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Oxygen supplementation in noninvasive home mechanical ventilation: the crucial roles of CO₂ exhalation systems and leakages

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Abstract

Background: When supplemental oxygen is added to noninvasive positive pressure ventilation (NPPV) using non-ICU ventilators, it is usually introduced with a preset flow rate into the ventilatory circuit at a site next to the ventilator; however, the impact of different CO₂ exhalation systems and leaks on actual inspired FiO₂ and gas exchange has not been elucidated.

Methods: In a randomized, open-label, four-treatment (two-by-two), four-period crossover design, four daytime measurements (60 minutes each) were performed in 20 patients receiving home mechanical NPPV plus ≥ 2 L O₂/min inserted proximally to the ventilator: active valve circuit or leak port circuit with or without artificial leakage (4mm I.D.). FiO₂ at the ventilator, FiO₂ at the mask, and blood gases were measured.

Results: Overall, FiO₂-mask (29 \pm 5%) was lower compared to FiO₂-ventilator (34 \pm 4%), with a mean (95%CI) difference of 5.1 (4.2 to 5.9, p<0.0001)%. With the leak port circuit, FiO₂-mask decreased by 3.2 (2.6 to 3.9, p<0.0001)% when compared to the active valve circuit. When artificial leakage was introduced into the circuit, FiO₂-mask decreased by 5.7 (5.1 to 6.4, p<0.0001)%, PaO₂ by 10.4 (3.1 to 17.7, p=0.006) mmHg, and PCO₂ increased by 1.8 (0.5 to 3.3, p=0.008) mmHg.

Conclusions: The use of leak port circuits and the occurrence of leakages around the interface significantly reduce FiO₂-mask and negatively impact on gas exchange in patients receiving home mechanical NPPV and supplemental oxygen.

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Keywords: Chronic obstructive pulmonary disease, mechanical ventilation, chronic respiratory failure, long-term oxygen therapy, fraction of inspired oxygen

Background

Noninvasive positive pressure ventilation (NPPV) via a face mask is a well established and increasingly used treatment option for acute and chronic respiratory failure that arises from different pathologies.¹⁻⁴ In many of those patients NPPV is either administered in addition to existing long-term oxygen therapy, or oxygen treatment and NPPV are commenced simultaneously, given that these patients frequently suffer from both hypoxemic and hypercapnic respiratory failure.^{5,6}

When using ICU ventilators a fixed inspiratory fraction of oxygen (FiO_2) is set during ventilatory support. In contrast, in smaller and portable ventilators outside the ICU oxygen is typically placed directly into the circuit using a constant flow rate. However, in the latter scenario the actual inspired FiO_2 is unknown and, importantly, is dependent on several factors: oxygen flow, leakage, circuit, and interface.⁷⁻⁹ The effect of an altered oxygen flow rate on inspired FiO_2 remains unclear in a clinical setting, as this is not regularly measured. Furthermore, conflicting results exist in the literature about whether FiO_2 is dependent on the location of oxygen insertion and the presence of leakages;^{7,10-13} this is likely attributable to the fact that the majority of relevant studies were performed in vitro using test lungs.^{7-9,11-13} So far, no study has been performed in patients with hypoxemic and hypercapnic respiratory failure where the impact on gas exchange may differ substantially depending on the underlying pathology. In addition, the impact of leaks on FiO_2 has yet not been conclusively investigated.

Two different single tube circuits are regularly used for NPPV: the leak port circuit and the active valve circuit.¹⁴ In the leak port circuit an intentional leak is integrated either into the circuit or the mask in order to wash-out CO_2 .¹⁵ In contrast, when using

an active valve circuit an exhalation port actively opens during expiration and closes during inspiration.

The present study was aimed at investigating the effects of (i) unintentional leakages that inevitably occur during NPPV application, and (ii) intentional leaks introduced into the circuit/mask to promote CO₂ elimination, on inspired FiO₂, oxygenation, dyspnea sensation, and alveolar ventilation. It was hypothesized that both intentional and unintentional leakages would contribute to reduced oxygenation and ventilation.

Methods

The study protocol was approved by the Institutional Review Board for Human Studies at the Albert-Ludwigs University, Freiburg, Germany, and was performed in accordance with ethical standards laid down in the Declaration of Helsinki. Written informed consent was obtained from all subjects.

