ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Original research article

At-home NIV initiation with telemonitoring in ALS patients: a retrospective study

T. Réginault, B. Bouteleux, P. Wibart, S. Mathis, G. Le Masson, O. Pillet, L. Grassion

Please cite this article as: Réginault T, Bouteleux B, Wibart P, *et al*. At-home NIV initiation with telemonitoring in ALS patients: a retrospective study. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00438-2022).

At-home NIV initiation with telemonitoring in ALS patients: a retrospective study

T. Réginault[1,2], B. Bouteleux[2], P. Wibart[1,2], S. Mathis[3], G. Le Masson[3], O. Pillet[1], L.Grassion[4]

Co-authors :

Thomas Réginault - 1. Département de Médecine, Service de Réanimation Médicale, Hôpital Pellegrin, Bordeaux, France. 2. Zéphyr Paramed, Bordeaux, France.

Benoit Bouteleux - 2. Zéphyr Paramed, Bordeaux, France.

Philippe Wibart - 1. Département de Médecine, Service de Réanimation Médicale, Hôpital Pellegrin, Bordeaux, France. 2. Zéphyr Paramed, Bordeaux, France

Stéphane Mathis - 3. Département de Neurologie et Centre de référence pour la SLA, Hôpital Pellegrin, Bordeaux, France.

Gwendal Le Masson - 3. Département de Neurologie et Centre de référence pour la SLA, Hôpital Pellegrin, Bordeaux, France.

Odile Pillet - 1. Département de Médecine, Service de Réanimation Médicale, Hôpital Pellegrin, Bordeaux, France.

Léo Grassion - 4. Département de Pneumologie, Service des Maladies Respiratoires, Hôpital du Haut Lévêque, Pessac, France.

Corresponding author :

Thomas Réginault - Département de Médecine, Service de Réanimation Médicale, Hôpital Pellegrin, place Amélie Raba Léon, 33000 Bordeaux, France. thomas.reginault@chu-bordeaux.fr.

At-home NIV initiation with telemonitoring in ALS patients: a retrospective study

Abstract

Background: Noninvasive ventilation (NIV) improves survival and quality of life in amyotrophic lateral sclerosis (ALS) patients. NIV initiation is mostly conducted at hospital, but a recurrent lack of hospital beds led to the necessity to explore an at-home initiation process. We report here data from our NIV initiation cohort in ALS patients.

Research Question: Could, our at-home NIV initiation process with telemonitoring in ALS patients, be an efficient solution for adherence and nocturnal hypoxemia correction?

Methods: We performed a retrospective analysis of data collected from the 265 ALS patients followed in the Bordeaux ALS Centre for whom NIV initiation has been carried out between September 2017 and June 2021 with two modalities: at-home initiation or in-hospital initiation. The primary outcome was adherence to NIV at 30 days. The secondary outcome was at-home NIV initiation-process efficiency on nocturnal hypoxemia correction.

Results: At 30 days, NIV adherence (mean >4h/day) was 66% in total population, 70% in the subgroup at-home NIV initiation and 52% in the subgroup in-hospital NIV initiation. Nocturnal

hypoxemia correction was observed in 79% of adherent patients in the subgroup at-home NIV initiation. Mean delay of NIV prescription and at-home NIV initiation was 8.7 days (+/- 6.5) vs 29,5% at hospital.

Conclusion: Our study shows that our at-home NIV initiation process in ALS patients is a good option to provide rapid access to NIV with good adherence and efficiency. Further literature on at-home NIV initiation benefit is welcomed especially to evaluate long-term efficiency and global cost analysis.

Keywords:

Amyotrophic lateral sclerosis, at-home initiation, noninvasive ventilation, telemonitoring.

Abbreviations list

ADH, adherence; AHI, apnea hypopnea index; ALS, amyotrophic lateral sclerosis; BMI, body mass index; EPAP, expiratory positive airway pressure; IPAP, inspiratory positive airway pressure; MIP, maximum inspiratory pressure; NIV, noninvasive ventilation; PaCO2, arterial pressure of CO2; PIF, peak inspiratory flow; RR, respiratory rate; SM, supplementary material; SNIP, sudden nasal inspiratory pressure; SpO2, pulsed oxygen saturation; Ti, inspiratory time ; FVC, forced vital capacity;

At-home NIV initiation with telemonitoring in ALS patients

Introduction

Amyotrophic lateral sclerosis (ALS) is one of the most common neurodegenerative conditions in adult life. ALS induces a rapid paralysis of the limbs, bulbar muscles (speech, mastication and swallowing) and respiratory muscles. After the onset of diaphragmatic weakness, the median survival without respiratory assistance is 7 months, (1) and most of the deaths are due to respiratory causes, (2). For these reasons, since 2006, noninvasive ventilation (NIV) is the reference treatment for ALS-related respiratory failure, (3). NIV relieves dyspnea, improves sleep, improves the quality of life and prolongs survival, (4).

NIV initiation is a critical point that raises two questions: when and where? Since

2006, guidelines and several studies have focused on the “When” question, (5) but there is no evident answer to the “Where” question.

French guidelines, (5, 6) recommend initiating NIV at the hospital (possibly as an outpatient) but propose initiating NIV at home, if there is good collaboration with the referral center and if the patient can be rapidly hospitalised in case of failure (7).

This practice was illustrated by a Dutch randomised controlled trial, (8) comparing hospitalised NIV initiation vs. at-home NIV initiation by a nurse on patient with all kind of pulmonary restrictive disorder, without a difference in nocturnal hypoxemia correction.

Inpatient NIV initiation seems not to be the best solution to promote the acceptance of this treatment. Discomfort from significant travel and anxiety-provoking hospital environments; recurrent issues with hospital bed capacity causing hospitalisation waiting times; an obligation for quick results; and a risk of nosocomial infections have led us to change our NIV initiation practice from an in-patient initiation model (1 to 2 days) to explore an at-home NIV initiation process to respond to these issues.

Another important point in NIV follow-up is treatment quality. In a previous study, half of the patients were inadequately ventilated at one month, with a negative impact on survival, (9). Indeed, the persistence of leaks, (10), obstructive events, (9) or desaturation, (11) are associated with reduced survival.

We are reporting here our own experience regarding NIV initiation in ALS patient with a 30 days at-home NIV initiation process with telemonitoring, in order to evaluate NIV adherence and NIV efficiency (define by a correction of nocturnal hypoxemia under NIV as an indirect criteria for hypoventilation).

Method

Patients

This was a retrospective monocentric study. Data were collected between September 2017 to June 2021 from all patients followed in the Bordeaux ALS Centre and for whom NIV initiation was decided.

