At-home noninvasive ventilation initiation with telemonitoring in amyotrophic lateral sclerosis patients: a retrospective study

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Shareable abstract (@ERSpublications)
At-home NIV initiation in ALS patients with close telemonitoring is a good option to provide rapid and highly efficient access to NIV. At 1 month, 69% of the participants were observant and their nocturnal oximetry was corrected to 78%. https://bit.ly/3OxzRX8

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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 of exploring an at-home initiation process. Here, we report data from our NIV initiation cohort of ALS patients. Could our at-home NIV initiation process with telemonitoring in ALS patients be an efficient solution for adherence and nocturnal hypoxaemia correction?

Methods We performed a retrospective analysis of data collected from 265 ALS patients treated at the Bordeaux ALS Centre for whom NIV initiation was 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 of nocturnal hypoxaemia correction.

Results At 30 days, NIV adherence (mean >4 h·day^{-1}) was 66% of the total population, 70% of the at-home NIV initiation subgroup and 52% of the in-hospital NIV initiation subgroup. Nocturnal hypoxaemia correction was observed in 79% of adherent patients in the at-home NIV initiation subgroup. Mean delay of NIV prescription and at-home NIV initiation was 8.7 days (+/−6.5) *versus* 29.5 days in 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 the benefits of at-home NIV initiation is welcomed, especially to evaluate long-term efficiency and global cost analysis.

Introduction

Amyotrophic lateral sclerosis (ALS) is one of the most common neurodegenerative conditions in adult life. ALS induces 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) has been the reference treatment for ALS-related respiratory failure [3]. NIV relieves dyspnoea, improves sleep, improves 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 centre and if the patient can be rapidly hospitalised in the case of failure [7].

This at-home NIV initiation practice was illustrated by a Dutch randomised controlled trial [8] comparing hospital *versus* at-home NIV initiation by a nurse on patients with all kinds of pulmonary restrictive disorder, which showed no difference in nocturnal hypoxaemia correction.

Inpatient NIV initiation does not seem to be the best solution to promote 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 inpatient 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 1 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 report here our own experience regarding NIV initiation in ALS patients with a 30-day at-home NIV initiation process with telemonitoring in order to evaluate NIV adherence and NIV efficiency (defined by a correction of nocturnal hypoxaemia under NIV as an indirect criterion for hypoventilation).

Methods

Patients

This was a retrospective monocentric study. Data were collected between September 2017 and 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: vital capacity <80%, nocturnal peripheral oxygen saturation (S_{pO_2}) <90%, time >5% (French recommendations [3])), sudden nasal inspiratory pressure (SNIP) <40 cmH_2O, maximum inspiratory pressure (MIP) <60cmH_2O) or hypercapnia.

Some patients refused to try NIV. For the others, home NIV initiation was then proposed, except in those with an arterial carbon dioxide tension (P_{aCO_2}) above 6.1 kPa, those without a caregiver and those who were already hospitalised and for whom NIV was initiated in the hospital.

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

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 a respiratory assessment before NIV initiation at a stable state. It was performed in the same hospital lab during the Bordeaux ALS Centre consultation and included plethysmography, spirometry, MIP measurement and arterial blood gases assessment. Nocturnal oximetry was performed at home or during hospitalisation. Some emergency patients were not able to have a respiratory assessment beforehand.

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) device with an integrated internal battery was used.

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

The ventilator was set up in the spontaneous timed mode with pressure support (PS) titrated to correct clinically spontaneous respiratory effort. PS was set initially at 4 cmH_2O and was gradually adapted according to patient tolerance and comfort to relieve dyspnoea and respiratory effort. In most cases, expiratory positive airway pressure (EPAP) was initially set at 4 cmH_2O and could be increased to 8 cmH_2O in the event of known obstructive events. Inspiratory triggering, pressurisation and inspiratory to expiratory cycling were adapted to obtain good clinical synchronisation and patient comfort.