Patients

Stable NPPV patients without evidence of acute respiratory failure, signs of respiratory infection (e.g. fever, purulent sputum), and severe obesity (BMI >35 kg/m²) were included in the study. Patients were recruited during a routine follow-up visit to the University Hospital Freiburg after previously being established on long-term NPPV.¹⁶ Home mechanical ventilation has been applied for at least two months prior to the study, with an additional oxygen flow rate of ≥2 L/minute.

Measurements

Lung function parameters (Masterlab-Compact[®] Labor, Jaeger, Hochberg, Germany) were assessed in accordance with international guidelines.^{17,18} Arterial blood gas

samples (AVL OMNI[®], Roche Diagnostics GmbH, Graz, Austria) were taken from the arterialized earlobe.

FiO₂ was measured using two sensors (Oxygensensor E-17/J, Nuova GmbH, Ratzeburg, Germany) connected to both ends of the ventilatory circuits (Figure 1).

Study design

The study had a randomized, open-label, four-treatment (two-by-two), four-period crossover design. It was performed as a single-center study at Department of Pneumology, University Medical Center Freiburg, Germany, between January and August 2010. The study setup is illustrated in Figure 1. Two ventilators capable of measuring FiO₂ (Vivo 50, BREAS Medical AB, Mölnlycke, Sweden) were used during all measurements. The first ventilator was used for ventilation in each patient. This ventilator also served as FiO₂ measurement site at the mask for distal FiO₂ (FiO₂-mask); the second ventilator was connected to a test lung and exclusively measured proximal FiO₂ next to the ventilator (FiO₂-ventilator). Ventilation parameters and oxygen flow rates were adopted from last-used settings of patient's home mechanical ventilation protocol and were not changed during any measurements. The oxygen flow was provided by hospital's wall socket and connected via oxygen adapter (Sauerstoff-Adapter Ref. 9-1963, Medisize Deutschland GmbH, Neuenkirchen-Seelscheid, Germany) to the ventilatory circuits proximal to the ventilator. All patients used a full-face mask (Ultra Mirage Fullface NV, ResMed Ltd, North Ryde, Australia) without integrated exhalation ports during all measurements.

An artificial leakage (inner diameter 4mm; Oxygen Adapter No. 1974, BpP Beatmungsprodukte GmbH, Neunkirchen-Seelscheid, Germany) was implemented into the circuit between exhalation port and mask to simulate unintentional leakage as described previously.¹⁶ The Patient Circuit with Exhalation Valve reusable 5055

(BREAS Medical AB, Mölnlycke, Sweden) was used for active valve circuit settings. For leak port circuit setups, patients were ventilated with a circuit (Patient Circuit with Leakage reusable 5065, BREAS Medical AB, Mölnlycke, Sweden) connected to a passive exhalation port (Silentflow 2, WM 23600, Weinmann GmbH & Co KG, Hamburg, Germany).

The effects of the circuit type (active valve vs. leak port) and the leakages (artificial leakage vs. no leakage) were each investigated. For this purpose, patients were ventilated during daytime with four different settings in a two-by-two design; each setting lasted for a period of 60 min (Figure 1):

- Setup A: Active valve circuit without artificial leakage
- Setup B: Leak port circuit without artificial leakage
- Setup C: Active valve circuit with artificial leakage
- Setup D: Leak port circuit with artificial leakage

Patients were randomized between sequences ABCD, BADC, CDAB, and DCBA. Measurements were performed on two consecutive days (two sequences/day). Between each sequence a wash-out period of 120 minutes was maintained while patients received oxygen using the flow rate established for home treatment without NPPV. After each measurement patients were asked to state their level of dyspnea according to Borg-Dyspnea-Scale.¹⁹

Study endpoints

The aim of the study was to assess the differences between active valve and leak port circuit. Furthermore, the impact of the unintentional leak produced by the additionally implemented artificial leakage was investigated. The primary endpoint was the difference in the mean FiO₂-mask between active valve and leak port circuit during 60 minutes of daytime NPPV. Here, it was hypothesised that FiO₂-mask, i.e.

the actual inspired FiO_2 , would yield a 10% lower FiO_2 (relative difference) when using a leak port compared to an active valve circuit. Further endpoints were FiO_2 -ventilator, PaO_2 , PaCO_2 , and Borg-Dyspnea-Scale.

