EVALUATING NIV USING A MONITORING SYSTEM COUPLED TO A VENTILATOR: A BENCH TO BEDSIDE STUDY

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Short title: Evaluating NIV by a simplified monitoring device

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ABSTRACT

Empirically determined NIV settings may not achieve optimal ventilatory support. Some ventilators include monitoring modules to assess ventilatory quality. We conducted a bench-to-bedside study to assess that of the VPAPIII-ResLink™.

Methods: 1) *Bench*: we tested the accuracy of minute ventilation (MV) and leak calculations given by VPAPIII-ResLink™, compared to those measured by a bench model at varied leak levels and ventilator settings. 2) *Bedside*: From 2003 to 2006, we systematically assessed NIV efficacy using this system. Ventilation was considered inadequate if leak (>24 l/min); continuous desaturation (>30% of the trace) or desaturation dips (>3%) were present.

Results: 1) On bench tests both methods were highly correlated (r=0.947; p>0.0001 for leak; r=0.959; p<0.0001 for MV). 2). We performed 222 assessments in 169 patients (age 66.42±16 y, 100 males). Abnormalities were detected on 147 of 222 occasions (66%). Leak was the most common abnormality (34.2%), then desaturation dips (23.8%). The most effective therapeutic solutions were a chin strap if leak was detected (61.2 %) and EPAP increase for desaturation dips (59.5%). In 15.7% of cases, when abnormalities persisted, a polygraphy was performed.

Conclusion: The systematic use of this device enables NIV to be optimised, limiting the indication of sleep studies to complex cases.

Abbreviations

ABG: Arterial blood gases

ARF: Acute respiratory failure

BMI: Body mass index

FVC: Forced Vital Capacity

CRF: Chronic respiratory failure

EPAP: Expiratory positive airway pressure

FEV1: Forced expiratory volume in the first second

FM: Facial mask

IPAP: Inspiratory positive airway pressure

LTMV: Long term mechanical ventilation

MV: Minute ventilation

NIV: Non invasive ventilation

NM: Nasal mask

PG: ventilatory polygraphy

PSG: full polysomnography

PtcCO2: transcutaneous PCO2 pressure

UA: Upper airway

Noninvasive ventilation (NIV) has been demonstrated to be effective treatment in respiratory failure. In some cases, however, the clinical results may be less than expected, despite using the correct technique. When NIV is initiated, the ventilator settings are determined empirically based on clinical evaluation of underlying disease, patient tolerance when awake, and diurnal blood gas variations [1]. However, NIV is predominantly applied at night [2], when profound ventilatory changes may occur, particularly in patients with respiratory failure [3]. Such changes include modifications of ventilatory control, upper airway patency and respiratory muscle recruitment. Consequently, modulating NIV settings during the day and underestimating these physiological differences may lead to suboptimal patient-ventilator interaction that reduces NIV efficacy. Moreover, NIV uses a non-hermetic technique, which poses the possible risk of leak. Leakage may be absent or minimal when the patient is awake and may worsen during sleep as a result of the loss of voluntary control and decreased muscle tone. Thus NIV settings chosen empirically on daytime evaluation may not predict optimal nocturnal ventilatory support. Consequently, NIV effectiveness may be more correctly assessed by sleep studies than through daytime assessment [1]. Ideally this requires complete polysomnography (PSG) or ventilatory polygraphy (PG) at the time of initiation to NIV. However, it is not technically feasible to perform repeated long term assesment by PG/PSG in these patients

Recently, NIV has been provided by portable ventilators capable of meeting high ventilatory demands [4]. Some of these ventilators include monitoring modules that can assess various ventilatory parameters, storing the data in memory, for subsequent analysis. Such technology and its clinical usefulness merits critical analysis

We wished to assess one of these systems, which consists in a ventilator (VPAPIII™) and its monitoring module (ResLink™). We assesed the accuracy of the parameters measured by this

device in a bench model. Secondly, we investigated the results of using the system by systematically assessing the efficacy of the NIV in different clinical situations.

Materials and Methods

The VPAPIII-ResLink™ (ResMed, North Ryde, Australia) is a bi-level ventilator that includes a monitoring system that provides trend data on minute ventilation (MV) (defined as estimated MV received by the patient after the removal of leak), respiratory rate, air leaks (above "intentional" ones), SpO_2 and heart rate, which are analysed by the software package AutoScan 5.7™. ResLink obtains this information from signals received at the mask and requires only an additional connection to a pulse oximeter (included). The oximeter has a sampling frequency of 1 Hz and averaging of the SpO_2 value is made over the last 4 beats. For the oxygen desaturation index, the averaging window is 5 seconds long. The data can be stored on a SmartMedia card and transferred to a computer for simultaneous onscreen viewing.

Bench study:

   - Lung model (Fig. 1): In an artificial lung model, we tested the accuracy of the MV and leak estimation calculated by the ResLink™, and compared these with a reference system. Details of this lung prototype could be seen in the online supplement.

   - Experimental procedure (Figure 1): The ventilator with its monitoring module was connected to the lung model by a 60-cm long tubing. The following were introduced into the circuit: 1) a variable-opening valve providing a variable leak joined to a first pneumotachograph; 2) a second flow measurement system located downstream, capable of measuring the actual MV. Both pneumotachographs are linear to the flow ranges studied.

The protocol consisted of a total of 48 recordings of 10 minutes each, at different leak levels and at different ventilatory settings and varying compliance and resistance. Data are recorded on a SmartCard, transferred to a PC and visualised via the AutoScan 5.7 program to compare them with reference values.

Clinical Study

We included patients recruited between 2003 and 2006 treated with NIV using VPAPIII™, either in the acute setting (ARF group) or electively, in patients for whom home mechanical ventilation was indicated (CRF group).

The efficacy of ventilation was monitored using ResLink™ under ventilation conditions (parameters and interfaces) present at the time of assessment. In patients discharged home with NIV, another trace was performed 4 to 6 months later to confirm NIV efficacy (Long term Mechanical Ventilation, LTMV group) under the parameters used at home. The Reslink criteria used to define ventilation as ineffective were as follows: 1) leakage >24 l/min for >20% of the trace duration; 2) continuous desaturation (>30% of the trace with SpO2 <90%), whether or not accompanied by a simultaneous reduction of MV (>10% of reduction of MV compared to baseline) estimated by the ResLink™, in the absence of significant leak; 3) cumulated desaturation dips (greater than 3%) for >10% of the trace duration. Otherwise, the ventilation was considered effective. The data were analysed using the AutoScan 5.7 software package. If one of these abnormality criteria were detected, one or more conditions were modified to optimise ventilation and another recording was performed. This procedure was repeated until the best results possible were obtained. When the trace could not be corrected despite these changes, we performed PG/PSG under ventilation. This PG/PSG included at least: pneumotachograph-based airflow, mask pressure, thoraco-abdominal movements and SpO2 recordings. Typical Reslink™ traces of the various abnormalities are shown in Figure 2. Arterial blood gases (ABG) during spontaneous ventilation were measured under the conditions of oxygenation at the time of assessment. In the ARF and CRF patient groups, ABG were sampled before the start of ventilation and in the LTMV group, during the first hour in the morning after the patient was disconnected from the ventilator.