Progress of the at-home NIV initiation protocol

In accordance with the French National Authority for Health recommendations of 2012 [7], a 30-day at-home NIV initiation protocol (figure 1) was performed by a specialised physiotherapist team in collaboration with the neurologists and the resuscitation consultant of the Bordeaux ALS Centre.

There were five interventions, which are described in the supplemental material (SM1), including three at-home visits and two teleconsultations with telemonitoring. Costs of physiotherapist actions were supported by home healthcare companies, which usually receive a reimbursement of €62.16 per week of NIV treatment <12 h by the French social security service.

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

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

On day 1, 3 and 30, NIV parameters were adjusted to improve respiratory comfort during at-home physiotherapist visits. Inspiratory positive airway pressure (IPAP) and EPAP were increased by 1 or 2 cmH_2O at each step, following patient tolerance and analysis of obstructive events using the ResScan® (ResMed®, Australia) software, to obtain an apnoea–hypopnoea index (AHI) lower than 10, a respiratory rate <20 cycles per minute and a target volume of 8–10 $mL \cdot kg^{-1}$. In cases of persistent AHI >10 despite an increased of positive end-expiratory pressure, polygraphy under NIV was considered to discriminate apnoeas with or without decrease of neural drive [13].

Telemonitoring on day 2 and 10 was used to control adherence, fractional use, leaks, tidal volume (V_T), respiratory rate 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.

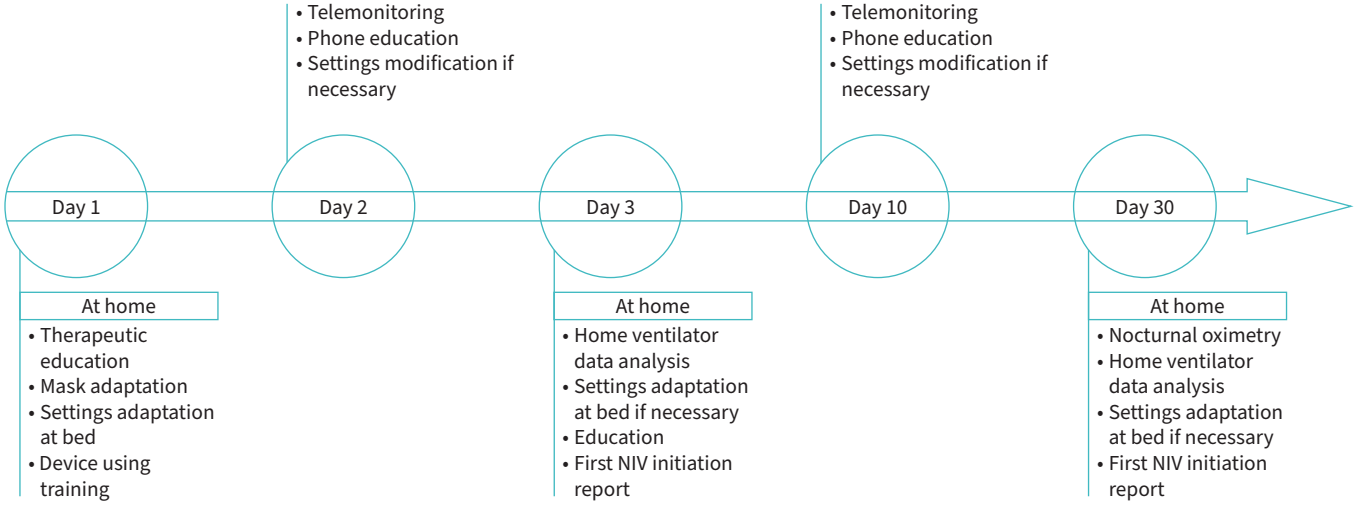

FIGURE 1 At-home noninvasive ventilation (NIV) initiation protocol. Five steps that comprise at-home NIV initiation with a nonexhaustive description of the actions performed by the different actors.