Statistics

Sample size calculation was based on the primary endpoint FiO_2 -mask. The study was designed to show at a two-sided significance level of 0.05 with a power of 0.90 a difference between active valve and leak port circuit (A and C vs. B and D), when the true absolute difference was 2.5% FiO_2 . A standard deviation in the difference of 3% FiO_2 was assumed according to previous findings.⁹ Under these assumptions, recruitment of 20 patients was required.

The effect of active valve vs. leak port circuit was analysed by comparing setups A and C vs. B and D, and the effect of the artificial leakage was analysed by comparing setups A and B vs. C and D. Additionally, an analysis of interaction between type of circuit and an additional leakage was performed.

All randomised patients who were ventilated with all four setups in the crossover setting were included in the analysis. Analysis of variance (ANOVA) models were used assuming normal distribution of data, with 'circuit', 'artificial leak', the interaction between 'circuit' and 'artificial leak', 'period', and 'randomised sequence' defined as fixed effects, and 'patient within sequence' defined as a random effect. For analysis of FiO_2 -mask, FiO_2 -ventilator measurement was included as a fixed effect in the model for adjustment. For analysis of PaO_2 and PaCO_2 after ventilation, the measurements at the start of ventilation were included as a fixed effect in the model for adjustment. Treatment effects and interactive effects were estimated with 95% confidence interval (95%CI) and tested with a two-sided level of 0.05.

For the endpoint Borg-Dyspnea-Scale, the assumption of a normal distribution was not fulfilled. For these data, a non-parametric analysis was performed using Wilcoxon tests and Hodges-Lehmann estimators of the cross-over differences.

In addition, tests for period and carry-over effects (i.e., treatment - period interactions) were performed, which showed no relevant effects.

Results

Twenty-three patients were included in the study and twenty patients completed all measurements. Two patients refused to be ventilated during setup C and one patient refused to be ventilated during setup D due to dyspnea, both periods reflecting setups with artificial leakage. Demographic data and lung function parameters of the twenty patients who completed the study are given in Table 1. Eleven patients suffered from COPD. Nine patients had restrictive ventilatory disorders (Non-COPD) due to obesity-hypoventilation-syndrome (n=3), kyphoscoliosis (n=3), unclassified interstitial lung disease, post polio syndrome and phrenic nerve paralysis (n=1, respectively). NPPV settings and oxygen flow rates are shown in Table 2.

After summarizing all measurements (setups A-D, n=80), the mean FiO_2 -mask (29.1 ± 4.5 % SD) was found to be lower compared to FiO_2 -ventilator (34.2 ± 4.0 % SD), with a mean difference of 5.1% (95%CI 4.2 to 5.9, $p < 0.0001$) during 60 minutes of NPPV and supplemental oxygen. The drop in FiO_2 along the circuit arose irrespective of the circuit being used or of the presence of an artificial leakage: Firstly, regarding the two circuits, the drop in FiO_2 incorporating the active valve was 3.4% (95%CI 2.4 to 4.4, $p < 0.0001$), while using the leak port led to a 6.6% drop (95%CI 5.6 to 7.7, $p < 0.0001$); this revealed a treatment effect of 3.2% (95%CI 2.6 to 3.9, $p < 0.0001$) in

the drop of FiO_2 (active valve vs. leak port) . Secondly, without the artificial leakage, the drop in FiO_2 was 2.2% (95%CI 1.1 to 3.2, $p=0.0001$), while inserting the leakage led to a drop of 7.9% (95%CI 6.8 to 8.9, $p<0.0001$), thus representing a treatment effect of 5.7% (95%CI 5.1 to 6.4, $p<0.0001$) in the drop of FiO_2 (artificial leakage, without vs. with). Results of the FiO_2 -mask and FiO_2 -ventilator measurements in the four setups are given in Table 3. The values for FiO_2 -ventilator and FiO_2 -mask for each setup are illustrated in Figure 2 and Figure 3. The hypothesis of the study was confirmed, since FiO_2 -mask using the leak port circuit was about 10% lower (relative difference) than the FiO_2 -mask obtained using active valve circuit, Table 3.