The indication for NIV was given by the neurologist according to guideline recommendations (12) and was based on the presence of symptoms of respiratory muscle weakness (at least one of the following dyspnoea, tachypnoea, orthopnoea, disturbed sleep due to nocturnal desaturation/arousals, morning headache, use of auxiliary respiratory muscles at rest, paradoxical respiration, daytime fatigue, excessive daytime sleepiness (ESS > 9)) and abnormal respiratory function tests (with at least one of the following elements: VC < 80%, nocturnal SpO2 < 90%, time

> 5% (French recommendations (3)), SNIP < 40 cmH2O, MIP <60cmH2O), or hypercapnia.

Some patients refused to try NIV. For the others, home NIV initiation were then proposed, except those with a PaCO2 above 6,1 Kpa, those without any caregiver and those who were already hospitalized for whom NIV was initiated in the hospital.

NIV prescription corresponded to the day of the NIV initiation request by the Bordeaux ALS center.

The duration of chart inclusion was from the first day of NIV initiation to the 30th day of the last patient included.

Respiratory assessment

All patients had respiratory assessment before NIV initiation at a stable state. It was performed in the same hospital lab during the Bordeaux ALS center consultation, including plethysmography, spirometry, maximal inspiratory pressure measurement, arterial blood gases. Nocturnal oximetry was performed at-home or during hospitalisation. Some emergency patients have not been able to have a respiratory assessment before.

NIV initiation

NIV initiation was defined as the first day of the NIV trial. It was performed by a specialised physiotherapist as soon as possible following the NIV prescription on a weekday for at-home initiation or any day of the week for in-hospital initiation.

To benefit telemonitoring, we provided NIV with an integrated telemonitoring device (LUMIS 100/150 VPAP ST (ResMed®, Australia), Airview (ResMed®, Australia)) for at-home initiation patients. For the in-hospital initiation patients, a STELLAR 150 (ResMed®, Australia) was used to benefit internal battery.

A face mask was proposed in the first place to avoid leaks from mouth control weakness.

The ventilator was set up in the spontaneous timed (S/T) mode with pressure support (PS) titrated to correct clinically spontaneous respiratory effort. PS was set initially at 4 cmH2O and was gradually adapted according to patient tolerance and comfort to relieve dyspnea and respiratory effort. In most cases, expiratory positive airway pressure (EPAP) was initially set at 4 and could have been increased to 8 cmH2O in the event of known obstructive events. Inspiratory triggering, pressurisation and I to E cycling were adapted to obtain a clinically good synchronisation and a good patient feeling.

Progress of the home NIV initiation protocol (Figure 1)

In accordance with the French National Authority for Health recommendations of 2012 (7), a 30 days at-home NIV initiation was performed by a specialised physiotherapist team in collaboration with the neurologists and the resuscitation consultant of the Bordeaux ALS center.

There are a total of 5 interventions, which are described in the supplemental material (SM1), including 3 at-home visits and 2 teleconsultations with telemonitoring. Costs of physiotherapists actions were suported by home healthcare companies which usually perceive a reimbursement of 62.16€/week of NIV treatment <12h by the French social security.

During the 30 days NIV initiation process, patients were able to contact the multidisciplinary care team (homecare assistance, coordination nurse, specialised physiotherapist) by phone at any time to receive support for any reason related to NIV and their clinical condition.

During the follow-up of 30 days, at each step of the protocol, the mask could be switched in case of leaks or discomfort.

On day 1, 3 and 30, NIV parameters were adjusted to improve respiratory comfort during at-home physiotherapist visits. IPAP and EPAP were increased by 1 or 2 cmH2O at each step, following patient tolerance and the analysis with the rescan software of obstructive events, to obtain an AHI lower than 10, a RR<20 cycles/minute and a target volume of 8-10 ml/kg. In case of persistent AHI>10 despite an increased of PEEP, polygraphy under NIV was considered to discriminate apneas with or without decrease of neural drive (13).

Telemonitoring on day 2 and 10 was used to control adherence, fractional use, leaks, tidal volume (Vt), respiratory rate (RR) and AHI before a phone call to the patient (Figure 1).

Nocturnal oximetry was performed with the Air10 oximeter adapter (ResMed®, Australia) on day 30 only when patients had nocturnal adherence.

NIV data evaluated

NIV data were collected from day 1 of initiation to day 30 from the NIV software (Rescan®, Resmed®, Australia).

The primary outcome was the adherence (ADH) to NIV at 30 days, defined by a mean use of NIV for more than 4 hours/day during the first 30 days.

The secondary outcome was the efficiency of NIV initiation on nocturnal hypoxemia correction, defined by a nocturnal SpO2 correction on day 30 (nocturnal

SpO2 < 90%, time < 5%). As nocturnal oximetry on day 30 was performed only in adherent patient, the secondary outcome was collected only in the adherent subgroup. As a lack of nocturnal oximetry performed at day 30 for in-hopital patients, the secondary outcome was collected only for adherent subgroup of at-home NIV initiation.

A fractional use was defined by the visualisation of 3 or more interruptions during the last night.

Leaks were considered relevant when non-intentional leaks were up to a mean of 24 L/min during the first 30 days above the fabricant's recommendation.

Persistent obstructive events were defined by an apnea–hypopnea index (AHI) detected by the software above a mean of 10/hours during the first 30 days.

Statistics

Data are presented as the mean (standard deviation [SD]) for continuous variables and as relative frequencies for categorical variables. Patients were divided into 2 groups according to their mean ADH to NIV on the first 30 days: 1) NIV ADH < 4 h/day, 2) NIV ADH > 4 h/day and 2 subgroups (SpO2 corrected defined as nocturnal SpO2<90% <5% night time (11) and SpO2 non corrected) in the NIV ADH > 4 h/day group. Loss of follow-up were excluded from analysis at day 30 due to an important lack of datas at day 30, especially in the in-hospital initiation subgroup. Emergency NIV initiation at hospital were excluded from the analysis for the calculation of the mean time between NIV prescription to NIV initiation.

Differences between groups and subgroups were assessed using a t test for continuous variables, a Chi2 test for categorical variables, and a McNemar test for paired categorical variables. The usual $p < 0.05$ threshold for significance was retained for all analyses. The statistical analysis was performed with GraphPad PRISM 5 (GraphPad Software, La Jolla, USA).

Ethics

This study was approved and registered by the Bordeaux hospital personal data officer (CHUBX2021RE0296) and complies with the protection of personal health data and the protection of privacy with the application framework provided for by article 65-2 of the amended Data Protection Act and the general data protection regulations of a personal nature.

