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RESEARCH ARTICLE

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Psychiatric disorders as predictor of adherence to non-invasive ventilation treatment in patients with acute exacerbation in chronic obstructive pulmonary disease – a real life study

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ABSTRACT

Introduction: Non-invasive ventilation (NIV) treatment is effective and potentially lifesaving in patients with respiratory acidosis and acute exacerbation of chronic obstructive pulmonary disease (AECOPD). However, feelings of anxiety during NIV treatment are common, potentially leading to premature patient-initiated termination of treatment.

The primary aim of this study is to examine whether psychiatric disorders are a risk factor of premature patient-initiated termination of NIV treatment. The secondary aim is to examine the patterns in use of sedative drugs during NIV treatment.

Methods: This retrospective cohort study includes 195 patients with AECOPD receiving NIV between 1 January and 31 December 2018, in hospitals in the Northern Region of Denmark. Information was obtained from medical records. Psychiatric disorders were defined by the use of psycholeptics at home, right before admission.

Primary outcome was premature patient-initiated termination of NIV treatment. Secondary outcome was the use of any sedative drug during NIV treatment.

Results: Patient-initiated premature termination was seen in 41 (21%) of cases. This group had a significantly higher mortality (43.9% vs. 19.5% in the total population, $p < 0.01$). A higher risk of patient-initiated premature termination was seen in patients with psychiatric disorders (Odds ratio 2.18, $p < 0.05$) and older age (Odds ratio 1.06, $p < 0.05$). No significant difference in the use of sedative drugs was seen (34.1% vs. 38.1% in the total population, p 0.12).

Conclusion: A significantly higher risk of premature patient-initiated termination of NIV treatment was seen in patients with psychiatric disorders and older patients, but not in patients with active smoking or excessive use of alcohol. No significant difference in the pattern of sedative drug use during treatment was seen.

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Introduction

Acute exacerbations in chronic obstructive pulmonary disease (AECOPD) are characterized by increased dyspnea, cough, and increased amount of sputum production in patients with COPD beyond regular day-to-day variation [1].

Non-invasive ventilation (NIV) treatment involves respiratory support with positive airway pressure without the need for endotracheal intubation [2]. In patients with respiratory acidosis, defined as pH < 7.35 and elevated pCO_2 due to AECOPD, NIV increases survival and decreases the risk of intubation [3,4]. There is strong evidence that NIV should be used for patients with respiratory failure and respiratory acidosis caused by AECOPD, when standard medical treatment fails to correct the condition [3,4]. Approximately 20% of patients admitted with AECOPD develop respiratory acidosis, and 12% receive NIV treatment, with an in-hospital mortality of 16–27% [5–7].

Patient acceptance and collaboration are crucial during NIV treatment. Patient anxiety or discomfort may lead to refusal or subsequent premature treatment discontinuation. Patients undergoing NIV treatment report a sensation of being trapped, fear, anxiety, and claustrophobia, which has been described as a traumatic experience [8]. Previous studies have found a discontinuation

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rate of approximately 30%, the risk increasing with higher degree of respiratory failure [9,10].

The use of sedatives in patients receiving NIV is reported to vary between 20 and 25% across the world [11,12]. However, previous studies have reported conflicting results regarding the effects of sedatives. One systematic review has shown a decreased risk of intubation and delirium in patients receiving sedative medication during NIV treatment [10], whereas another study found an increased risk of premature termination in patients receiving sedative medication [13]. Supportive care and information from staff have also been shown to increase the success rate of NIV [14].

Where physician-initiated termination is based on treatment failure or patient recovery, patient-initiated termination can be caused by a sensation of discomfort, claustrophobia, or anxiety [8]. However, to the best of our knowledge, no study has investigated predisposing factors for premature patient-initiated termination of NIV. Mental health and substance abuse have previously been shown to be predictive of non-adherence to different treatment regimens, such as inhaled medication [15–17]. Whether this is a risk factor for patient terminated NIV treatment is unknown.