Statistical analysis

Values are shown as means ± SD. Values for minute ventilation and leak obtained by the two methods in the bench study were correlated by linear regression using Pearson's correlation coefficient. We also calculated the bias (where d = the mean difference between reference bench measures and the ResLink™ estimated values) and the limits of agreement between the parameters as described by Bland and Altman [5]. For the clinical study, data were compared using the unpaired t-test and Mann-Whitney U test. Differences between the groups were assessed using ANOVA. A χ^2 analysis was performed to study categorical data. A p value of 0.05 was considered as significant.

Results

Bench study

The correlations between values obtained by pneumotachograph and those estimated by the VPAPIII™-ResLink™ are shown in Figure 3a. Both sets of measurement were highly correlated (for leak r=0.947; p>0.0001 for MV; r=0.959; p<0.0001) as was the correlation for data subgroups (for both MV and leak), but the correlation of leak was not as good at low leak levels (at 18 l/min r=0.853; p<0.001)

Figure 3b shows Bland-Altman plots of the agreement between pneumotachograph-measured leak and MV and ResLink™ values. For all observed values of leak and MV, the mean observed bias was 0.736 ± 1.68 and 0.077 ± 0.97 l/min, respectively, and the limits of agreement between both techniques were -4.04 and 2.57 l/min for leak and -1.82 and 1.97 l/min for MV. Again the agreement was less for low leak values (<22 l/min)

Bedside study

NIV efficacy was assessed for 222 different hospital admissions in 169 patients (mean age 66.42 ± 16 years, 100 males). During each admission one or more traces (t) were performed. The total number of recordings performed was 542. Amongst them, 500 were useful for analysis (2.25 ± 1.45 t/admission) and 42 traces (8.4%) were not suitable for analysis because of technical problems. 69 assessments (31.08%) were performed in patients in the ARF group (180 valid traces, 2.6 ± 1.72 t/pt), 53 (23.8%) in the CRF group (147 valid traces, 2.77 ± 1.75 t/pt) and 100 (44.59%) in those from the LTMV group (173 valid traces, 1.73 ± 0.95 t/pt).. Oxygen therapy was added on 112 occasions to ensure diurnal $PaO2 > 60$ mm Hg (69/69 in ARF, 20/53 in CRF and 23/100 in LTMV). The difference between the number of traces/admission was significant between ARF and LTMV and between CRF and LTMV, but not between ARF and CRF (Table 2). 50 patients were assessed on 2 different occasions and two patients on three occasions. A nasal mask (NM) was used on 167 occasions (75.2%), and a facial mask (FM) on 55 (24.8%). Patients in the ARF group are significantly more aged that those in both other groups.

Table 1 illustrates the classification of patients according to the categories defined in the Eurovent survey [6]. Patient characteristics, ventilatory parameters and ABG values are shown in Table 2. There were no significant differences in ventilatory settings for the three groups. However, differences in the types of interfaces used were observed, with a gradual increase in the use of NMs compared to FMs as patients progressed from an acute to a more stable situation (nasal mask ARF<CRF<LTMV) ($p<0.01$).

Results of the Reslink monitoring traces

Abnormalities were detected on 147 of the 222 occasions (66%). In the group as a whole, 129 out of 169 patients presented with abnormalities in some of the assessments (76.3%), most commonly in ARF (53/69 occasions, 76.8%) and CRF (41/53 occasions, 77.3%) groups compared to the LTMV group (53/100 occasions, 53.0%). The differences in the number of abnormalities were significant between ARF and LTMV and between CRF and LTMV ($p<0.05$) but not between ARF and CRF. These abnormalities were significantly more common when using a NM in ARF ($p<0.02$) but not in CRF or LTMV. The proportion of patients with suboptimal ventilation was similar, independently of the disease category or ventilatory parameters. There were no differences regarding subjective perception of quality of sleep as evaluated by a categorical scale (poor-fair-good) between patients with and without abnormalities

Leak was the most common abnormality in the overall population (76 occasions, 34.2%) and also in the ARF (30 occasions, 43.4%) and CRF (21 occasions, 39.6%) groups. In the LTMV group, leak was less common (25 occasions, 25%), and the number of cases was significantly smaller compared with ARF ($p<0.02$) but not with CRF. Leak seems to be unrelated to IPAP levels and was significantly more common in the overall population when a NM was used ($p<0.01$). The second most common abnormality was 3% desaturation dips that were observed on 53 occasions (23.8%) with no significant differences between the three groups. A significantly greater prevalence of desaturation dips was observed with FM than with NM ($p<0.04$), but only the ARF group contributed to this difference. Finally, episodes of continuous desaturation were observed on 18 occasions (8.1%) with no significant differences between the three groups, and a similar prevalence of these events with both interfaces. On 10 occasions (4.5% of the total) the desaturation episodes were accompanied by a significant reduction in MV.

Figure 4 illustrates the results of the recordings, categorized by clinical situation, and subsequent therapeutic modifications. The results classified by type of abnormality and interface can be seen in Table 3.

Comparison between patients with normal and abnormal traces

 - Relationship between ABG and monitoring results

Table 4 shows a comparison of ABG between patients with normal (N) and abnormal (AN) Reslink traces. These were sampled prior to the start of the ventilation in ARF and CRF and on spontaneous ventilation after disconnecting the ventilator in LTMV. When ABG values in LTMV patients with abnormal traces were compared according to the type of Reslink abnormality, we did not find significant differences between the three groups of abnormalities as regards $PaCO_2$ and pH. PaO_2 was significantly worse in patients with an abnormal trace, with continuous desaturation being associated with the lowest PaO_2, followed by the desaturation dips, group with leak having the least impact.

- Additional data concerning the LTMV group

  Comparative mean compliance

There were no differences in terms of daily duration of ventilator use between patients with N and AN Reslink traces (7.92±2.2 and 7.90±2.0 hours/day, respectively).

- Modifications in ventilation as a result of the monitoring

Figure 4 and Table 3 illustrate the modifications made as a result of monitoring, classified by situation and interface, respectively. If leaks were detected, the most common approach was to add a chin strap (49/76 patients ventilated with a NM, 64%), which was effective in 30 patients (61.2 %). The efficacy of this was similar in the 3 clinical situations. In the case of

desaturation dips, the most common approach used was to increase EPAP (42/53 occasions, 79.2%), which was effective in 25/42 cases (59.5%). For continous desaturation, the effective modifications were to increase IPAP (10/18 cases: 55.55%) or add oxygen (8/18 cases: 44.4%). Only one modification was required in 81 cases, two in 33 patients and three or more in 30 patients. In 35 cases (15.7%), it was judged necessary to perform PG/PSG under ventilation (see online supplement). The need for PG was significantly more common in ARF (19/69: 27.5%) than in LTMV (7/100: 7%) (p<0.01). The abnormality that most frequently indicated a PG/PSG was desaturation dips (21/35 cases: 60%).