This study was approved by the Bordeaux University Hospital Ethics Committee with the reference number CER-BDX-2022-19.

Results

NIV initiation

Between September 2017 and June 2021, 265 ALS patients had an indication for NIV with the same criteria as previously described. As reported in the flow chart (Figure 2), 81 were initiated during hospitalisation, and 184 were initiated at home.

Of the patients who have accepted to try NIV and had no counter-indication for home NIV initiation, all of them accepted the at-home NIV initiation model.

Patient characteristics are presented in Table 1. Briefly, patients had a mean age of 68±11 years and were predominantly male (63%). Half of them had bulbar symptoms , as determinated by the neurologist, and the mean time from symptom onset to NIV initiation was 29±25 months.

The subgroup of in-hospital NIV initiation patients present more severe respiratory impairment than at-home NIV initiation subgoup with respectively a mean FVC of 59,4% vs 71,6% (p<0,001), a mean percentage of nighttime with SpO2<90% of 23,2% vs 15,2% (p=0,023), and a mean PaCO2 of 6,21 vs 5,07 (p<0,001).

The mean time from NIV prescription to NIV initiation was 12,5 days for the total population, 8.7±6.5 days for at-home initiation subgroup vs 29±31.1 days for in-hospital initiation subgroup (p<0,001).

NIV parameters at initiation are presented in the supplemental material (SM2). IPAP, back-up and rise time were statistically significantly different between the two subgroups.

NIV parameters and data at 1 month (Table 2)

At 1 month, 153 patients (66%) were using NIV for more than 4 h a day, 80 (34%) were using it for less than 4 h a day (including 12 deaths, 4 total intolerance). 126 patient (70%) in the subgroup at-home NIV initiation vs 27 patients (52%) in the subgroup in-hospital initiation had an ADH >4h (p=0,018).

ALSFRS-R and FVC were significantly higher in adherent patients than in nonadherent patients (34±6.36 vs 30,5±8.21, p=0,003 and 71.5±21,5 vs. 62,9±18,2, p = 0.007 respectively). Proportion of initial nocturnal hypoxemia (defined by nocturnal SpO2 < 90% more than 5% of the recording time) was significantly higher in adherent patient vs non adherent patient (62 vs 50% p = 0.024).

We also found significant differences in NIV data at one month between adherent and nonadherent patients with a lower EPAP and IPAP in the nonadherent group (SM3).

As reported in table 3, At 1 month, NIV parameters were significatively higher for the in patients initiation group (IPAP 14±2,81 vs 11,8±1,98, p = <0,001, back up rate 14,2±1,46 vs 13,4±1,17 p= < 0,001). We also find difference in NIV monitoring with

a more fractional use (13 (31) vs 10 (6), p = < 0, 001), a higher proportion of relevant leaks and obstructive events (6(14) vs 4(2) p = < 0,001, and 11,1±10,6 vs 5,48±8,77, p= <0,001, respectively) for the in patients group.

NIV efficiency at 1 month

Nocturnal oximetry under NIV was performed only on nocturnal adherent patients of at-home NIV initiation patients. In the subgroup of patients with an ADH of 4 hours or more (126 patients), NIV normalised nocturnal oximetry occurred in 99 (79%) patients (Table 4), this represent 55% of the total at-home NIV initiation cohort.

Twenty-one patients (17% of the adherent patients) still had pathological nocturnal oximetry. Their characteristics at initiation are presented in the supplemental material 4 (SM4), and show a significantly higher body mass index (BMI) (26 vs. 24, p = 0,028) and a significantly higher mean nocturnal time percentage with SpO2 < 90% (21% vs. 15.9, p = 0.041). At day 30, they had a significantly higher EPAP (7.75 vs. 6.75, p = 0.006), and a higher but non significant AHI (10.1 vs. 5.63, p = 0,066), and we did not find any difference in the monitoring at D30 (Table 4).

Discussion

Here, we report original data from a real-life practices of at-home NIV initiation in 184 ALS patients with a PaCO2 under 6,1KPa and 81 patients with in-hospital NIV initiation, showing in the subgroup home NIV initiation a very short delay in NIV instauration and a good nocturnal hypoxemia correction in adherent patients, even if we report 30% of non adherent.

One of the main results was the short delay between NIV prescription and NIV initiation in the sub group at-home NIV initiation. Decreasing the time between NIV prescription and NIV initiation is one of the main goals of NIV initiation in ALS patients. Sherrs and col. have shown that shortening the delay between prescription and initiation tends to reduce mortality in ALS patients, (14). In a recent study performed by Van den Biggelaar, their delay times were 19.9 days for home initiation and 31.2 days at the hospital, (8). We have reported a mean time from NIV requirement assessment to home initiation of 8.7±6.5 days and 29±31.1 days at the hospital. The problem of bed availability in hospitals is recurrent, a phenomenon exacerbated during the COVID period. Using this at-home process, we didn’t have a decrease in NIV initiation during the COVID period. This study shows that at-home NIV initiation can be a good option to accelerate the implementation of NIV, especially in ALS patients with quick disease evolution.

Our data show that at-home NIV initiation is possible, accepted by all patients, that a large majority of patients (70%) are adherent to the therapy and that NIV

allows the correction of nocturnal hypoxemia.

Unfortunately, we also had 34% of the whole cohort who did not support NIV for more than 4 hours per day, .30% in the subgroup at-home NIV initiation and 48% in the subgroup in- hopital NIV initiation. This higher rate of nonobservant patients in the in-hospital initiation subgroup should be moderate by the fact that patient were more severe and the mortality at day 30 (consider as non adherent patient in our analysis) is much higher in the in hospital initiation subgroup. Of the total 184 at-home initiations, only 4 did not tolerate NIV at all. This is a higher rate of NIV initiation failure than can be described in the literature. Nuria Gonzalez Calazada reported an NIV failure rate of 15%, (15) ; however, in that study, patients were mainly initiated at the hospital, at a more advanced stage with a mean FVC of 51% compared to 71,6% in our cohort. In most studies evaluating at-home NIV initiation, the rate of NIV initiation failure has not been reported, (8, 16). Enrica Bertella reported 22% at-home NIV initiation intolerance (vs. 2.1% in our study) and 32% of patients who did not support NIV more than 4 h/day at 3 months, (17). These results should also be moderated by another study that reported a level of NIV use < 4 h at one month of 48%, (18). Concerning NIV ADH, we found that adherent patient had a significant higher nocturnal time percentage with SpO2<90% at initiation that suggest nocturnal symptomatology is related to tolerance and therefore observance of NIV.