Effects on gas exchange after 60 minutes of NPPV according to the different setups are provided in Table 3. Here, PaO_2 tended to be lower after 60 minutes of NPPV when the leak port was compared to the active valve circuit. The addition of artificial leakage in the circuits led to a substantial drop in PaO_2 ($p=0.006$) and an increase in PaCO_2 ($p=0.008$, Table 3).

The Borg-Dyspnea-Scales scores (median and quartiles) reached 0 (0-2.75) during Setup A, 0 (0-2.5) in Setup B, 0 (0-2) in Setup C, and 1 (0-3) when patients were treated by Setup D. Treatment effects in terms of Borg-Dyspnea-Scale scores were detectable neither between the two circuits (active valve vs. leak port: -0.125 (95%CI -0.5 to 0, $p=0.12$), nor with the insertion of the artificial leakage (no vs. yes: 0 (95%CI -0.25 to 0.5, $p=0.83$) .

Discussion

Three major findings arise from this study: Firstly, there is a substantial drop in FiO_2 along the tubing from the ventilator to the interface, irrespective of the circuits used or the presence of unintentional leakage.

Secondly, differences in the FiO_2 measured at the mask are evident when different ventilatory circuits and their exhalation ports are compared. Here, the FiO_2 measurement at the mask is lower with a leak port circuit than with a ventilatory circuit and active valve, despite the fact that the same rate of oxygen flow is fed into the ventilator circuit proximal to the ventilator.

Finally, adding an artificial leakage next to the full face mask to simulate unintentional leakage led to a drop in FiO_2 -mask. This, in turn, has a detrimental effect on gas exchange, with a decrease in PaO_2 and an increase in PaCO_2 .

These findings have two clinically important implications: Firstly, FiO_2 -mask was found to be lower with a leak port than with an active valve circuit. As a consequence, PaO_2 values were approximately 10 mmHg lower at end of the trial when leakage was present. This drop in PaO_2 is very important, even if PaO_2 -levels did not decrease to a critical value in the clinical stable patients investigated here. In a study using test lungs and healthy volunteers, obtaining FiO_2 values higher than 50% was not feasible with the leak port system, despite increases in oxygen flow rate up to 16 L/min.⁷ Preferably, patients who also require supplemental oxygen should receive NPPV by the means of an active valve circuit if portable ventilators are used. In addition, the authors do not recommend using supplemental oxygen flow inserted into a t-piece proximal to the ventilator in patients suffering from acute hypoxemic respiratory failure, in which adequate oxygenation is the primary aim of acute NPPV.^{1,2,20} In this scenario, ICU-ventilators in which a fixed FiO_2 ratio can be set are

preferable for NPPV in pure acute hypoxemic respiratory failure patients. As pointed out above regarding blood gas deteriorations, a substantial drop in PaO_2 would harm patients with acute or more severe chronic hypoxemic respiratory failure.

Secondly, leakages during NPPV should be kept to a minimum, since leaks in the present study were responsible for a reduction in FiO_2 , a decrease in PaO_2 , and an increase in PaCO_2 . In addition, the deleterious effects of leaks on inspired FiO_2 and gas exchange are exacerbated when a leak port circuit is used. Therefore, if leakage is unavoidable, active valve circuits would be preferable in order to minimize the negative impact of leakage on gas exchange. Today most patients receive pressure-preset NPPV for home mechanical ventilation,⁴ since this is better tolerated by the patients, is less expensive, and has leak compensation capabilities. In contrast, volume-preset NPPV produces more gastrointestinal side effects, is more expensive, and does not compensate for leakage.^{16,21} Pressure-pre-set NPPV is also primarily being used in acute respiratory failure patients.² However, when the pressure-preset mode increase the inspiratory flow rate as a means of leak compensation, higher amounts of room air with FiO_2 of 21% are mixed with the constant amount of oxygen delivered according to the preset oxygen flow rate. As a consequence, inspired FiO_2 decreases in different etiologies of chronic ventilatory failure and their settings of ventilatory support as clearly demonstrated in this study. A further drop of FiO_2 in the circuit can be attributed to the presence of expiratory positive airway pressure, which maintains a flow rate during expiration. In line with previous findings¹⁶ the current results suggest that leaks cause a decrease in minute ventilation as demonstrated by the increase of PaCO_2 which negatively impacts on oxygenation. Thus, the advantage of pressure-preset NPPV in terms of leak compensation can also serve as a disadvantage for the oxygenation of patients receiving supplemental oxygen in

addition to NPPV, and this seems to be valid for both acute and chronic respiratory failure patients.