Discussion

NIV is a non-hermetic system compared to invasive ventilation, and the ventilator-lung assembly cannot be considered as a single-compartment model because of the presence of variable resistance in the upper airway (UA) [7]. Therefore, increasing the volume or the delivered inspiratory pressure do not necessarily result in increased effective ventilation reaching the lungs [8,9,10]. It is therefore essential to assess the clinical efficacy of NIV in all patients and this evaluation should include at least a clinical assessment and measurement of ABG and nocturnal SpO2 under NIV [11,12]. However, this may not be sufficient. For example, while an abnormal SpO2 reflects, on the whole, inoptimal ventilation, it does not determine the underlying mechanism [11,12]. Moreover, even a "normal" SpO2 does not rule out the possibility of nocturnal hypoventilation, particularly if the patient is receiving supplemental oxygen [12-14]. Consequently, more specific monitoring is necessary. Some authors have suggested that all patients under NIV should be tested by PSG to verify its efficacy [1,15,16] but, in reality this practice is infrequent [3]. This is on account of the workload and the lack of available PSG devices, but also due to the difficulty in interpreting the ventilatory signals under NIV, which needs a high level of experience. In addition, in

order to understand patient-ventilator interactions, the PSG must include at least one signal to detect inspiratory activity (oesophageal pressure or diaphragmatic EMG), and, monitoring of this type may itself change sleep quality. Therefore, "interpreting polysomnography under NIV is a very difficult task" [17]. Finally it is impossible to perform polysomnography after every therapeutic modification. Thus the systematic use of PSG would be very difficult. In addition there has been an exponential growth in the number of patients under NIV in recent years and therefore performing polysomnography on all ventilated patients becomes increasingly difficult.

Some portable ventilators include technologies that allow monitoring of ventilatory parameters. In this study we assessed the efficacy of NIV using the VPAP-ResLink™. We first wished to evaluate the accuracy of the parameters measured in a bench model. We tested the system at different settings, "prompting" various leak ranges, at different compliance and resistance levels, to reproduce situations observed in clinical practice. These tests confirmed the accuracy of this system in terms of leak detection and MV. The correlation between the bench test and Reslink was less reliable with low leak levels, but, since such leak levels would not degrade the quality of ventilation they are probably not clinically relevant.

We have assessed the usefullness of the Reslink device in monitoring NIV in clinical practice. This approach is pertinent since, to date, only a limited number of studies have specifically addressed the question of NIV evaluation during the night. Moreover, the validity of several parameters estimated by NIV devices is questionable and must be validated by independent clinical and/or bench test studies [17]

One can estimate that by permitting evaluation of some "critical signals" (for instance SaO2, leaks and MV) this system could give useful information about the global quality of ventilation. The occurrence of oxygen desaturations (both desaturation dips and continous

desaturation) is highly sensitive to detect breathing abnormalities in NIV users. Moreover, unintentional leaks are probably the main phenomena that impair ventilatory effectiveness [17] and are extremely frequent in patients under NIV [18,19]. Finally, whereas the main goal of ventilatory assistance is to ensure physiological MV, it allows us to estimate this parameter. Therefore, an analysis combining the three signals provided by this device may offer a global estimation of NIV quality. Using this procedure enabled us to observe abnormalities liable to change the efficacy of the NIV in 66% of cases. This is higher than reported in the literature (between 5 and 60%) [20,21] perhaps because the efficacy criteria selected were very rigorous, but also because a more subtle methodology of analysis was used in order to rule out false negative results. We defined ventilation as ineffective when we observed one of the following abnormalities: leak, episodes of continuous desaturation or desaturation dips. Suboptimal ventilation was more common at the start of ventilation treatment, and therefore the number of traces and PG/PSG required (and consequently, the number of modifications made) was higher in that period. The better ventilation performance in patients assessed at a later period may reflect greater clinical stability or a "training effect" [22], but may also reflect that many of these patients had undergone monitoring at the start of the NIV, making early intervention possible. The abnormalities were less common when a FM was used, but this difference was only significant in the acute phase. The better results with FM in the acute phase is found in clinical practice, given that in acute NIV, facial masks are most commonly used, while for chronic NIV nasal mask use predominates [4,23]. Finally, the proportion of patients with suboptimal ventilation was unrelated to the type of underlying disease.

In the acute setting greater hypercapnia at the start of the ventilation correlated with a greater probability of inefficacy of NIV. This can be explained by the need, in these patients, to modify the PaCO2 to a greater extent, which could cause "resistance" to the ventilation, as

has been described [24]. For stable patients, there was a significant correlation between the presence of abnormalities in Reslink data and a reduced efficacy of NIV particularly in terms of PaO2, pH and HCO3⁻. Serum bicarbonate levels reflect as well as PaCO2 the effectivenes of nocturnal ventilation [25,26]. Given that compliance in both groups (N and AN) was similar, these differences in blood gases cannot be explained by a difference in the use of the ventilator. If one assumes that the primary objective of ventilation is to correct the ABG [2], these findings call attention to the importance of monitoring results as markers of ineffective ventilation.

Leak was the most commonly found abnormality as is expected in a non-hermetic system such as NIV [21,26] and can compromise the efficacy of the method, reduce compliance and disturb sleep quality [18,19,27]. Generally, a leak of less than 24 l/min is considered clinically tolerable [18,20,25,27]. Different portable ventilators allow leak to be estimated, but the performance of their algorithms is variable [26]. In addition, for most of these algorrithms, intentional leaks are included in the leak estimations, which are variable and proportional to the level of pressure and different for each interface. The ResLink™ has the particular feature of taking into account the intentional leak and sustracting it, thereby estimating the "undesired" leak level. Solutions for reducing leak include chin straps and using a FM or mouth interfaces [18]. Although the use of chin straps has been reported to reduce leak volume by less than 50% [25], in our and in others experience [28], this was effective in a large number of patients.

Desaturation dips reflect intermittent obstruction of the UA under NIV and are related to two mechanisms. The first corresponds to obstructive events at the oropharyngeal level because of UA collapse, as a result of insufficient EPAP. This mechanism may be present in patients with an unstable UA, such as patients with OSA [29,30]. Another mechanism corresponds to episodes of intermittent obstruction at the glottal level reflecting cyclic glottal

closure induced by hyperventilation, a type of "ventilation resistance" reflex [9,31-33]. Interestingly, desaturation dips were more frequent when a FM was used, particularly in patients in an acute situation. There are several possible explanations for this. One is that greater modification of PaCO2 as a result of more hermetic ventilation could promote the occurrence of glottal closure episodes [24]. Another is that the use of FM induces predominantly mouth breathing, which may promote significant narrowing of the retropalatal distance predisposing to oropharyngeal obstruction [34]. The application of positive pressure in the mouth could worsen this situation even further [34].