Initially, we thought that very early initiation would be a negative predictive factor of at-home NIV initiation success, but adherent patients seemed to be at an earlier stage (FVC and ALSFRS score significantly higher).In the literature, Vitacca et al. did not find any ADH difference between early and late NIV initiation, (19). Although we did not find presence of bulbar symptoms at NIV initiation as a negative factor of NIV success, presence of bulbar symptoms was defined by clinical consideration by the neurologists.–We did not have an objective evaluation such as the Norris bulbar score to attest to this clinical condition, nor re-evaluation over time of this bulbar degradation which has a major impact on NIV tolerance (4).

Concerning NIV parameters, as expected the hospital patients were more severe and therefore their ventilation parameters were higher at initiation and at 1 month.

At home, we started the initiation with a low level of inspiratory pressure to facilitate the acceptance of NIV. In our experience, as recommended by new French recommendations, (20) a very gradual increase of the pressures allowed by a long adaptation time and close telemonitoring has permitted a very low total intolerance percentage. The initial objective was to find the right compromise between efficacy and tolerance. On day 30, we did not manage to obtain pressure support as high as expected and similar to what is described in the literature, (8, 11, 19) and these parameters might be too low for this kind of population even though it could be explained by an early NIV initiation which led us to promote treatment acceptation in this quite low symptomatic population. Although nocturnal oximetry was normalised in 79% of cases in adherent patients, we did not evaluate nocturnal hypoventilation

by capnography, asynchrony, or proportion of the capture cycle, which could estimate the underassistance of NIV. These measures might result in a less aggressive strategy during at-home NIV initiation compared to hospital initiation and should be taken into account in our future practice and future studies.

But this less aggressive strategy could also have a negative impact on NIV adherence because on day 30 in the subgroup of non-adherent patients, on one hand, mean IPAP is significantly lower, and on the other hand, RR monitoring is significantly higher. That would suggest non-adherent patients could be under-assisted. It is difficult to conclude because the question is whether patients are under-assisted because of NIV tolerance or patients are non-adherent due to under-assistance?

We did not report the blood gas results at 1 month due to the fact that if patients were not hypercapnic at NIV initiation, blood gases were not routinely measured at 1 month but at the next visit in the Bordeaux ALS center (mean each 4 months).

In at-home NIV initiation subgroup, NIV efficiency (54% of patients who had a normalised night oximetry) was slightly higher compared to results from Gonzalez-Bermejo and col. who reported that 49% of patients had normalised night oximetry at 1 month, (11). The incidence rates of leaks and obstructive events were also very low and might be explained by the telemonitoring carried out during the whole initiation period and the several setting adaptations made at each step of the NIV initiation protocol. Those results are supported by the fact that in the in patients subgroup, at 1 months there is a higher rate of leaks and obstructive events, but it is difficult to conclude as patients are at a more severe stage of their disease.

At D30, in at-home NIV initiation subgroup, 17% of adherent patients still had non corrected nocturnal SpO2; they had a higher BMI, which was associated with a significantly higher EPAP and a higher but not significant AHI. This may suggest more obstructive events, and optimal EPAP not reached at D30. In those cases, polygraphy under NIV should be discussed to discriminate apneas with or without decrease of neural drive improve.

One of the main limitation to take into account is the monocentric retrospective nature of the study, with all associated biases such as selection biais–(we had no information for patients who had totally refused NIV initiation), and memorization bias with a significant number of loss of follow-up at day 30, especially at the in-hospital NIV initiation subgroup.

The other main limitation of this study is the lack of specific data on bulbar involvement. As previously reported, bulbar involvement is a major limiting factor in tolerance and adherence to NIV (4) and apart from a clinical evaluation by the neurologist at the initiation of NIV, we have no quantifiable evaluation or data on the evolution of the involvement.

Another limitation is the absence of long-term assessment of ADH and efficiency (> 1 month); indeed, NIV ADH might change during the follow-up, as reported by Vitacca and col, with 10% of ALS patients being at risk of reducing their ADH, (19). Progressive NIV adaptation over 1 month is just the beginning of treatment. The first month of NIV is a very important period, especially for immediate acceptance and ADH, but setting modifications must be continued thereafter.

As retrospective study on a real-life process, we were not able to provide information about suppementary interventions during this one-month NIV initiation process (patient phone calls or tecnicians' home visits) even if, to our opinion, there were no substantially more interventions than there were with the anterior in-patient model.

Moreover, Van Den Biggelaar and colleagues have shown significant cost savings when NIV was initiated at home, and it would have been interesting to add a global cost analysis to our study to help perpetuate this type of patient care, (8).

And lastly the Bordeaux ALS center has an active cohort of 350 patients from all the Nouvelle Aquitaine region (population of 6 million) with rural, suburban and urban zones. The radius of action to perform theses at-home NIV initiation processes was 200 kilometres from the Bordeaux hospital, so this model may be generalized in other hospital.

Conclusion

To our knowledge, we have reported the largest cohort of ALS patients with at-home NIV initiation. Our results show that NIV can be initiated at home very quickly, but patients need to be closely monitored because 1 out of 5 did not tolerate NIV at 1 month. When adherent at-home NIV initiation combined with telemonitoring is not efficient, the strategy must include close follow-up for more than one month to adapt NIV parameters in order to achieve optimum settings.

Acknowledgments

Thomas Réginault is the guarantor of the content of the manuscript, including the data and analysis, taking responsibility for the integrity of the work as a whole, from incepton to published article.

TR, BB, PW and LG were involved in the conception and design, acquisition of data, analysis, interpretation of data, drafting of the work or revising. SM, GLM and OP were involved in the conception and design, interpretation of data, drafting of the work or revising.

Funding from the Bordeaux University Foundation was received to facilitate the at-home NIV initiation.

We would like to thank Mrs. S. Bonnabaud and B. Dupiol from Bordeaux ALS center for her precious coordination help. We appreciate the effort of all partners (ALIZE SANTE, AVAD, SOS O2 and VIVISOL) involved in this study.

References

1. Arnulf I, Similowski T, Salachas F, Garma L, Mehiri S, Attali V, et al. Sleep disorders and diaphragmatic function in patients with amyotrophic lateral sclerosis. Am J Respir Crit Care Med. 2000 Mar;161(3 Pt 1):849–56.

2. Gil J, Funalot B, Verschueren A, Danel-Brunaud V, Camu W, Vandenberghe N, et al. Causes of death amongst French patients with amyotrophic lateral sclerosis: a prospective study. Eur J Neurol. 2008 Nov;15(11):1245–51.