There are some limitations in the current study, which need to be addressed. Firstly, all measurements were performed during daytime, with one ventilator, and with an oronasal mask. Consequently, these results cannot directly be extrapolated to nocturnal circumstances, to different ventilators, or other interfaces available for NPPV. However, the amount of leakage arising from the artificial leakage used¹⁶ was overall comparable to leak levels encountered during nocturnal NPPV.²¹⁻²³ The artificial leak used in the present study remained constant throughout the entire ventilation procedure. In clinical practice the degree of leakage changes over time due to the individual circumstances of the patient. Thus, it could be speculated that higher amounts of leakage could have an even more deleterious impact on inspired FiO_2 and gas exchange. However, this needs further investigation.

Secondly, in this clinical trial only two different exhalation ports and their ventilatory circuits were analyzed. Additional systems for NPPV are available, and these systems may vary both in dead space and resistance, thus potentially influencing inspired FiO_2 .^{6,14} In particular, exhalation ports directly integrated into the face mask were not investigated in this study. Interfaces with exhalation ports embedded into the mask were excluded since their influence to FiO_2 could not have been monitored with the FiO_2 -sensor used in this study. However, in line with the current findings, a previous study showed a drop in FiO_2 when using these interfaces.⁹ Furthermore, oxygen was integrated into the circuit next to the ventilator, and hence was not in the vicinity of the patient's interface. Indeed, there are conflicting results in the literature regarding the favored site of oxygen insertion. While some studies reported an increase in FiO_2 when supplemental oxygen was inserted at a site more proximal to

the patient or the mask,^{7,9,13} others demonstrated opposite results, with a lower FiO_2 when oxygen was implemented next to the mask.^{11,12} One study showed no effect of changing the position of oxygen insertion.¹⁰ However, the insertion of oxygen proximal to the ventilator is recommended by many manufacturers as well as guidelines,⁶ and is suggested to be more convenient because the risk of disconnection is lower than that when oxygen is inserted close to the mask. This rationale therefore supported the decision in the present study to insert oxygen proximal to the ventilator, and different results by inserting oxygen at other ports could not be excluded.

Thirdly, arterial blood gas analysis was performed obtaining a blood sample from the arterialized earlobe. This may have led to different results analyzing arterial blood samples, especially focusing PaO_2 . However, patients in this study were clinically stable and therefore the insertion of an arterial line was avoided. Furthermore, a recently published meta-analysis demonstrated that results of capillary pH and PaCO_2 accurately reflect arterial values, and capillary PaO_2 can be appropriate replacing arterial PaO_2 , respectively.²⁴

Conclusion

In conclusion, the FiO_2 reading at the mask of patients receiving NPPV and supplemental oxygen is lower when a leak port system is used compared to when an active valve circuit is implemented. A further reduction in inspired FiO_2 occurs in the presence of air leakage, and this directly translates into a deterioration of gas exchange. As a consequence, active leak valves are preferable to leak port systems when oxygen is administered in addition to NPPV.

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Figure Legends

Figure 1: Setup of measurements: active valve circuit or leak port circuit with additional artificial leakage (Setup C+D) or without additional artificial leakage (Setup A+B) (4mm I.D.) next to the full-face mask.

Figure 2: FiO_2 -ventilator during 60 min of NPPV/oxygen. Mean values for all patients (n= 20) are given for each measurement point and setup: Active valve circuit without artificial leakage (filled circle), leak port circuit without artificial leakage (blank circle), active valve circuit with artificial leakage (filled triangle), leak port circuit with artificial leakage (blank triangle).

Figure 3: FiO_2 -mask during 60 min of NPPV/oxygen. Mean values for all patients (n= 20) are given for each measurement point and setup: Active valve circuit without artificial leakage (filled circle), leak port circuit without artificial leakage (blank circle), active valve circuit with artificial leakage (filled triangle), leak port circuit with artificial leakage (blank triangle).

Tables

Table 1. Demographic data and lung function parameters. Values for mean \pm standard deviation are given.