The fact that it is impossible to identify the underlying mechanism of these desaturation dips explains that this abnormality was the one that led most frequently to performing a PG/PSG. In these situations, the purpose of PG/PSG was to identify the mechanism of the UA obstruction [21,35]. If obstruction occurs at the oropharyngeal level it will be accompanied by progressively increased inspiratory activity, indicating a struggle against UA collapse. Conversely, if the mechanism is glottal closure it will be accompanied by reduced inspiratory effort, the result of an excessive level of ventilation promoting respiratory pauses [31,36]. In the case of oropharyngeal apnoea, the approach is to increase the level of EPAP to stabilise the UA. In the case of glottal apnoea, however, it is to reduce the MV [31].

The third pathological Reslink pattern was represented by regular desaturation episodes, whether or not accompanied by a simultaneous reduction of MV. Two mechanisms could explain this abnormality: 1) the inefficacy of the system to ensure adequate ventilation, which is generally accompanied by diurnal hypercapnia; 2) a worsening of the ventilation perfusion imbalance, known as a cause of nocturnal hypoxemia in patients with respiratory failure [29]. Monitoring transcutaneous PCO2 (PtcCO2) is a useful tool for the differential diagnosis between these mechanisms, although this assessment is under-utilised [29]. In our

bench study, the Reslink™ device gives a good estimate of MV and may thus be useful for differentiation between the mechanisms of regular desaturations, but this needs to be confirmed by other studies.

A number of criticisms may be made with regard to our study. Concerning the bench study, the tests were performed using a passive lung model, which may not accurately reproduce physiological conditions. The estimate of leak by the ResLink™ may be less accurate with assisted breathing, given that the velocity of the turbine (and accordingly the estimate of leak level) can vary in the presence of inspiratory effort.

Regarding the clinical study: **firstly**, the study includes patients with various pathologies and heterogeneous clinical situations, and additionally, the parameters defined as a threshold of normality are arbitrary. However, our objective was to propose a screening method that can be used in daily practice. Thus it was necessary to include a representative sample of practice and establish criteriae that reflect the quality of ventilation and which have already been suggested as markers of NIV inefficacy [12,25]. **Secondly**, our definition of ineffective ventilation was based only on the results of the traces without taking into account ABG or clinical response. Future research should assess the importance of combining the results of this monitoring with other variables. **Thirdly**, since Reslink provides only trend data and not raw data of ventilation, this system does not allow an analysis of patient-ventilator interaction to detect asynchrony. Nevertheless, it has been well established that, in patients under NIV, major leak is probably the most important contributor to these events [12], and our evaluation includes its detection. Finally, as with all oximeters, O2 supplementation may affect reliability of SaO2 mesured by this device.

In summary, monitoring by this system makes it possible, with accessible technology, to assess the quality of the ventilation and interpret the results easily, which facilitates its application in screening patients in a real-life situation. If the results prove to be less than expected, this system makes it possible to first clarify the pathophysiological mechanism responsible, and, if changes are required, to subsequently check the results of these changes. The systematic use of this system enables NIV to be optimised, limiting the indication of PG/PSG to complex cases. The importance of including the results of this simplified monitoring with other assessment variables of ventilation quality should be the objective of future research.

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Aetiological group	n (pts)	%
Lung and airways	85	50.3
COPD	45	
Overlap syndrome	35	
Cystic fibrosis	4	
Others	1	
Chest wall abnormalities	54	32
Obesity Hypoventilation Syndrome	32	
Tuberculosis sequelae	12	
Kyphoscoliosis	10	
Neuromuscular diseases	30	17.7
Myopathy	12	
Amyotrophic Lateral Sclerosis	10	
Phrenic nerve paralysis	5	
Others	3	

Table 1: Classification of disease categories according to the Eurovent survey [6] **for patients included in the study**

	Acute Setting (ARF)	At the start of long-term ventilation (CRF)	At steady state (LTMV)	P
Age	69.5±16	60,8±18 [a]	65.6±16	
BMI (kg/cm²)	29.2±9	29.7±10	32.2±11	NS
FEV1 (l/s)	0.97±0.68[¶]	1.15±0.6 [a]	1.09±0.53	
FEV1 (% th.)	40.9±19.7	45.3±17	45.5±18	
FVC (l)	1.56±0.77 [¶]	1.51±0.74	1.61±0.75	NS
FVC (% th.)	51.4±17	49.3±20	53.1±19	
Mask type (nasal/facial)[1]	36/33	41/12 [a]	90/10 [a,b]	
IPAP (cm H2O)	16.6±1.9	16.6±2.0	17.0±2.1	NS
EPAP (cm H2O)	5.2±1.8	5.4±2.2	5.6±2.3	NS
Backup respiratory rate	14.5±1.10	14.0±1.5	14.1±1.3	NS
PaO2 (mm Hg) *‡	61.3±12.8	65.3±11.6	66.1±10.7 [a]	
PaCO2 (mm Hg) *‡	68.6±13.8	55.9±9.3 [a]	44.8±8.3 [a,b]	
pH*‡	7.32±6.0	7.37±3.5 [a]	7.40±2.8 [a,b]	
Number of traces / clinical situation	2.6± 1.7	2.7±1.5	1.70±0.9 [a,b]	
Number of polygraphies / clinical situation	19/69	9/53 [c]	7/100 [a,b]	

Table 2: Ventilation settings, arterial blood gases and number of studies performed, classified by clinical situation. All patients were ventilated in ST mode.

[1] Since the device makes it possible to set parameters for the type of mask used in order to abstract the amount of intentional leak, preference was given to the types of masks that could be preset in the device. If this was not possible, the mask used was that with the closest intentional leak. Accordingly, we measured the intentional leak for each mask previously in our laboratory.

* Breathing room air or under supplemental oxygen therapy.

‡ Prior to the start of the ventilation in ARF and during the first hour in the morning after the patient was disconnected from the ventilator in CRF and LTMV

[¶] Data lacking in 10 patients of this group

[a] indicates a significant difference ($p<0.05$) compared to ARF, and [b] indicates a difference ($p<0.05$) compared to CRF using the Mann-Whitney rank sum test. [c] *indicates* $p<0.056$ compared with ARF.