3. HAS 2006. Prise en charge des personnes atteintes de Sclérose latérale amyotrophique. Revue neurologique. 2006;162(Hs2) : 4s188-4s99.

4. Bourke SC, Tomlinson M, Williams TL, Bullock RE, Shaw PJ, Gibson GJ. Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial. Lancet Neurol. 2006 Feb;5(2):140–7.

5. Morelot-Panzini C, Bruneteau G, Gonzalez-Bermejo J. NIV in amyotrophic lateral sclerosis: The “when” and “how” of the matter. Respirology. 2019;24(6):521–30.

6. Rabec C, Gonzalez-Bermejo J, Arnold V, Rouault S, Gillet V, Perrin C, et al. Initiation of

domiciliary non-invasive ventilation: proposals of the Casavni working party. Rev Mal Respir. 2010 Oct;27(8):874–89.

7. HAS.Ventilation mécanique à domicile. Dispositifs médicaux et prestations associées pour traitement de l'insuffisance respiratoire. 20 novembre 2012: 59-63.

8. Van den Biggelaar RJM, Hazenberg A, Cobben NAM, Gaytant MA, Vermeulen KM, Wijkstra PJ. A Randomized Trial of Initiation of Chronic Noninvasive Mechanical Ventilation at Home vs In-Hospital in Patients With Neuromuscular Disease and Thoracic Cage Disorder: The Dutch Homerun Trial. Chest. déc 2020;158(6):2493-501.

9. Georges M, Attali V, Golmard JL, Morélot-Panzini C, Crevier-Buchman L, Collet JM, et al. Reduced survival in patients with ALS with upper airway obstructive events on non-invasive ventilation. J Neurol Neurosurg Psychiatr. 2016 Oct;87(10):1045–50.

10. Gonzalez J, Sharshar T, Hart N, Chadda K, Raphaël JC, Lofaso F. Air leaks during mechanical ventilation as a cause of persistent hypercapnia in neuromuscular disorders. Intensive Care Med. 2003 Apr;29(4):596–602.

11. Gonzalez-Bermejo J, Morelot-Panzini C, Arnol N, Meininger V, Kraoua S, Salachas F, et al. Prognostic value of efficiently correcting nocturnal desaturations after one month of non-invasive ventilation in amyotrophic lateral sclerosis: a retrospective monocentre observational cohort study. Amyotroph Lateral Scler Frontotemporal Degener. 2013 Sep;14(5–6):373–9.

12. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, Andersen PM, Abrahams S, Borasio GD, De Carvalho M, Chio A, Van Damme P, *et al.* **EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) – revised report of an EFNS task force.Eur J Neurol, 19 (2012), pp. 360-375**

13. **Janssens JP, Borel JC, Pépin JL, Group S. Nocturnal monitoring of home non-invasive ventilation: the contribution of simple tools such as pulse oximetry, capnography, built-in ventilator software and autonomic markers of sleep fragmentation. Thorax. (2011) 66:438–45.**

14. Sheers N, Berlowitz DJ, Rautela L, Batchelder I, Hopkinson K, Howard ME. Improved survival with an ambulatory model of noninvasive ventilation implementation in motor neuron disease. Amyotroph. Lateral Scler. Frontotemporal Degener. 2014; 15: 180–4.

15. Gonzalez Calzada N, Prats Soro E, Mateu Gomez L, Giro Bulta E, Cordoba Izquierdo A, Povedano Panades M, et al. Factors predicting survival in amyotrophic lateral sclerosis patients on non-invasive ventilation. Amyotroph Lateral Scler Frontotemporal Degener. 2016;17:337–42.

16. Chatwin M, Hawkins G, Panicchia L, Woods A, Hanak A, Lucas R, et al. Randomised crossover trial of telemonitoring in chronic respiratory patients (TeleCRAFT trial). Thorax 2016;71:305–311.

17. Bertella E, Banfi P, Paneroni M, Grilli S, Bianchi L, Volpato E, et al. Early initiation of night-time NIV in an outpatient 46 setting: a randomized non-inferiority study in ALS patients. European journal of physical and rehabilitation medicine. 2017;53(6):892-899.

18. Jackson CE, Heiman-Patterson TD, Sherman M, Daohai YU, Kasarskis EJ, NUTRITION/NIV STUDY GROUP. Factors associated with Noninvasive ventilation compliance in patients with ALS/MND. Amyotroph Lateral Scler Frontotemporal Degener. 2021;22(sup1):40-47.

19. Vitacca M, Banfi P, Montini A, Paneroni M. Does timing of initiation influence acceptance and adherence to NIV in patients with ALS? Pulmonology, 26: 45-48.

20. Georges M, Perez T, Rabec C, Jacquin L, Finet-Monnier A, Ramos C, et al. Proposals from a French expert panel for respiratory care in ALS patients. Respir Med Res. 3 mars 2022;81:100901.

TABLE 1

Population characteristics

Patient characteristics at initiation	Total	At home patients	In patients	P value
Anthropometric data				
Patients	265	184	81	
Age (yr)	68±11	68±11	69±9	0.577
Male	157(63)	114 (62)	43(65)	0.645
BMI (kg/m2)	24±4	24±4	23±4	0.141

Smoking greater than 20 pack-years		23(9)	16 (9)	7(11)	0.684
Neurological assessment					
ALS-FRS-R score		33±7	33±7	33±7	0.854
Time from symptoms onset to NIV initiation (months)		29±25	29±24	27±26	0.521
Time from diagnostic to NIV initiation (months)		15±18	17±20	10±13	**0.016**
Bulbar symptoms at NIV initiation		131(53)	94(51)	37(56)	0.513
Gastrostomy in the follow-up		13(5)	9(5)	4(6)	0.714
Frontotemporal dementia		19(8)	15(8)	4(6)	0.582
Respiratory assessment					
FVC (L)		2.32±0.89	2.40±0,84	2.07±0.10	**0.042**
FVC (%)		68.9±20.9	71.60±19,97	59.4±21.7	**<.001**
Peak flow (L/s)		4.59±2.02	4.75±1,98	4.01±2.10	0.066
Peak flow (%)		63.4±24.8	65.65±24,65	54.8±23.7	**0.017**
MIP (cmH2O)		44.4±23.9	44.26±23,96	45.1±24	0.877
SNIP (cmH20)		45.9±20.8	47.88±23,89	43.2±17.5	0.692
SpO2 nighttime < 90% (%)		17±21.4	15.16±18,59	23.2±28.1	**0.023**
SpO2 < 90% more than 5% of nighttime		142(68)	114(62)	28(58)	0.118
SpO2 min.		80.4±7.85	80.7±7.77	79.4±8.12	0.345
SpO2 mean		91.9±2.36	92.1±1.98	91.3±3.29	0.070
ODI		9.63±10.1	9.25±8.92	10.9±13.4	0.357
PaCO2 (Pka)		5.39±1.04	5.07±0,58	6.21±1.44	**<.001**
NIV initiation criteria					
Clinical signs +	PCO2>6.1 KPa	34(13)	0	34(42)	
	FVC < 80% only	84(32)	65(35)	19(24)	0.056
	SpO2 < 90%, time > 5% only	74(28)	72(39)	2(2)	**<.001**
	Both FVC < 80% and SpO2 < 90%, time > 5%	42(16)	42(23)	0(0)	**<.001**