NIV data evaluated

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

The primary outcome was the adherence to NIV at 30 days, defined by a mean use of NIV for more than 4 h·day^{-1} during the first 30 days.

The secondary outcome was the efficiency of NIV initiation on nocturnal hypoxaemia correction, defined by a nocturnal S_{pO_2} correction on day 30 (nocturnal S_{pO_2} <90%, time <5%). As nocturnal oximetry on day 30 was only performed in adherent patients, the secondary outcome was only collected in the adherent subgroup. As there was a lack of nocturnal oximetry performed at day 30 for in-hospital patients, the secondary outcome data was only collected for the adherent at-home NIV initiation subgroup.

Fractional use was defined by the visualisation of three or more interruptions during the last night.

Leaks were considered relevant when nonintentional leaks were up to a mean of 24 L·min^{-1} during the first 30 days above the manufacturer's recommendation.

Persistent obstructive events were defined by an AHI detected by the software above a mean of 10 h during the first 30 days.

Statistics

Data are presented as the mean (standard deviation) for continuous variables and as relative frequencies for categorical variables. Patients were divided into two groups according to their mean adherence to NIV during the first 30 days: 1) NIV adherence <4 h·day^{-1}; and 2) NIV adherence >4 h·day^{-1} and two subgroups (S_{pO_2} corrected, defined as nocturnal S_{pO_2} <90% <5% night-time [11] and S_{pO_2} noncorrected) in the NIV adherence >4 h·day^{-1} group. Loss of follow-up was excluded from analysis at day 30 due to an important lack of data at day 30, especially in the in-hospital initiation subgroup. Emergency NIV initiation at the hospital was excluded from the analysis of 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 Chi^2 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 flowchart (figure 2), 81 were initiated during hospitalisation and 184 were initiated at home.

Of the patients who agreed to try NIV and had no contraindications 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 determined 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 presented more severe respiratory impairment than the at-home NIV initiation subgroup with, respectively, a mean forced vital capacity (FVC) of 59.4% *versus* 71.6% ($p<0.001$), a mean percentage of night-time S_{pO_2} <90% of 23.2% *versus* 15.2% ($p=0.023$) and a mean P_{aCO_2} of 6.21 kPa *versus* 5.07 kPa ($p<0.001$).

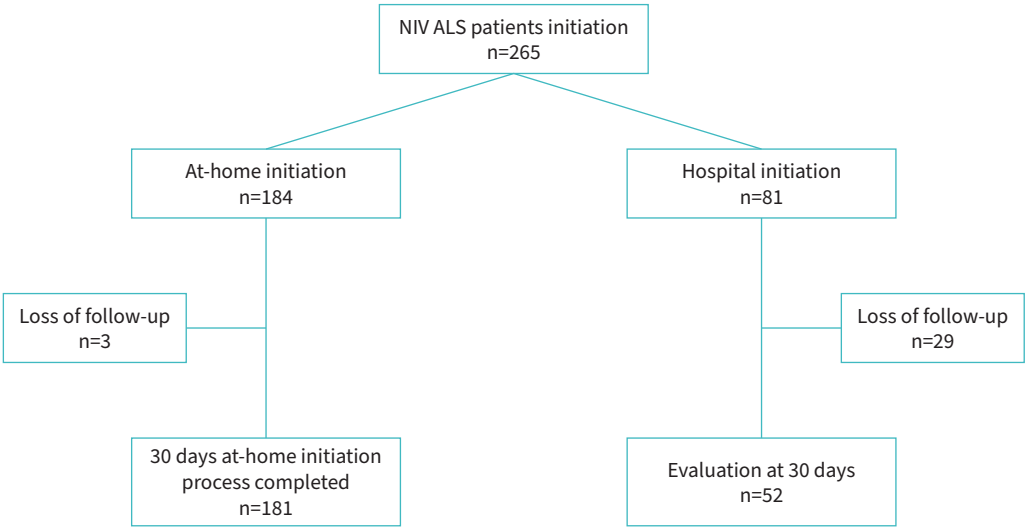

FIGURE 2 Flowchart of patients included between September 2017 and June 2021. ALS: amyotrophic lateral sclerosis; NIV: noninvasive ventilation.