	Abnormalities detected/ patients evaluated in each situation [2]	Effective therapeutic intervention [3]	PG/PSG needed
Nasal mask [1] *(n:167)*			
Leak n = 69 (41.3%)	ARF: 25/36 (69.4%) CRF: 20/41 (48.7%) LTMV: 24/90 (26.6%)	Chin strap: 30/69 (43.5%) Mask change: - nasal → facial: 18/69 (26 %) -other of the same type: 8/69 (11.6%) Decreasing IPAP: 2/69 (2.9%)	n=11/69 (16 %)
Desaturation dips n = 34 (20.4 %)	ARF: 4/36 (11.1%) CRF: 10/41 (24.4%) LTMV: 20/90 (22.2%)	Increasing EPAP: 18/34 (52.9 %) Decreasing IPAP: 5/34 (14.7 %)	n=11/34 (32.4%)
Continuous desaturation n = 10 (5.9 %)	ARF: 3/36 (8.33%) CRF: 3/41 (7.3%) LTMV: 4/90 (4.4%)	Increasing IPAP: 5/10 (50%) O2 addition: 5/10 (50%)	n= 0/10
Facial mask (n:55)			
Leak n= 7 (12.7%)	ARF: 5/33 (15.1%) CRF: 1/12 (8.3%) LTMV: 1/10 (10.0%)	Mask change: 3/7 (42.9%) Humidifier: 1/7 (14.2%)	n=3/7 (42.9 %)
Desaturation dips n = 19 (34.5 %)	ARF: 11/33 (33.3%) CRF: 5/12 (41.7%) LTMV: 3/10 (30.0%)	Increasing EPAP: 7/19 (36.8 %) Decreasing IPAP: 2/19 (10.5 %)	n=10/19 (52.7%)
Continuous desaturation n = 8 (14.5 %)	ARF: 5/33 (15.1%) CRF: 2/12 (16.7%) LTMV: 1/10 (10%)	Increasing IPAP: 5/8 (62.5 %) O2 addition: 3/8 (37.5%)	n= 0/8

Table 3: Monitoring results: classified by type of abnormality for each interface and effective therapeutic modifications

[1] Percentages in this column corresponds to the proportion of patients with each abnormality/total of patients classified by interface

[2] Percentages in this column corresponds to the proportion of patients with each abnormality/total of patients in a given situation

[3] Percentages in this column corresponds to the proportion of patients improved by each therapeutic intervention/total number of patients as classed by abnormality

ARF: acute respiratory failure group

CRF: chronic respiratory failure group

LTMV: long term mechanical ventilation group

PG/PSG: polygraphy / polysomnography

	Acute Setting (ARF)			At the start of long-term ventilation (CRF)			At steady state (LTMV)		
	N	**AN**		**N**	**AN**		**N**	**AN**	
PaO2	62±13	61.1±12	NS	68.2±12	64.4±11	NS	68.5±11	63.9±10	p<0.03
PaCO2	63.2±12	70.3±14	p<0.03	54.5±7	56.8±10	NS	42.9±6	46.5±9	NS (p<0.07)
pH	7.33±0.04	7.31±0.06	NS	7.38±0.03	7.37±0.03	NS	7.41±0.02	7.39±0.03	p<0.01
HCO3⁻	*******	********		*********	********		30,4±4.5	32,3±3.0	p<0.02

Table 4. Comparison in terms of ABG between patients with normal (N) and abnormal (AN) traces.

Values correspond to ABG performed before the start of the ventilation in the ARF and CRF groups and during the first hour in the morning after the patient was disconnected from the ventilator in the LTMV group. As PaCO2 varies rapidly, lack of difference in terms of PaCO2 between normal and abnormal traces in the LTMV group may be explained by the ABG sample timing. Note that the PaO2 difference between N and AN in LTMV group cannot be explained by a different prescription of oxygen (15/53 patients in the AN group, 9/47 in the N group, NS).

Legends for Figures

Figure 1: Schematic representation of the bench model. The artificial lung is composed of two 40-litre Nalgene® polycarbonate canisters. (Details on the lung prototype may be seen in Figure 1, in the online supplement). We included in the circuit: 1) a variable-opening valve providing a variable leak of 0 to 180 l/min joined by a Y-connection to a first pneumotachograph (RT200™, Timeter Instruments, St. Louis, Missouri, USA); 2) a second flow measurement system located downstream, capable of measuring the actual MV. A ventilator-testing device (Ventest™, Soderel, Heillecourt, France) was used to measure MV, and also calculate compliance and resistance. To simulate physiological ventilation conditions, a leak device corresponding to the intentional leak of the mask stated in the system was included. ("calibrated leak" in the chart). With the VPAPIII™-ResLink™, the type of mask and circuit length can be registered, which enables the device to "know" the value of the intentional leak and subtract it from the estimated leak. We used an intentional leak corresponding to a standard mask (25 l/min at 10 cm H2O), and the length of the circuit was 3 metres. These were the values registered in the system.

The protocol consisted of a total of 48 recordings of 10 minutes each, at leak levels of 0, 18, 24 and 30 l/min (when the apparatus was tested in bi-level mode, this value corresponded to the maximum leak during the inspiratory phase) at different ventilatory settings (see [1] in the figure), varying compliance (C) and resistance (R) as follows:

    1) C: 50 ml/cm H20, R: 4 cm H2O/L/s (physiological)

    2) C: 50 ml/cm H20, R: 15 cm H2O/L/s (increased resistance)

    3) C: 25 ml/cm H20, R: 4 cm H2O/L/s (reduced compliance)

Reslink estimates averaged values while the pneumotachograph measures instant flow in inspiration and expiration. Therefore we expressed a mean leak for pneumotachograph measures. This was the maximum instantaneous leak in inspiration and expiration weighted to the duration of inspiratory and expiratory phases. The device was set in 'T-mode' with an I/E ratio of 1/2