	SNIP < 60 cmH2O	1(0)	1(1)	0(0)	0.506
	Other	30(11)	4(2)	26(32)	**<.001**
Time from NIV requirement assessment to initiation (Days)		12.5±16.5	8.72±6,47	29±31.1	**<.001**

Data are presented as mean±sd and n (%). BMI: body mass index; ALS-FRS-R: ; NIV: noninvasive ventilation; FVC: forced vital capacity; MIP: maximal inspiratory pressure; SNIP: sniff nasal inspiratory pressure; SpO2: pulsed oxygen saturation; ODI: oxygen desaturation index

TABLE 2

Population characteristics at NIV initiation depending on adherence assessment at Day 30

Patient characteristics at initiation	**Total**	**ADH>4 h**	**ADH<4 h**	**P value**
Anthropometric data				
Patients	233	153(66)	80(34)	
Age (yr)	68±11	68.1±10.6	68±11.2	0.907
Male	148(63)	101(66)	47(59)	0.274
BMI (kg/m2)	24±5	24.4±4.64	23±4.13	**0.028**
Smoking greater than 20 pack-years	21(9)	12(7.8)	9(11)	0.381
Initiation modality				
At-home	181(78)	126(82)	55(69)	**0.018**
In-hospital	52(22)	27(18)	25(31)	**0.018**
Time from NIV requirement assessment to initiation (Days)	12.3±16.6	12.6±19.1	11.5±10.2	0.647
Died before the 30th day	12(5)	0(0)	12(15)	
Neurological assessment				

ALS-FRS-R score	32.9±7.28	34.3±6.36	30.5±8.21	**0.003**
Time from symptoms onset to NIV initiation (months)	28.2±24.1	28.9±24.7	26.6±22.9	0.519
Time from diagnostic to NIV initiation (months)	14.9±18.6	15.3±18.2	14±19.5	0.623
Bulbar symptoms at NIV initiation	122(52.6)	75(49)	47(59)	0.173
Gastrostomy in the follow-up	13(5.6)	8(5)	5(6)	0.747
Frontotemporal dementia	18(7.7)	11(7)	7(9)	0.672
Respiratory assessment				
FVC (L)	2.33±0.871	2.4±0.842	2.17±0.921	0.108
FVC (%)	68.7±20.9	71.5±21.5	62.9±18.2	**0.007**
Peak flow (L/s)	4.58±1.99	4.8±2.04	4.08±1.81	**0.036**
Peak flow (%)	63.2±24.7	65.6±25.3	57.6±22.5	0.053
MIP (cmH2O)	44.7±23.7	46.6±22.8	40.2±25.6	0.178
SNIP (cmH20)	45.4±22.4	56±24.4	34.8±15.7	0.104
SpO2 nighttime < 90% (%)	17.1±21.3	17.8±20.6	15.8±22.6	0.531
SpO2 < 90% more than 5% of nighttime	135(68.2)	95(62)	40(50)	**0.024**
SpO2 min.	80.4±7.88	80.8±8.33	79.6±7.01	0.317
SpO2 mean	91.9±10.3	91.8±2.43	92.1±2.37	0.468
ODI	9.91±10.3	9.49±11.9	10.6±11.9	0.477
PaCO2 (KPa)	5.36±1	5.39±1.04	5.29±0.9	0.489

Data are presented as mean±sd and n (%). ADH: adherence; BMI: body mass index; NIV: noninvasive ventilation; FVC: forced vital capacity; MIP: maximal inspiratory pressure; SNIP: sniff nasal inspiratory pressure; SpO2: pulsed oxygen saturation; ODI: oxygen desaturation index

TABLE 3

NIV parameters and monitoring at Day 30 for the whole cohort

NIV parameters and monitoring at Day 30 for the whole cohort		**Total**	**At-home patients**	**In patients**	**P value**
NIV Parameters	N	221	179	42	
	IPAP (cmH20)	12.2±2.31	11.8±1.98	14±2.81	**<.001**
	EPAP (cmH20)	6.7±1.49	6.66±1.48	6.85±1.53	0.465
	Back up RR (acts/min)	13.5±1.25	13.4±1.17	14.2±1.36	**<.001**
	Rise Time (ms)	428±138	439±134	372±149	**0.007**
	Trigger (L/min)	5.89±0.88	5.97±0.62	5.53±1.62	**0.007**
	Cycling (%IPF)	23.4±5.67	23.1±5.24	25±7.66	0.082
	Ti min (s)	0.664±0.640	0.644±0.570	0.769±0.922	0.293
	Ti max (s)	1.78±0.305	1.80±0.289	1.70±0.371	0.078
NIV Monitoring					
	Days (n)	31.4±10.1	30.6±7.07	35.3±18.2	**0.009**
	Days without use (n)	4.26±8.66	3.88±7.01	5.95±13.8	0.172
	Patients with fractional use (n)	23(10)	10(6)	13(31)	**<.001**
	NIV use (hr)	6.15±3.23	5.99±2.87	6.85±4.48	0.126
	Vt (ml)	439±118	427±89.7	490±193	**0.002**
	RR (acts/min)	16.8±3.13	16.5±2.73	18±4.32	**0.007**
	Leaks (L/min)	5.57±15.1	3.69±10.7	13.7±25.6	**<.001**

Leaks > 24 L/min (n)	10(5)	4(2)	6(14)	**<.001**
AHI	6.52±9.36	5.48±8.77	11.1±10.6	**<.001**
AHI > 10 (n)	41(19)	27(15)	14(33)	**0.004**

12 death before day30 were excluded from analysis. Data are presented as mean±sd and n (%). NIV: noninvasive ventilation; ADH: adherence; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; RR: respiratory rate; IPF: inspiratory peak flow ; Vt: tidal volume; Ti: inspiratory time; AHI: apnea hypopnea index