Therefore, the primary hypothesis of this study was that patients with pre-existing psychiatric disorders have a higher risk of patient-initiated termination of NIV, leading to increased mortality. The secondary hypothesis was that patients with pre-existing psychiatric disorders have a higher need for sedative drugs during NIV.

The primary aim of this study was to investigate whether psychiatric disorders increased the risk of premature patient-initiated termination of NIV and subsequent in-hospital mortality. The secondary aim was to investigate patterns in the use of sedative medications in patients receiving NIV treatment.

Methods

Study setting

In this retrospective cohort study, patients were identified from the *EXAcerbations of COPD; Identification of riSkfactors for rEadmission EXAcise* database (EXAcise) [18], containing every first admission due to AECOPD from 1 January to 31 December 2018, at the hospitals in the Northern Region of Jutland, Denmark (One teaching hospital and three regional hospitals). Tax-funded health care is available to all Danish inhabitants. Data were obtained from the patients' medical records.

Selection criteria

Patients were eligible for enrolment in the EXAcise cohort if admitted to any of the aforementioned hospitals in the inclusion period with AECOPD, defined by the following International Classification of Diseases 10-codes (ICD-10): Either a primary diagnosis of COPD (DJ44) or a combination of pneumonia (DJ13–18) and respiratory failure (DJ96) with COPD as a secondary diagnosis. In a previous study, this combination of ICD-10 codes had a positive predictive value for AECOPD of 92% in Danish hospital admissions [19].

Patients receiving NIV treatment for AECOPD because of respiratory acidosis ($pH \leq 7.35$, $paCO_2 < 6.0$ kPa) were included. AECOPD was defined by increased sputum, cough, and/or dyspnoea [20].

The exclusion criteria were continuation of previously initiated home NIV during AECOPD or intubation before receiving NIV treatment.

Covariate definitions and outcomes

Baseline information consisted of age, sex, duration of admission, in-hospital mortality, and 30-day mortality.

Smoking status (former smoker, active smoker, never smoker) and drinking habits (number of units per week) were obtained from the admission records. Excessive alcohol consumption was defined as more than 7 units per week for women and 14 units per week for men, as was the Danish definition in 2018 [21].

Patients receiving treatment at admission with psycholeptics were considered to have a psychiatric disorder. Psycholeptics recorded were antidepressants (anatomical therapeutic chemical code (ATC) N06A), anxiolytics (ATC N05B), neuroleptics (ATC N05A), hypnotics (ATC N05CD, N05CF, N05CH), and other (e.g. Lithium (N05AN)). The use of opioid droplets ('Oramorph' ATC N02AA01) was also recorded, as it is commonly used to relieve anxiety in patients with end-stage COPD in Denmark [22]. Information about the use and type of sedative drugs used during NIV treatment was obtained from medical records. The categories were opioids (ATC N02A), neuroleptics (ATC N05A), antihistamines (ATC R06A), benzodiazepines (ATC N05B), hypnotics (ATC N05CD, N05CF, N05CH), and others.

Information about pH and $paCO_2$ from arterial puncture was obtained from the last measurement taken before starting NIV treatment, as not every patient was acidotic at admission.

Treatment settings (teaching hospital vs. peripheral hospital), information about living arrangements (alone or not), mortality, and admission duration were obtained from the medical records. Thirty days readmission rates were calculated only for patients who survived the initial admission period.

Forced expiratory volume in one second in percentage of expected value (FEV1%) and FEV1/FVC were obtained from medical records if they were available from 3 months prior to or 3 months after admission.

Outcome groups

Patients were divided into four groups defined by the outcome of their NIV treatment: Fulfilment of NIV treatment (A), Patient-initiated termination (B), and Physician-initiated premature termination because of treatment failure (C). Group A includes patients receiving less than 72 h of NIV treatment because of rapid improvement of the condition, where the termination of the treatment is initiated by the physician.