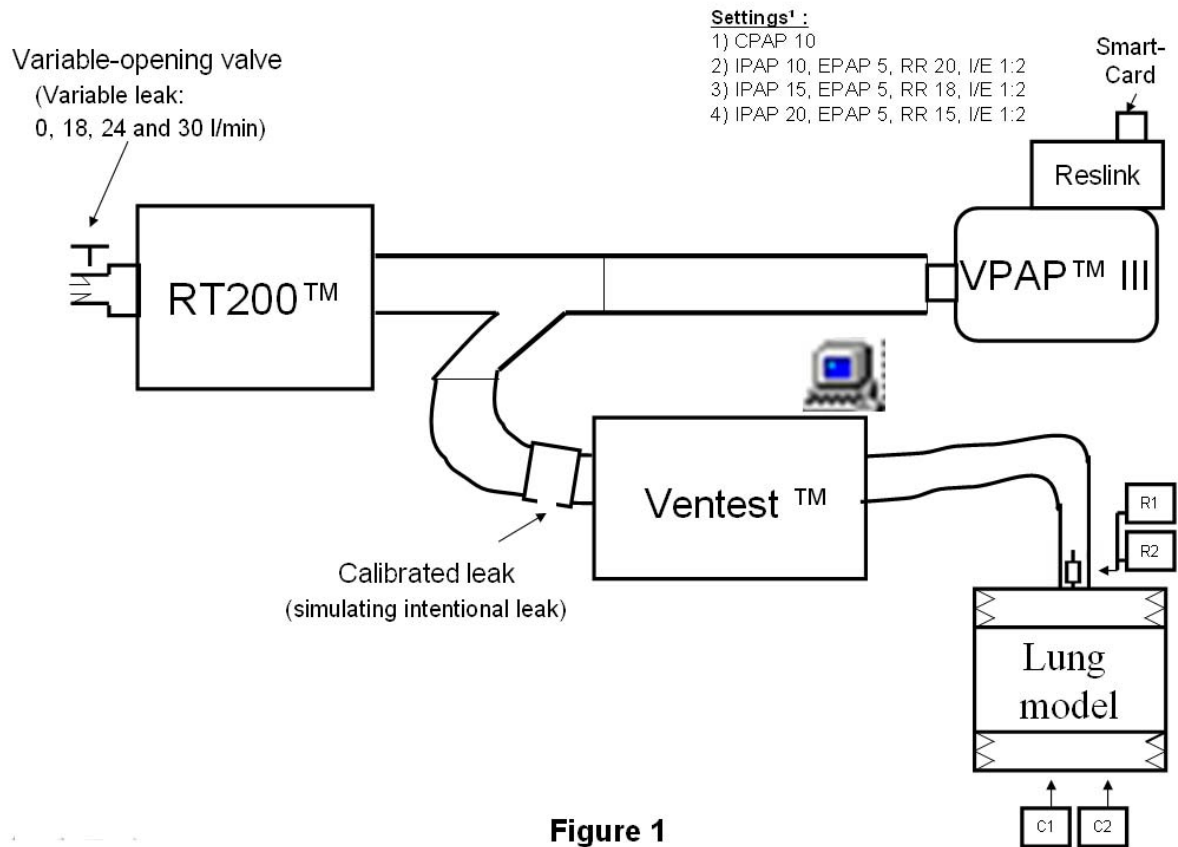*Abbreviations:* MV, minute ventilation

Figure 1

Figure 2: VPAP™ III ResLink System characteristic traces (2-hours per page)

a) Normal trace

b) Trace showing leaks > 0.40 l/sec followed by drop in SaO2

c) Trace showing continuous desaturation accompanied by a drop in minute ventilation as estimated by the ventilator (without leaks)

d) Trace showing desaturation dips (see oscillations in respiratory rate and minute ventilation as a reflection of desaturation dips)

Abbreviations: RR, respiratory rate (as estimated by the ventilator); MV, minute ventilation (as estimated by the ventilator)
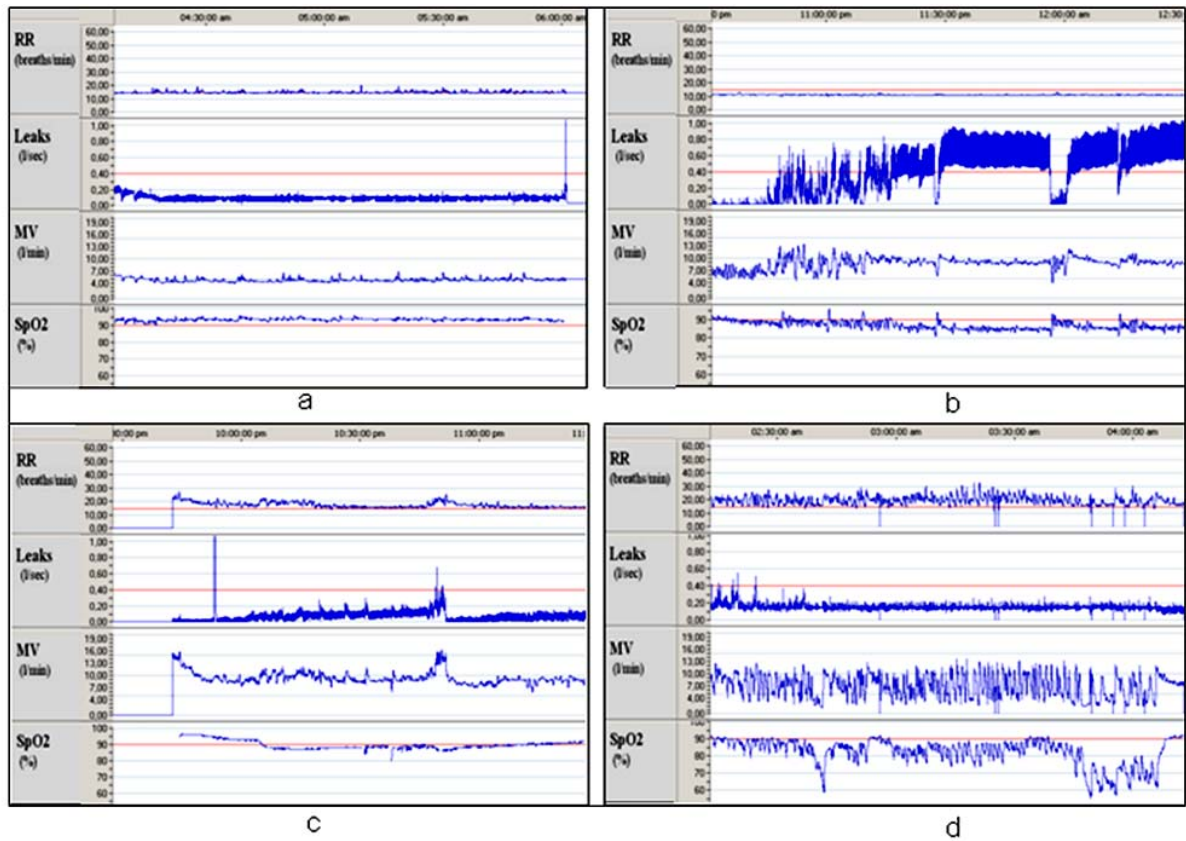
Figure 2

Figure 3: a) Correlation between values of measurements obtained by pneumotachograph and those estimated by the VPAP™ III- ResLink system (Pearson). b) Differences against mean for MV (n: 45) and leaks (n: 48) data according to Bland and Altman