TABLE 4

NIV parameters and monitoring at Day 30 for adherent patients of at-home NIV initiation subgroup

		D30	**Corrected SpO2**	**No corrected SpO2**	**P value**
NIV	N	126	99(79)	21(17)	
Parameters	IPAP (cmH20)	12.1±1.97	12±1.9	12.8±2.29	0.118
	EPAP (cmH20)	6.86±1.52	6.75±1.47	7.75±1.37	**0.006**
	Back up RR (acts/min)	13.4±1.17	13.5±1.15	13.3±1.03	0.531

	Rise Time (ms)	444±134	447±140	439±115	0.602
	Trigger (L/min)	5.96±0.57	5.95±0.64	6±0	0.736
	Cycling (%IPF)	23±5.39	22.7±5.47	24±5.53	0.345
	Ti min (s)	0.674±0.67	0.698±0.7	0.6±0.16	0.566
	Ti max (s)	1.8±0.3	1.80±0.3	1.81±0.31	0.862
	Face mask	121 (96)	96 (97)	18 (90)	0.156
NIV	Days (n)	29.5±3.07	29.6±3.18	28.6±2.58	0.169
Monitoring	Days without use	1.57±1.57	1.55±3.45	0.286±0.72	0.099
	Patients with fractional use	3 (2)	2 (2)	1 (5)	0.444
	NIV use (hr)	7.58±1.50	7.45±1.48	8.17±1.36	**0.043**
	Vt (ml)	426±88	420±80.9	456±113	0.099
	RR (acts/min)	16.2±5.55	16.3±2.62	15.4±1.79	0.131
	Leaks (L/min)	4.04±12.2	3.98±13.2	4.74±8.66	0.805
	Leaks > 2 4 L/min	4 (3)	3 (3)	1 (5)	0.656
	AHI	6.33±9.71	5.63±8.38	10.1±14.9	0.066
	AHI > 10	24 (19)	16 (16)	6 (30)	0.146
SpO2	SpO2 nighttime < 90 (%)	3.62±7.01	1.38±1.56	14.2±11.8	**<.001**
assessment					

There were 6 missing data. Data are presented as mean±sd and n (%). NIV: noninvasive ventilation; SpO2: pulsed oxygen saturation; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; RR: respiratory rate; IPF: inspiratory peak flow; Ti: inspiratory time; Vt: tidal volume; AHI: apnea hypopnea index

Figure legends

Figure 1. At-home NIV initiation protocol

Legend: this figure shows the five steps that compose the at-home NIV initiation with a nonexhaustive description of the actions performed by the different actors.

Figure 2. Flow-chart of patients included between september 2017 and june 2021

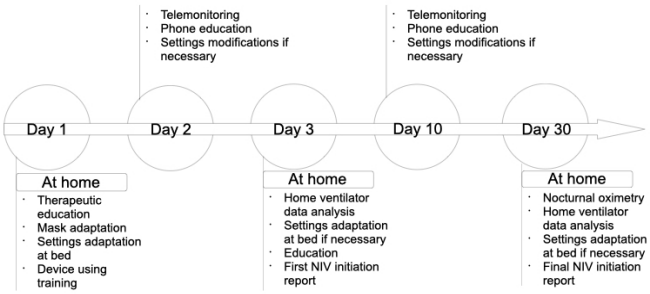
Conflict of Interest:

Thomas Réginault reports support for the present manuscript from Bordeaux University Foundation; travel support from Vivisol; personal fees from Zéphyr paramed; outside the submitted work.

Benoit Bouteleux reports personal fees from Zéphyr paramed, outside the submitted work.

Philippe Wibart reports support for the present manuscript from Bordeaux University Foundation; personal fees from Zéphyr paramed; outside the submitted work.

All other authors have nothing to disclose.


Telemonitoring
Phone education
Settings modifications if necessary
Telemonitoring
Phone education
Settings modifications if necessary
Day 1
Day 2
Day 3
Day 10
Day 30
At home
Therapeutic education
Mask adaptation
Settings adaptation at bed
Device using training
At home
Home ventilator data analysis
Settings adaptation at bed if necessary
Education
First NIV initiation report
At home
Nocturnal oximetry
Home ventilator data analysis
Settings adaptation at bed if necessary
Final NIV initiation report

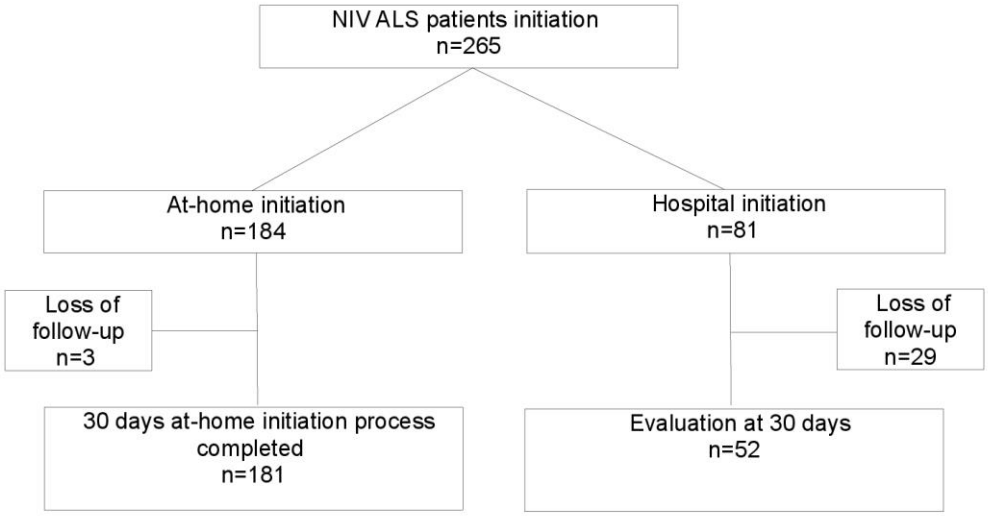


Figure 2 – Flow chart of patients included between 09/2017 and 06/2021

Supplemental material 1 (SM1): Progress of the at home NIV initiation protocol

Day1 : at home, the specialized physiotherapist gives education on the ALS pathology and its consequences. The ventilator, humidifier, mask, and corresponding telemonitoring devices were presented to the patients and their families by both the specialized physiotherapist and the home care assistance technician. The first use of the ventilator was done under supervision of the specialized physiotherapist for titrating the therapy as previously described. Patient was in supine position.

Day 2 : after telemonitoring checking, the physiotherapist makes a call to the patient to debrief the first night. Parameters could be modified if necessary.