The mean time from NIV prescription to NIV initiation was 12.5 days for the total population, 8.7±6.5 days for the at-home initiation subgroup *versus* 29±31.1 days for the 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

At 1 month, 153 patients (66%) were using NIV for more than 4 h·day^{-1}, 80 (34%) were using it for less than 4 h·day^{-1} (including 12 deaths and four total intolerance) (table 2). 126 patients (70%) in the at-home NIV initiation subgroup *versus* 27 patients (52%) in the in-hospital initiation subgroup had an adherence >4 h (p=0.018).

ALS Functional Rating Scale-Revised (ALSFRS-R) scores and FVC were significantly higher in adherent patients than in nonadherent patients (34±6.36 *versus* 30.5±8.21, p=0.003 and 71.5±21.5 *versus* 62.9±18.2, p=0.007, respectively). Proportion of initial nocturnal hypoxaemia (defined by nocturnal S_{pO_2} <90% more than 5% of the recording time) was significantly higher in adherent patients *versus* nonadherent patients (62 *versus* 50% p=0.024).

We also found significant differences in NIV data at 1 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 inpatients initiation group (IPAP 14±2.81 *versus* 11.8±1.98, p⩽0.001, back-up rate 14.2±1.46 *versus* 13.4±1.17, p⩽0.001). We also found differences in NIV monitoring with a more fractional use (13 (31) *versus* 10 (6), p⩽0.001) and a higher proportion of relevant leaks and obstructive events (6 (14) *versus* 4 (2), p⩽0.001 and 11.1±10.6 *versus* 5.48±8.77, p⩽0.001, respectively) for the inpatients group.

NIV efficiency at 1 month

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

21 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 *versus* 24 kg·m^{-2}, p=0.028) and a significantly higher mean nocturnal time percentage

TABLE 1 Population characteristics

Patient characteristics at initiation	Total	At-home patients	Inpatients	p-value
Anthropometric data				
Patients, n	265	184	81	
Age (years)	68±11	68±11	69±9	0.577
Male	157 (63)	114 (62)	43 (65)	0.645
BMI ($kg \cdot m^{-2}$)	24±4	24±4	23±4	0.141
Smoking greater than 20 pack-years	23 (9)	16 (9)	7 (11)	0.684
Neurological assessment				
ALSFRS-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 diagnosis 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	<0.001
Peak flow ($L \cdot s^{-1}$)	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 (cmH_2O)	44.4±23.9	44.26±23.96	45.1±24	0.877
SNIP (cmH_20)	45.9±20.8	47.88±23.89	43.2±17.5	0.692
S_{pO_2} night-time <90% (%)	17±21.4	15.16±18.59	23.2±28.1	0.023
S_{pO_2} <90% more than 5% of night-time	142 (68)	114 (62)	28 (58)	0.118
S_{pO_2} minimum	80.4±7.85	80.7±7.77	79.4±8.12	0.345
S_{pO_2} 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
P_{aCO_2} (kPa)	5.39±1.04	5.07±0.58	6.21±1.44	<0.001
NIV initiation criteria				
Clinical signs +				
P_{aCO_2} >6.1 kPa	34 (13)	0	34 (42)	
FVC <80% only	84 (32)	65 (35)	19 (24)	0.056
S_{pO_2} <90%, time >5% only	74 (28)	72 (39)	2 (2)	<0.001
Both FVC <80% and S_{pO_2} <90%, time >5%	42 (16)	42 (23)	0 (0)	<0.001
SNIP <60 cmH_2O	1 (0)	1 (1)	0 (0)	0.506
Other	30 (11)	4 (2)	26 (32)	<0.001
Time from NIV requirement assessment to initiation (days)	12.5±16.5	8.72±6.47	29±31.1	<0.001