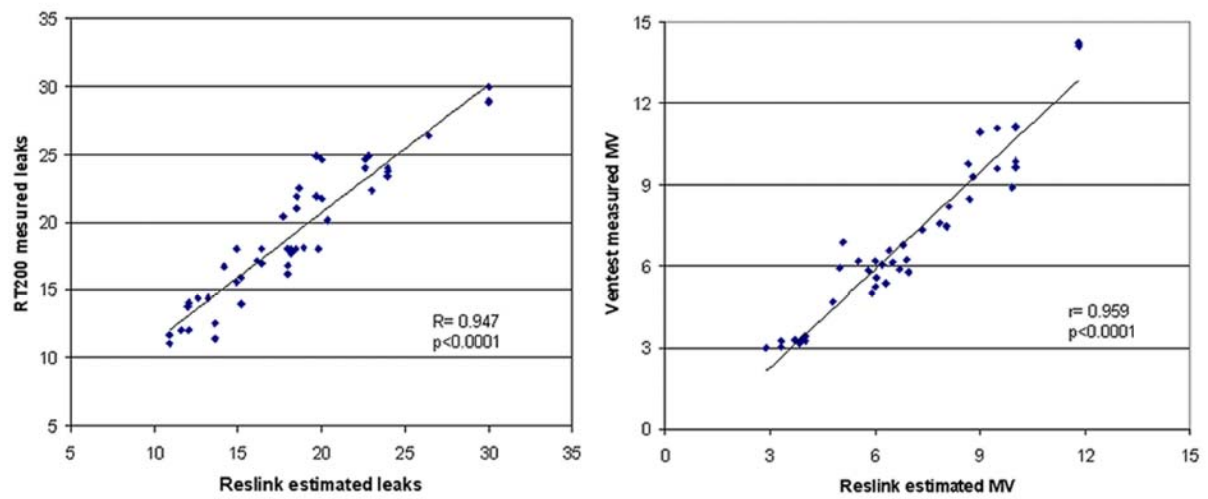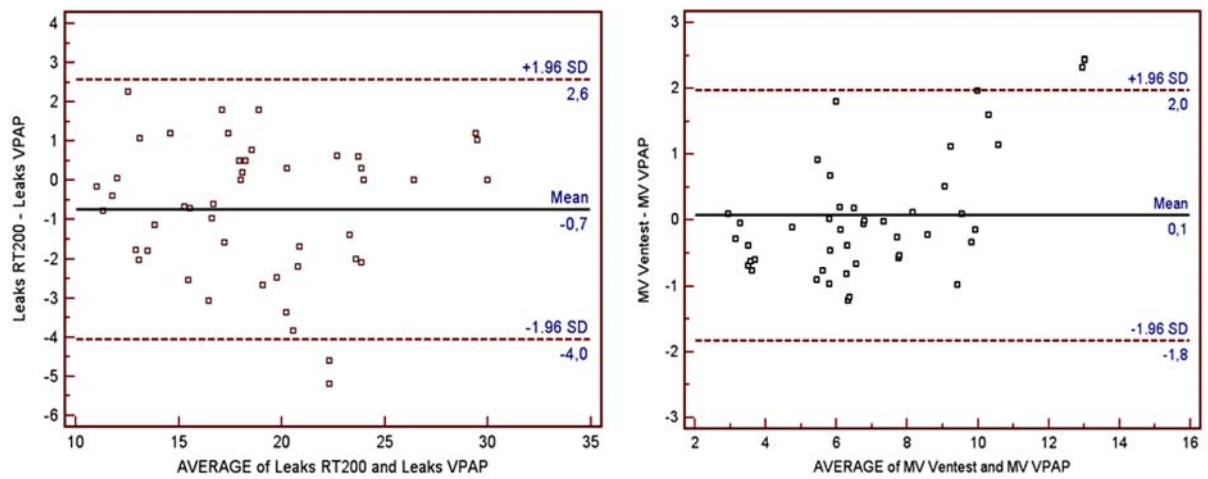Figure 3a

Figure 3b

Figure 4: Monitoring results classified by clinical situation and subsequent therapeutic modifications
   a) Acute setting (ARF group)
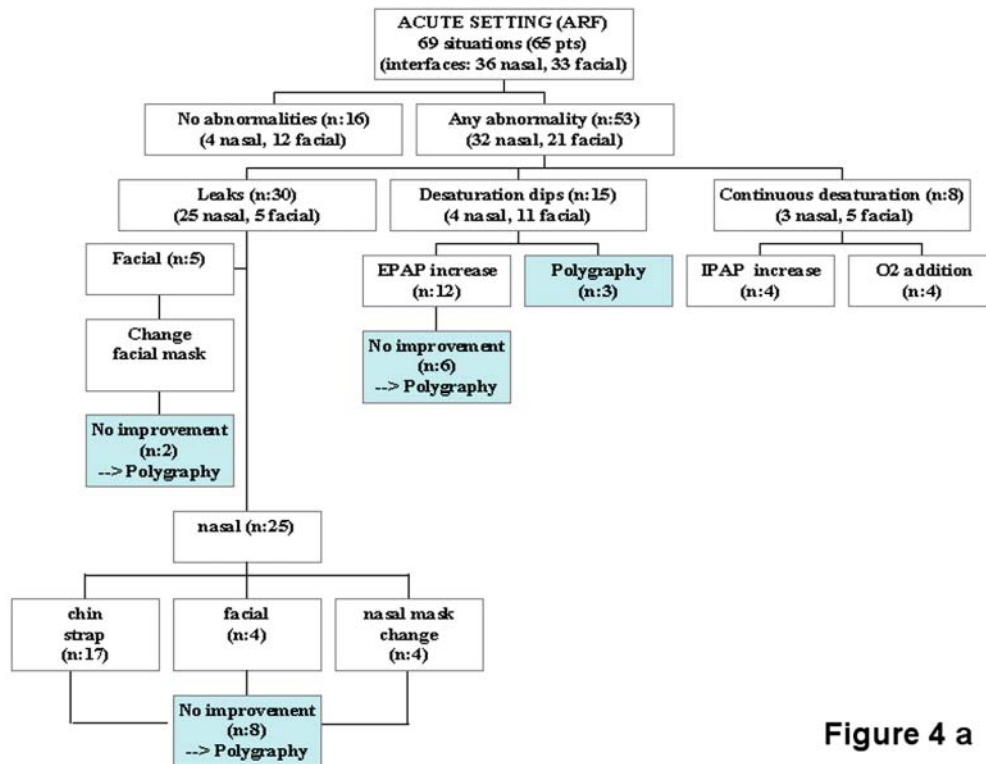   b) Elective ventilation (CRF group)
   c) At steady state (LTMV group)