Day 3 : at home, the physiotherapist gives once again education on the use of the material. They check the high resolution data from the device and elaborate a report. Adjustment of the settings are made if necessary.

Day 10 : after telemonitoring checking, the physiotherapist makes a call to the patient to debrief. Parameters could be modified if necessary. The home care assistance can be solicited to adjust a new mask or give technical informations if necessary.

Day 30 : at home, the specialized physiotherapist checks the high resolution data and the nocturnal oximetry from the device and elaborate an expert report. Adjustment of the settings are made if necessary.

During the 1-month of initiation, patients were able to contact by phone at any time the multidisciplinary care team (Home care assistance, coordination nurse, specialized physiotherapist), to receive support for any reason related to NIV and their clinical condition.

Supplemental material 2 (SM2) : NIV parameters at initiation

		Total	Out patients	In patients	P value
NIV Parameters	N	265	184	81	
	IPAP (cmH20)	11.9±2.38	11.36±1,94	13.5±2.79	**<.001**
	EPAP (cmH20)	6.44±1.36	6.36±1,32	6.68±1.46	0.108
	Back up RR (acts/min)	13.3±1.32	13.07±1,24	14.1±1.27	**<.001**
	Rise time (ms)	425±132	437.91±128,82	378±134	**0.004**
	Trigger (L/min)	5.9±0.85	5.95±0,47	5.72±1.72	0.078
	Cycling (%IPF)	23.8±5.35	23.49±4,78	25.1±7.54	0.096
	Ti min (s)	0.59±0.14	0.59±0,13	0.59±0.17	0.960
	Ti max (s)	1.76±0.3	1.77±0,28	1.71±0.41	0.228
	Face mask	245(100)	183(99)	62(100)	0.561

Data are presented as mean±sd and n (%).NIV: noninvasive ventilation; ADH: adherence; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; RR : respiratory rate; IPF: inspiratory peak flow ; Ti: inspiratory time

Supplemental material 3 (SM3) : NIV parameters and monitoring at Day 30 for the whole cohort

NIV parameters and monitoring at Day 30 for the whole cohort		Total	ADH>4 h	ADH<4 h	P value
NIV Parameters	N	221	153	78	
	IPAP (cmH20)	12.2±2.31	12.5±2.34	11.4±2.07	**<.001**
	EPAP (cmH20)	6.7±1.49	6.89±1.52	6.28±1.33	**0.005**
	Back up RR (acts/min)	13.5±1.25	13.6±1.21	13.3±1.33	0.107
	Rise Time (ms)	428±138	434±139	414±138	0.333
	Trigger (L/min)	5.89±0.88	5.88±0.826	5.94±0.994	0.639
	Cycling (%IPF)	23.4±5.67	23.3±5.78	23.5±5.44	0.816
	Ti min (s)	0.664±0.640	0.7±0.76	0.583±0.124	0.220
	Ti max (s)	1.78±0.305	1.78±0.291	1.78±0.338	0.932
NIV Monitoring					
	Days (n)	31.4±10.1	31.7±9.5	30.9±11.4	0.609
	Days without use (n)	4.26±8.66	1.80±6.36	9.95±10.5	**<.001**
	Patients with fractional use (n)	23(10)	7(4.6)	16(21)	**<.001**
	NIV use (hr)	6.15±3.23	7.9±1.96	1.97±1.18	**<.001**
	Vt (ml)	439±118	442±122	430±108	0.508
	RR (acts/min)	16.8±3.13	16.5±3.04	17.5±3.27	**0.038**
	Leaks (L/min)	5.57±15.1	5.84±16.7	4.82±9.25	0.668
	Leaks > 24 L/min (n)	10(5)	8(5.2)	2(2.5)	0.636
	AHI	6.52±9.36	6.86±9.74	5.54±8.22	0.375
	AHI > 10 (n)	41(19)	32(20)	9(12)	0.501
SpO2 assessment	SpO2 nighttime < 90 (%)	3.58±7.7	3.58±6.96	3.58±10.3	0.999

12 death before day30 were excluded from analysis. Data are presented as mean±sd and n (%). NIV: noninvasive ventilation; ADH: adherence; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; RR: respiratory rate; IPF: inspiratory peak flow ; Vt: tidal volume; Ti: inspiratory time; AHI: apnea hypopnea index

There were 7 missing data. Data are presented as mean±sd and n (%). ADH: adherence; SpO2: pulsed oxygen saturation; BMI: body mass index; NIV: noninvasive ventilation; ALSFRS-R: revised amyotrophic lateral sclerosis functional rating scale; FVC: forced vital capacity; SNIP: sniff nasal inspiratory pressure.

Supplemental material 4 (SM4) : patients characteristics at initiation in sub group ADH > 4h

		Total (ADH > 4h)	**Corrected SpO2**	**No corrected SpO2**	**P value**
Anthropometric data					
Patients; no(%)		127	99	21	
Age (yr)		68(±11)	68(±11)	67(±10)	0.698
Male; no(%)		83(65%)	66(67)	15(71)	0.672
BMI		24(±5)	24(±5)	26(±5)	**0.028**
Neurological assessment					
Time from diagnostic to NIV initiation (months)		17(±20)	18.8(±21)	13(±13)	0.240
Bulbar onset; no(%)		64(51)	51(52)	11(52)	0.977
Frontotemporal dementia; no(%)		8(6)	5(5)	3(14)	0.123
ALSFRS-R		34,2(±6.48)	34,2(±6.06)	34(±8.83)	0,917
Respiratory assessment					
FVC (L)		2.47(±0,82)	2.43(±0,79)	2.73(±0,93)	0.159
FVC (%)		74.03(±20,47)	72.9(±19.1)	77.2(±19)	0.369
SpO2 night time < 90% (%)		16.27(±18,77)	15.9(±19.1)	21(±18.9)	**0.041**
SpO2 < 90% more than 5% of nighttime; no(%)		83(75%)	62(73%)	18(95%)	0.301
NIV initiation criteria					
NIV Initiation criteria; no(%)					
Clinical signs +	FVC < 80% only	42(33%)	36(37)	3(14)	**0.050**
	SpO2 < 90%, time > 5% only	52(41%)	39(39)	11(53)	0.273
	Both FVC < 80% and SpO2 < 90%, time > 5%	31(25%)	23(23)	7(33)	0.332
	SNIP < 60cmH2O	0(0%)	0(0)	0(0)	
	Other	1(1%)	1(1)	0(0)	0.644
Time from NIV requirement assessment to home initiation (Days)		8.65(±6,47)	8.94(±6,77)	8.71(±5.64)	0.888