Data are presented as mean±SD or n (%) unless otherwise stated. ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; BMI: body mass index; FVC: forced vital capacity; MIP: maximal inspiratory pressure; ODI: oxygen desaturation index; NIV: noninvasive ventilation; P_{aCO_2}: arterial carbon dioxide tension; SNIP: sniff nasal inspiratory pressure; S_{pO_2}: oxygen saturation measured by pulse oximetry.

with S_{pO_2} <90% (21% *versus* 15.9% , p=0.041). At day 30, they had a significantly higher EPAP (7.75 *versus* 6.75, p=0.006) and a higher but nonsignificant AHI (10.1 *versus* 5.63, p=0.066), but we did not find any difference in the monitoring at day 30 (table 4).

Discussion

Here, we report original data from real-life practices of at-home NIV initiation in 184 ALS patients with a P_{aCO_2} under 6.1 kPa and 81 patients with in-hospital NIV initiation. The data for the home NIV initiation subgroup show a very short delay in NIV instauration and a good nocturnal hypoxaemia correction in adherent patients, even though we report 30% of nonadherence.

One of the main results was the short delay between NIV prescription and initiation in the at-home NIV initiation subgroup. Decreasing the time between NIV prescription and initiation is one of the main goals of NIV initiation in ALS patients. Sheers *et al.* [14] have shown that shortening the delay between prescription and initiation tends to reduce mortality in ALS patients. In a recent study performed by van den Biggelaar *et al.* [8], their delay times were 19.9 days for home initiation and 31.2 days at the hospital.

TABLE 2 Population characteristics at noninvasive ventilation (NIV) initiation depending on adherence assessment at day 30

Patient characteristics at initiation	Total	Adherence >4 h	Adherence <4 h	p-value
Anthropometric data				
Patients	233	153 (66)	80 (34)	
Age (years)	68±11	68.1±10.6	68±11.2	0.907
Male	148 (63)	101 (66)	47 (59)	0.274
BMI ($kg \cdot m^{-2}$)	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				
ALSFRS-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 diagnosis 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 ($L \cdot s^{-1}$)	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 (cmH_2O)	44.7±23.7	46.6±22.8	40.2±25.6	0.178
SNIP (cmH_20)	45.4±22.4	56±24.4	34.8±15.7	0.104
S_{pO_2} night-time <90% (%)	17.1±21.3	17.8±20.6	15.8±22.6	0.531
S_{pO_2} <90% more than 5% of night-time	135 (68.2)	95 (62)	40 (50)	0.024
S_{pO_2} minimum	80.4±7.88	80.8±8.33	79.6±7.01	0.317
S_{pO_2} 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
P_{aCO_2} (kPa)	5.36±1	5.39±1.04	5.29±0.9	0.489

Data are presented as mean±SD or n (%) unless otherwise stated. ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; BMI: body mass index; FVC: forced vital capacity; MIP: maximal inspiratory pressure; ODI: oxygen desaturation index; P_{aCO_2}: arterial carbon dioxide tension; SNIP: sniff nasal inspiratory pressure; S_{pO_2}: oxygen saturation measured by pulse oximetry.

We have reported mean times from NIV requirement assessment to initiation of 8.7±6.5 days at home and 29±31.1 days at the hospital. The problem of bed availability in hospitals is recurrent and has exacerbated during the coronavirus disease 2019 (COVID-19) period. Using this at-home process, we did not have a decrease in NIV initiation during the COVID-19 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 fast 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 hypoxaemia.