The primary outcome was defined as patient-initiated discontinuation of NIV in less than 3 days of treatment (Group B). The discontinuation was defined as patient-initiated if the patient expressed a wish to stop the treatment, and the physician complied even though continued treatment was advised. The cutoff of 3 days was used as the Danish Respiratory Society guidelines recommend this duration when treating respiratory acidosis in patients with AECOPD, with a gradual step-down [23].

Statistics

Categorical variables were described using proportions and counts, while continuous variables were described using means. The 95% confidence intervals and p-values were used to assess significance.

Baseline information, when normally distributed, is presented as mean (standard deviation) when continuous and as proportions when binomial. Baseline information in patients grouped according to outcome (patient-initiated discontinuation, physician-initiated discontinuation, and fulfilment of treatment) was compared using ANOVA. The assumptions were visually investigated to determine if they were met before the analysis. P-values <0.05 were considered significant. The variables showing significant differences among the groups were analyzed using a two-tailed t-test, comparing the group fulfilling NIV treatment and the group with patient-initiated termination. Missing data were excluded.

To evaluate the primary outcome, all covariates were graphically assessed before multiple regression analyses to check for normality. A multiple regression model was run using patient-initiated discontinuation as the outcome variable. The covariates included age, sex, active smoking, excessive alcohol consumption, and use of psychopharmaceuticals, as previous studies have shown these covariates might be associated with frailty in patients with COPD [24–26]. Patients with missing data in the included variables were excluded.

The secondary outcome was evaluated by calculating the proportion of patients receiving sedative drugs pro necessitate (PN) in the various groups and specific medications (opioids, hypnotics, neuroleptics, antihistamines, and benzodiazepines). The groups were compared using ANOVA test.

Data were collected in REDCap (13.1.37). The analysis was conducted using R version 4.4.1.

Ethical approval

This study was approved by the Danish Patient Safety Authority (31-1521-34). The project is approved by the Northern Region of Denmark (ID F2024–039).

Results

Selection process

The selection process is illustrated in Figure 1. Of the 1,532 patients included in the database, 203 received NIV during admission. In total, 195 patients were included in this study.

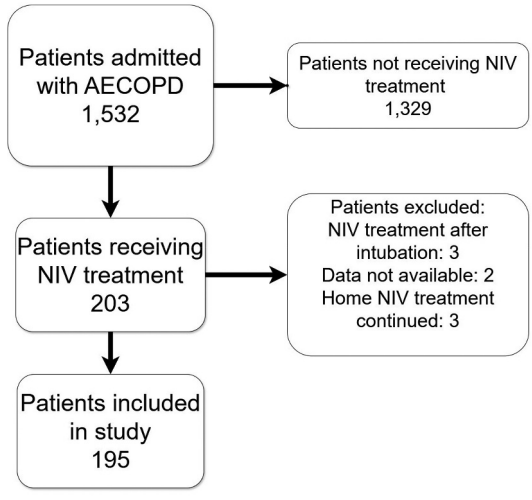

Figure 1. Flowchart describing the selection process.

Table 1. Baseline information.