	COPD	Non-COPD	p-value
	(N=11)	(N= 9)	
Male/female	6/5	6/3	
Age (years)	55.2 \pm 8.3	72.1 \pm 10.1	<0.001
BMI (kg/m ²)	26.7 \pm 8.7	27.9 \pm 5.6	0.287
NPPV use (months)	28.0 \pm 34.8	62.3 \pm 56.8	0.323
LTOT use (months)	35.4 \pm 36.6	52.2 \pm 57.8	0.761
FEV ₁ (% predicted)	24.7 \pm 11.1	38.3 \pm 8.3	0.010
FVC (% predicted)	48.4 \pm 11.1	43.2 \pm 17.7	0.430
FEV ₁ /FVC (%)	43.6 \pm 11.3	73.6 \pm 10.6	<0.001
RV (% predicted)	261.4 \pm 63.0*	84.8 \pm 35.9	<0.001
TLC (% predicted)	127.3 \pm 33.0*	58.6 \pm 19.3	<0.001

BMI = body mass index, FEV₁ = forced expiratory volume in one second, FVC = forced vital capacity, LTOT = long-term oxygen therapy, RV = residual volume, TLC = total lung capacity. *N=9.

Table 2. NPPV settings and oxygen flow rates. Values given as mean \pm standard deviation.

	COPD (N= 11)	Non-COPD (N= 9)	p-value
Oxygen flow rate (L/min)	2.6 \pm 0.2	2.7 \pm 1.3	0.858
Interface (Small / Medium / Large)	3 / 7 / 1	3 / 4 / 2	
Mode (PSV / PCV / ASSPCV)	2 / 0 / 9	1 / 2 / 6	
IPAP (mbar)	25.9 \pm 5.1	22.9 \pm 4.2	0.170
EPAP (mbar)	4.7 \pm 1.3	3.9 \pm 1.8	0.254
RR _{set} (/min)	17.0 \pm 3.2	18.8 \pm 2.7	0.206
Inspiratory time (sec) ^a	1.1 \pm 0.1 ^b	1.2 \pm 0.2 ^c	0.094
Inspiratory trigger ^d	3.7 \pm 1.6	4.6 \pm 1.8	0.302
Expiratory trigger (PSV only) ^e	3.5 \pm 0.7 ^f	5 ^g	
Rise time	1.6 \pm 0.7	3.1 \pm 2.7	0.212

ASSPCV = assisted pressure controlled ventilation, EPAP = expiratory positive airway pressure, IPAP = inspiratory positive airway pressure, Interface = Ultra Mirage Fullface NV (ResMed Ltd, North Ryde, Australien), PCV = pressure controlled ventilation, PSV = pressure support ventilation, RR_{set} = preset respiratory rate (including back-up frequency in pressure support mode).

^aInspiratory time (min to max) was set in PSV to 0.5-2.0 sec, ^bN=9, ^cN=8, ^dInspiratory flow trigger: sensitive (1) to non-sensitive (9), ^eExpiratory trigger dependent on peak flow: 90% (1) to 10% (9), ^fN=2, ^gN=1.

Table 3. Effects of the exhalation circuit and artificial leakage on FiO₂ at proximal and distal sensors during 60 minutes of NPPV/oxygen and measurements of gas exchange after 60 minutes of NPPV/oxygen. N=20 for each setup (A, B, C or D).

Setup	exhalation	artificial	Mean [95% CI]	Effect of treatment, Difference [95% CI], p-value		
	circuit	leakage		exhalation circuit	artificial leak	Interactive effect
				active valve (A+C)	no (A+B)	(A-B)
				vs.	vs.	vs.
				leak port (B+D)	yes (C+D)	(C-D)
FiO ₂ (%) proximal at the ventilator						
A	active valve	no	36.2 [34.4, 37.9]			
B	leak port	no	33.8 [32.0, 35.5]	1.7 [0.3, 3.1]	1.4 [0.0, 2.8]	1.4 [-1.4, 4.2]
C	active valve	yes	34.0 [32.3, 35.7]	0.019	0.045	0.31
D	leak port	yes	33.0 [31.3, 34.7]			
FiO ₂ (%) distal at the interface						
A	active valve	no	33.9 [32.8, 35.1]	3.2 [2.6, 3.9], <0.0001	5.7 [5.1, 6.4] <0.0001	1.1 [-0.1, 2.3] 0.08
B	leak port	no	30.1 [29.0, 31.2]			
C	active valve	yes	27.6 [26.5, 28.8]			