Unfortunately, 34% of the whole cohort did not tolerate NIV for more than 4 h per day, this included 30% in the at-home NIV initiation subgroup and 48% in the in-hospital NIV initiation subgroup. This higher rate of nonobservant patients in the in-hospital initiation subgroup should be moderated by the fact that the symptoms of those patients were more severe and the mortality at day 30 (consider as nonadherent patient in our analysis) was much higher in the in-hospital initiation subgroup. Of the total 184 at-home initiations, only four did not tolerate NIV at all. This is a higher rate of NIV initiation failure than described in the literature. Gonzalez Calazada *et al.* [15] reported an NIV failure rate of 15%; however, in that study, patients were mainly initiated at the hospital at a more advanced stage and had a mean FVC of 51% compared to 71.6% in our cohort. In most studies evaluating at-home NIV initiation, the rate of NIV

TABLE 3 Noninvasive ventilation (NIV) parameters and monitoring at day 30 for the whole cohort

	Total	At-home patients	Inpatients	p-value
NIV parameters				
Patients, n	221	179	42	
IPAP (cmH_20)	12.2±2.31	11.8±1.98	14±2.81	<0.001
EPAP (cmH_20)	6.7±1.49	6.66±1.48	6.85±1.53	0.465
Back-up respiratory rate (acts per minute)	13.5±1.25	13.4±1.17	14.2±1.36	<0.001
Rise time (ms)	428±138	439±134	372±149	0.007
Trigger ($L{\cdot}min^{-1}$)	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
t_I min (s)	0.664±0.640	0.644±0.570	0.769±0.922	0.293
t_I 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)	<0.001
NIV use (h)	6.15±3.23	5.99±2.87	6.85±4.48	0.126
V_T (mL)	439±118	427±89.7	490±193	0.002
Respiratory rate (acts per minute)	16.8±3.13	16.5±2.73	18±4.32	0.007
Leaks ($L{\cdot}min^{-1}$)	5.57±15.1	3.69±10.7	13.7±25.6	<0.001
Leaks >24 $L{\cdot}min^{-1}$ (n)	10 (5)	4 (2)	6 (14)	<0.001
AHI	6.52±9.36	5.48±8.77	11.1±10.6	<0.001
AHI >10 (n)	41 (19)	27 (15)	14 (33)	0.004

12 deaths before day 30 were excluded from analysis. Data are presented as mean±SD or n (%) unless otherwise stated. AHI: apnoea–hypopnoea index; EPAP: expiratory positive airway pressure; IPAP: inspiratory positive airway pressure; IPF: inspiratory peak flow; V_T: tidal volume; t_I: inspiratory time.

initiation failure has not been reported [8, 16]. Bertella *et al.* [17] reported 22% at-home NIV initiation intolerance (*versus* 2.1% in our study) and 32% of patients did not support NIV for more than 4 $h{\cdot}day^{-1}$ at 3 months. 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 adherence, we found that adherent patients had a significantly higher nocturnal time percentage with S_{pO_2} <90% at initiation, which suggests that 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-R score significantly higher). In the literature, Vitacca *et al.* [19] did not find any adherence difference between early and late NIV initiation. Although we did not find presence of bulbar symptoms at NIV initiation as a negative factor of NIV success, their presence was defined by clinical consideration by the neurologists. We did not use an objective evaluation metric such as the Norris bulbar score to attest to this clinical condition and did not re-evaluate bulbar degradation over time, which has a major impact on NIV tolerance [4].

As expected in the hospital patient subgroup, NIV parameters were more severe and, therefore, their ventilation parameters were higher at initiation and at 1 month.

In the at-home subgroup, we started with a low level of inspiratory pressure to facilitate the acceptance of NIV. In our experience, and as recommended by new French recommendations [20], a very gradual increase of pressure allowed by a long adaptation time and close telemonitoring 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 PS as high as expected and similar to what is described in the literature [8, 11, 19]; these parameters might be too low for this restrictive population even though it could be explained by an early NIV initiation (mean FVC of 71.6% at initiation), which led us to promote treatment acceptance. Although nocturnal oximetry was normalised in 79% of adherent patients, we did not evaluate nocturnal hypoventilation by capnography, asynchrony or proportion of the capture cycle, which could estimate the under-assistance 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 future practice and studies.

