patient activity cause errors in the determination of RC. Time constants below 1 s are overestimated, above 1 s they are underestimated [23].

The derivation of the ventilation pattern using the Test-Breath method

There is a good correlation between the anatomical deadspace determined by the Fowler method and the patient's body size [24]. The correlation between the respiratory deadspace (VD_{Bohr}) determined by the Bohr formula and the patient's body weight is also obvious [19]. The weight can be used to estimate the necessary tidal volume (V_T) [19] and the CO_2 production [20] from which the necessary alveolar ventilation (V'_A) can be estimated. Therefore VD_{Bohr} can be considered as an estimation base for V_T and the alveolar ventilation (V'_A). The series deadspace (V_{dS}), which represents the volume of the conducting airways, correlates well with VD_{resp} under normal circumstances. However, pathology and mode of ventilation can influence V_{dS} and VD_{resp}. Therefore the use of a standardized breath pattern is necessary to make the use of V_{dS} as a measure of VD_{resp} more reliable. The patient's weight is estimated from the series deadspace (V_{dS}) using Radfords formula [19]:

$$\text{weight} = V_{dS} * 0.45 \qquad [2]$$

where the weight is in kg and V_{dS} in ml.
V_T is derived from the weight by the formula

$$V_T = 12 * \text{weight} \qquad [3]$$

where V_T is in ml. Thus substituting eq. 2 for the weight in eq. 3 yields the following expression for the computer estimated tidal volume V_T^C (all values in ml):

$$V_T^C = 5.4 * V_{dS} \qquad [4]$$

The CO_2 production is estimated to be 6 ml/min/kg for infants and 3 ml/min/kg for adults [20]. If the weight is above 45 kg (V_{dS} above 100 ml), the patient is assumed to be an adult. For patients with a smaller weight the CO_2 production per body weight is increased linearly with decreasing weight up to 6 ml/min/kg for a weight of 0. Using Radford's correlation between weight and deadspace, V'_{CO2} can thus be expressed as follows:

$$V'CO_2 = \begin{cases} V_{dS} * (1.35 + (100 - V_{dS}) * 0.0135), \text{ if } V_{dS} < 100 \text{ ml} \\ V_{dS} * 1.35 \text{ otherwise} \end{cases} \qquad [5]$$

where V'_{CO2} is in ml/min BTPS and V_{dS} is in ml. Alveolar ventilation (V'_A) can be defined in terms of the CO_2 production (V'_{CO2}) and the alveolar CO_2 concentration (F_{ACO2}). Assuming an F_{ACO2} of 5%, V'_A can be expressed as

$$V'_A = V'_{CO2} / 0.05. \qquad [6]$$

This is the alveolar ventilation needed to eliminate CO_2 at an alveolar concentration of 5%. To allow for increased metabolism due to sepsis V'_A is increased by 50% [21]. The determination of the optimal respiratory frequency is based on the assumption that the work of breathing should be minimal. Otis and Mead have suggested that the respiratory frequency depends on the alveolar ventilation (V'_A), the expiratory time constant (RC) and a 'deadspace portion' (V_D) [15, 16]. If one equals V_D and V_{dS}, the following formula for the computer-proposed respiratory frequency f^c is obtained:

$$f^c = 30 \frac{\sqrt{1 + \frac{200}{3} \pi^2 RC \frac{V'A}{VdS}} - 1}{\pi^2 RC} \qquad [7]$$

where f^c is in breaths/min, RC in seconds, V'_A in l/min, and V_{ds} in ml. Finally MV^c is the product of f^c and V_T^c:

$$MV^c = f^c * V_T^c \qquad [8]$$

The derivation of the ventilation pattern using the House-Rule

V_T^H, f^H and MV^H are calculated according to the following formulae:

$$V_T^H = 12 * \text{weight} \qquad [9]$$

where V_T^H is given in ml and weight is the patient's body weight in kg.

$$f^H = \begin{cases} 20/\text{min, if weight} > 10 \text{ kg} \\ 15/\text{min, if } 10 \text{ kg} \leq 25 \text{ kg} \\ 10/\text{min, if weight} > 25 \text{ kg} \end{cases} \qquad [10]$$

and

$$MV^H = f^H * V_T^H \qquad [11]$$

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