D	leak port	yes	24.9 [23.8, 26.1]			
PaO ₂ (mmHg) after 60 minutes of NPPV/oxygen						
A	active valve	no	87.7 [78.2, 97.2]			
B	leak port	no	84.9 [75.4, 90.4]	6.3 [-1.0, 13.7]	10.4 [3.1, 17.7]	-7.1 [-21.8, 7.6]
C	active valve	yes	80.8 [71.1, 90.5]	0.09	0.006	0.34
D	leak port	yes	71.0 [61.5, 80.5]			
PaCO ₂ (mmHg) after 60 minutes of NPPV/oxygen						
A	active valve	no	45.7 [44.0, 47.4]			
B	leak port	no	47.6 [45.9, 49.3]	-0.5 [-1.9, 0.8]	-1.8 [-3.2, -0.5]	-2.8 [-5.5, -0.1]
C	active valve	yes	48.9 [47.2, 50.6]	0.43	0.008	0.044
D	leak port	yes	48.0 [46.4, 49.7]			

CI = confidence interval, FiO₂ = inspired fraction of oxygen, NPPV = noninvasive positive pressure ventilation, PaCO₂ = arterial partial pressure of carbon dioxide, PaO₂ = arterial partial pressure of oxygen.

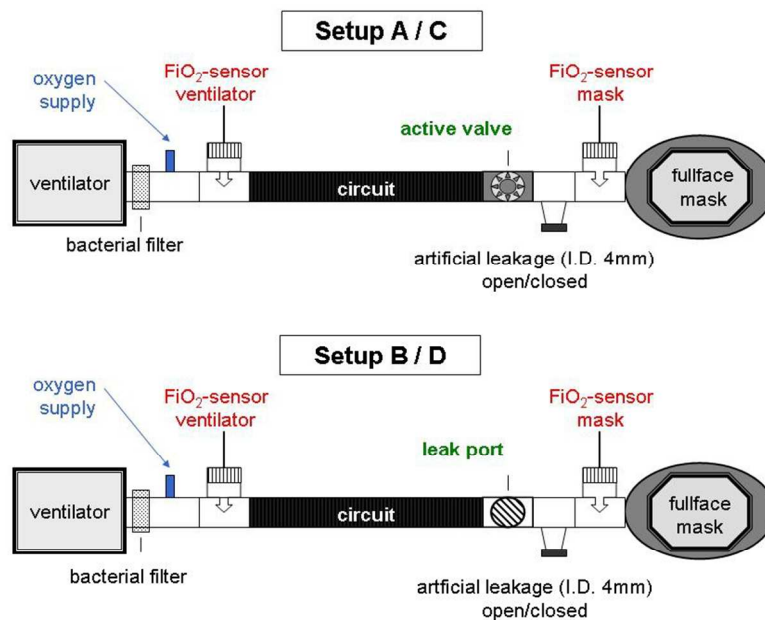


Figure 1: Setup of measurements: active valve circuit or leak port circuit with additional artificial leakage (Setup C+D) or without additional artificial leakage (Setup A+B) (4mm I.D.) next to the full-face mask.
285x190mm (96 x 96 DPI)