TABLE 4 Noninvasive ventilation (NIV) parameters and monitoring at day 30 for adherent patients of the at-home NIV initiation subgroup

	Day 30	Corrected S_{pO_2}	Noncorrected S_{pO_2}	p-value
NIV parameters				
Patients, n	126	99 (79)	21 (17)	
IPAP (cmH_20)	12.1±1.97	12±1.9	12.8±2.29	0.118
EPAP (cmH_20)	6.86±1.52	6.75±1.47	7.75±1.37	0.006
Back-up respiratory rate (acts per minute)	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 ($L{\cdot}min^{-1}$)	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
t_I min (s)	0.674±0.67	0.698±0.7	0.6±0.16	0.566
t_I 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 monitoring				
Days (n)	29.5±3.07	29.6±3.18	28.6±2.58	0.169
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 (h)	7.58±1.50	7.45±1.48	8.17±1.36	0.043
V_T (mL)	426±88	420±80.9	456±113	0.099
Respiratory rate (acts per minute)	16.2±5.55	16.3±2.62	15.4±1.79	0.131
Leaks ($L{\cdot}min^{-1}$)	4.04±12.2	3.98±13.2	4.74±8.66	0.805
Leaks >24 $L{\cdot}min^{-1}$	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
S_{pO_2} assessment				
S_{pO_2} night-time <90 (%)	3.62±7.01	1.38±1.56	14.2±11.8	<0.001

There were six missing results. Data are presented as mean±SD or n (%) unless otherwise stated. AHI: apnoea-hypopnoea index; EPAP: expiratory positive airway pressure; IPAP: inspiratory positive airway pressure; IPF: inspiratory peak flow; S_{pO_2}: oxygen saturation measured by pulse oximetry; t_I: inspiratory time; V_T: tidal volume.

This less aggressive strategy could also have a negative impact on NIV adherence because, on one hand, on day 30 in the nonadherent subgroup, mean IPAP was significantly lower and, on the other hand, respiratory rate monitoring was significantly higher. This suggests that nonadherent patients could be under-assisted. The question is whether patients are under-assisted because of NIV tolerance or nonadherent due to under-assistance.

We did not report the blood gas results at 1 month because 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 Centre (mean 4 months).

In the 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 *et al.* [11] who reported that 49% of patients had normalised night oximetry at 1 month. 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 inpatient subgroup, at 1 month there is a higher rate of leaks and obstructive events, but it is difficult to conclude as patients were at a more severe stage of their disease.

At day 30, in the at-home NIV initiation subgroup, 17% of adherent patients still had noncorrected nocturnal S_{pO_2}; 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 day 30. In those cases, polygraphy under NIV should be discussed to discriminate apnoeas with or without a decrease of neural drive improvement.

One of the main limitations to take into account is the monocentric retrospective nature of the study, with all associated biases such as selection bias (we had no information for patients who had totally refused NIV initiation), and memorisation bias with a significant number of loss of follow-up at day 30, especially in 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 information or data on the evolution of its involvement.

Another limitation is the absence of long-term assessment of adherence and efficiency (>1 month); indeed, NIV adherence might change during the follow-up, as reported by Vitacca *et al.* [19], with 10% of ALS patients being at risk of reducing their adherence. 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 adherence, but setting modifications must be continued thereafter.

As a retrospective study on a real-life process, we were not able to provide information about supplementary interventions during this 1-month NIV initiation process (patient phone calls or technician home visits) even if, in our opinion, there were no more substantial interventions than there were with the anterior inpatient model.

Moreover, van den Biggelaar *et al.* [8] showed 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.

Lastly, the Bordeaux ALS Centre has an active cohort of 350 patients from the Nouvelle Aquitaine region (population of 6 million) with rural, suburban and urban zones. The radius of action to perform these at-home NIV initiation processes was 200 km from the Bordeaux hospital, so this model may be generalised in other hospitals.

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 one in five did not tolerate NIV at 1 month. When adherent at-home NIV initiation combined with telemonitoring is not efficient, the strategy must include a close follow-up for more than 1 month to adapt NIV parameters in order to achieve optimum settings.

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