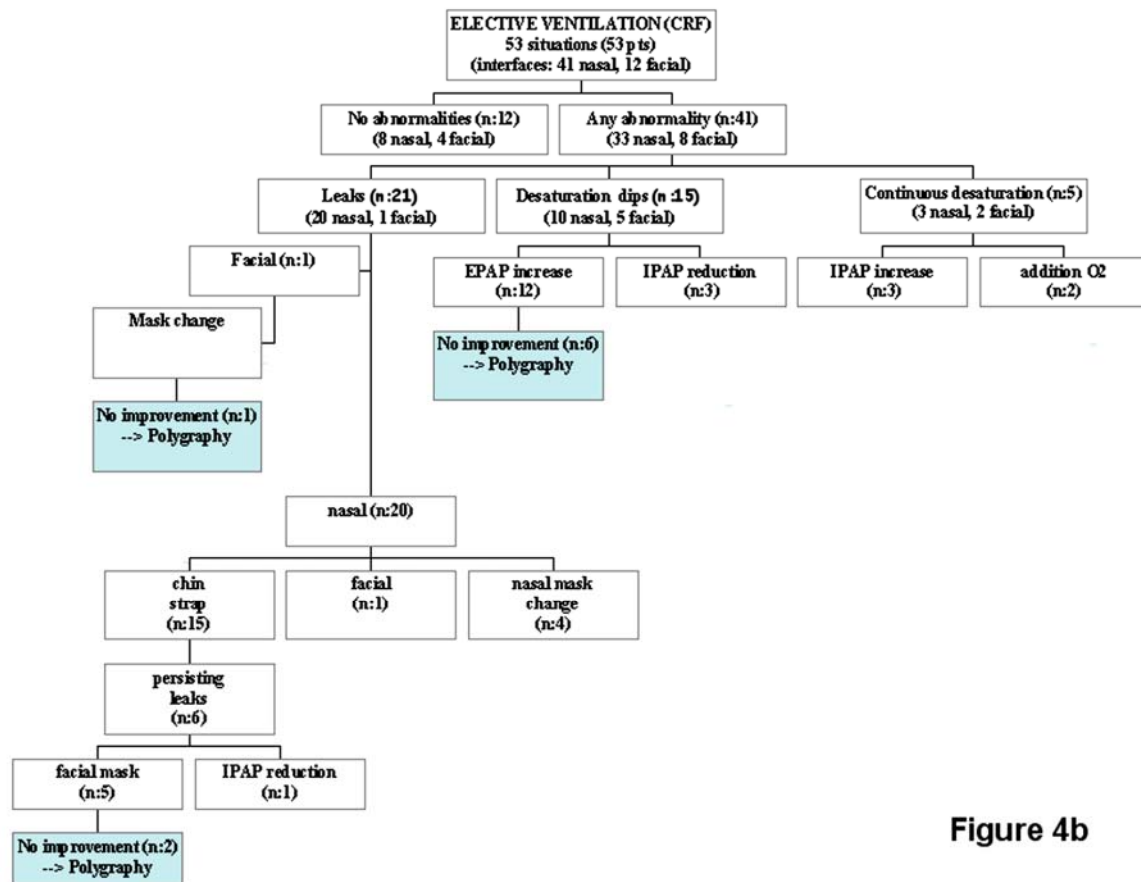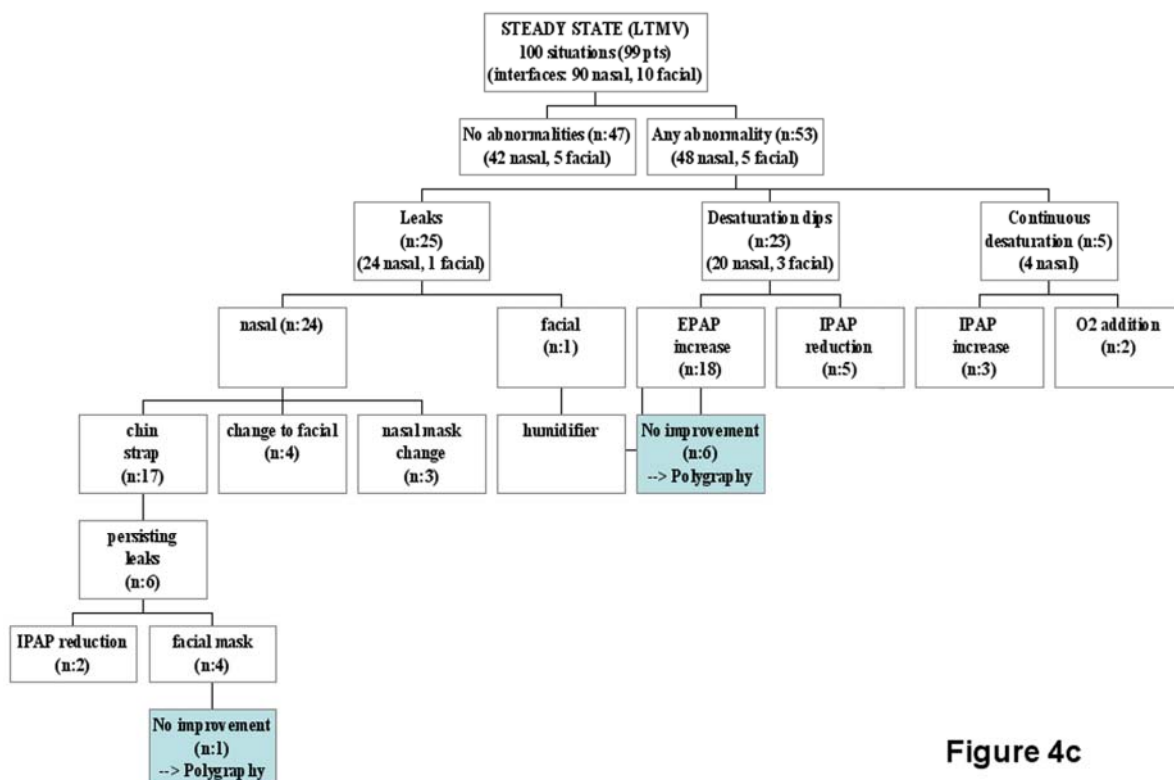Figure 4 a

ELECTIVE VENTILATION (CRF)
53 situations (53 pts)
(interfaces: 41 nasal, 12 facial)

No abnormalities (n:12) (8 nasal, 4 facial)

Any abnormality (n:41) (33 nasal, 8 facial)

Leaks (n:21) (20 nasal, 1 facial)

Desaturation dips (n:15) (10 nasal, 5 facial)

Continuous desaturation (n:5) (3 nasal, 2 facial)

Facial (n:1)

EPAP increase (n:12)

IPAP reduction (n:3)

IPAP increase (n:3)

addition O2 (n:2)

Mask change

No improvement (n:6) --> Polygraphy

No improvement (n:1) --> Polygraphy

nasal (n:20)

chin strap (n:15)

facial (n:1)

nasal mask change (n:4)

persisting leaks (n:6)

facial mask (n:5)

IPAP reduction (n:1)

No improvement (n:2) --> Polygraphy

Figure 4b

STEADY STATE (LTMV)
100 situations (99 pts)
(interfaces: 90 nasal, 10 facial)

No abnormalities (n:47) (42 nasal, 5 facial)

Any abnormality (n:53) (48 nasal, 5 facial)

Leaks (n:25) (24 nasal, 1 facial)

Desaturation dips (n:23) (20 nasal, 3 facial)

Continuous desaturation (n:5) (4 nasal)

nasal (n:24)

facial (n:1)

EPAP increase (n:18)

IPAP reduction (n:5)

IPAP increase (n:3)

O2 addition (n:2)

chin strap (n:17)

change to facial (n:4)

nasal mask change (n:3)

humidifier

No improvement (n:6) --> Polygraphy

persisting leaks (n:6)

IPAP reduction (n:2)

facial mask (n:4)

No improvement (n:1) --> Polygraphy

Figure 4c