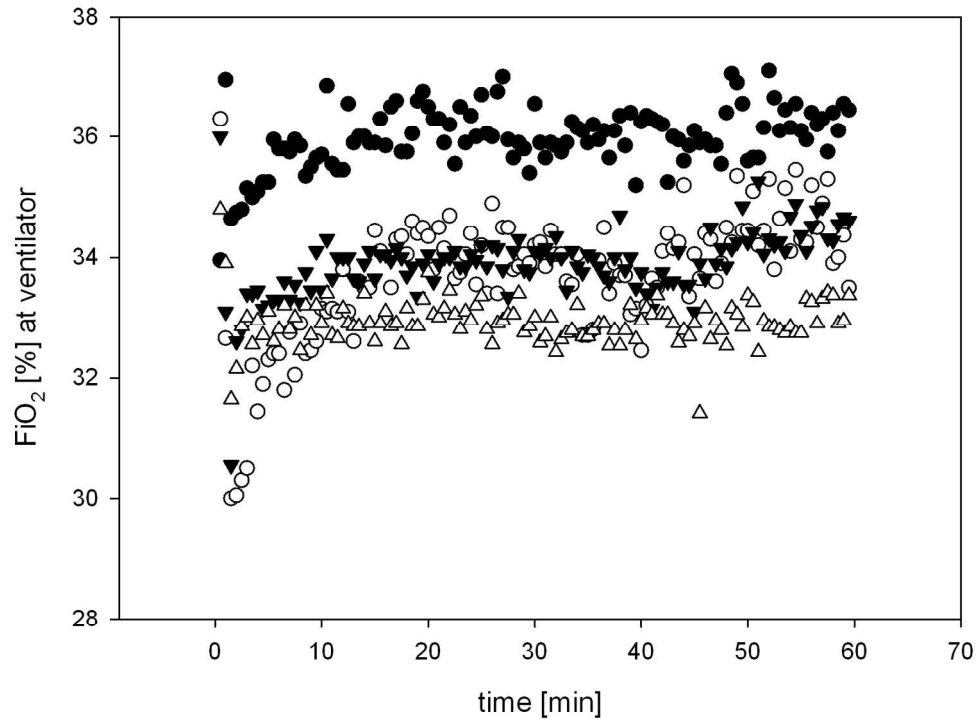


Figure 2: FiO₂-ventilator during 60 min of NPPV/oxygen. Mean values for all patients (n= 20) are given for each measurement point and setup: Active valve circuit without artificial leakage (filled circle), leak port circuit without artificial leakage (blank circle), active valve circuit with artificial leakage (filled triangle), leak port circuit with artificial leakage (blank triangle).

148x117mm (300 x 300 DPI)

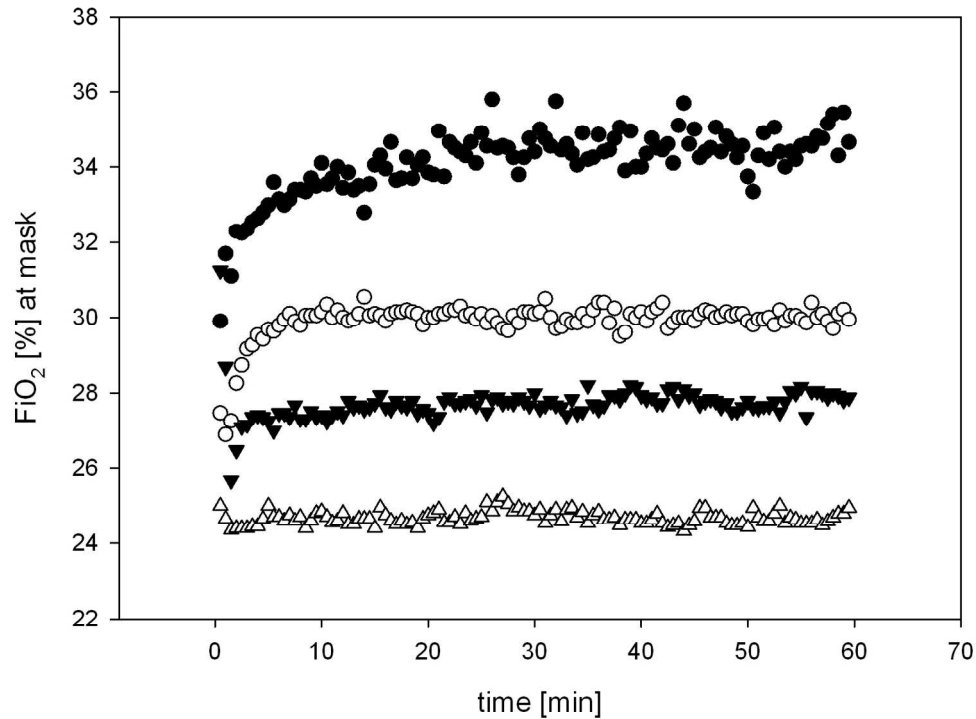


Figure 3: FiO₂-mask during 60 min of NPPV/oxygen. Mean values for all patients (n= 20) are given for each measurement point and setup: Active valve circuit without artificial leakage (filled circle), leak port circuit without artificial leakage (blank circle), active valve circuit with artificial leakage (filled triangle), leak port circuit with artificial leakage (blank triangle).

148x117mm (300 x 300 DPI)