	Total population	Fulfilment of NIV treatment (Group A)	Premature termination of NIV, patient initiated (Group B)	Premature termination of NIV, physician initiated (treatment failure) (Group C)	P-value
Number	195	131	41	23	–
Age (years)	72.6 (9.7)	71.2 (9.6)	75.3 (9.5)	75.3 (9.6)	**<0.05**
Sex, male	42.6%	45.0%	34.1%	43.5%	0.47
BMI	28.8 (9.8) NA: 26.7%	30.2(9.9) NA: 22.1%	24.7 (7.1) NA: 36.6%	26.9 (11.4) NA: 34.8%	**<0.05**
FEV1%	33.8% (14.9) NA: 47.2%	33.6% (14.1) NA: 41.2%	32.4% (14.1) NA: 63.4%	37.1% (21.3) NA: 52.2%	0.72
In-hospital mortality	19.5%	5.3%	43.9%	56.5%	**<0.01**
Mortality, 30 days	23.1%	9.2%	46.3%	60.9%	**<0.01**
Readmission, 30 days	65.6%	65.6%	56.5%	40.0%	**<0.01**
Length of hospital stay (Days)	8.8 (8.2)	9.2 (8.1)	7.1 (7.0)	9.9 (10.6)	0.29
Intubation	6.7%	2.3%	2.4%	39.1%	**<0.01**
Stay at ICU	45.6%	44.3%	39.0%	65.2%	0.11
Stay at university hospital	53.8%	51.9%	51.2%	69.6%	0.28
Daily use of psycholeptics (Psychiatric disorder)	49.2%	50.4%	61%	21.7%	**<0.01**
Daily use of inhaled medications	88.2%	91.6%	73.9%	85.4%	**<0.01**
Active smoker	47.7%	44.3%	48.8%	65.2%	0.18
Excessive use of alcohol	9.7%	10.7%	7.3%	8.7%	0.81
PH before NIV	7.24 (0.9)	7.24 (0.1)	7.25 (0.1)	7.20 (0.1)	**<0.05**
Standard Bicarbonate before NIV (mmol/L)	27.4 (5.7)	27.8 (5.7)	27.2 (6.4)	25.5 (3.7)	0.22
$PaCO_2$ before NIV (kPa)	10.7 (3.2)	10.8 (3.4)	10.0 (2.6)	11.7 (2.8)	0.13
Living alone	51.3%	48.1%	61.0%	52.2%	0.36
Receiving home care	62.6%	59.5%	75.6%	56.5%	0.25

Binomial values are presented as percentages, continuous variables as mean (standard deviation). P-value obtained by ANOVA including all outcome groups. Significant p-values are highlighted. NA: Not available in number.

Study population and baseline information

The baseline information is presented in Table 1. Patient-initiated termination occurred in 41 of 195 patients (21.0%).

In Group A, 103 received NIV treatment for 72 or more, while 28 had a rapid improvement and received treatment for less than 72 h. These two subgroups differed regarding differences in mortality ($p < 0.01$), BMI ($p < 0.05$), and stay at ICU ($p < 0.01$). Baseline information is presented in Appendix A.

A total of 103 patients (52.8%) had recently undergone spirometry. Only 13 of 45 (28.8%) patients who died within 30 days after admission had a recent spirometry.

Further specification of type of psycholeptics is shown in Appendix B. Antidepressants was the most commonly used psycholeptic (30.8% of the total population), and the only specific treatment showed significant differences across outcome groups ($p < 0.05$).

A two-sided t-test was performed to compare the variables with significant differences across all outcome groups with ANOVA (Table 1) of Group A with Group B. No significant differences were found regarding the use of psycholeptics (p 0.24), stay in the ICU (p 0.56), daily inhaled medications (p 0.31), pH-value (p 0.56), and intubation rates (p-value 0.95), while 1 month readmission ($p < 0.01$), in-hospital mortality ($p < 0.01$), 30-day mortality ($p < 0.01$), and BMI ($p < 0.01$) still showed significant differences.

In-hospital mortality and association between psychiatric disorders and risk of patient-initiated termination: primary outcome

Patients in Group B had a significantly higher mortality rate during admission than in Group A (43.9% and 5.3%, respectively, $p < 0.01$), and the same applies to the 30-days mortality (46.3% vs. 9.2%, respectively, $p < 0.01$).

Figure 2 shows a multiple regression analysis of the risk of patient-initiated premature termination. A significant association was found between psychiatric disorders ($p < 0.05$), increasing age (p-value <0.05), and the odds of patient-initiated termination. No significant associations were found between excessive use of alcohol, active smoking, and sex.

Sedation during non-invasive ventilation treatment

The use of sedatives is summarized in Table 2. Of the total population, 38.1% received sedatives. Opioid use was the most prevalent among all outcome groups, whereas only few (<1%) used sedative antihistamines. No significant differences were found in the patterns of sedative drug use among outcome groups.

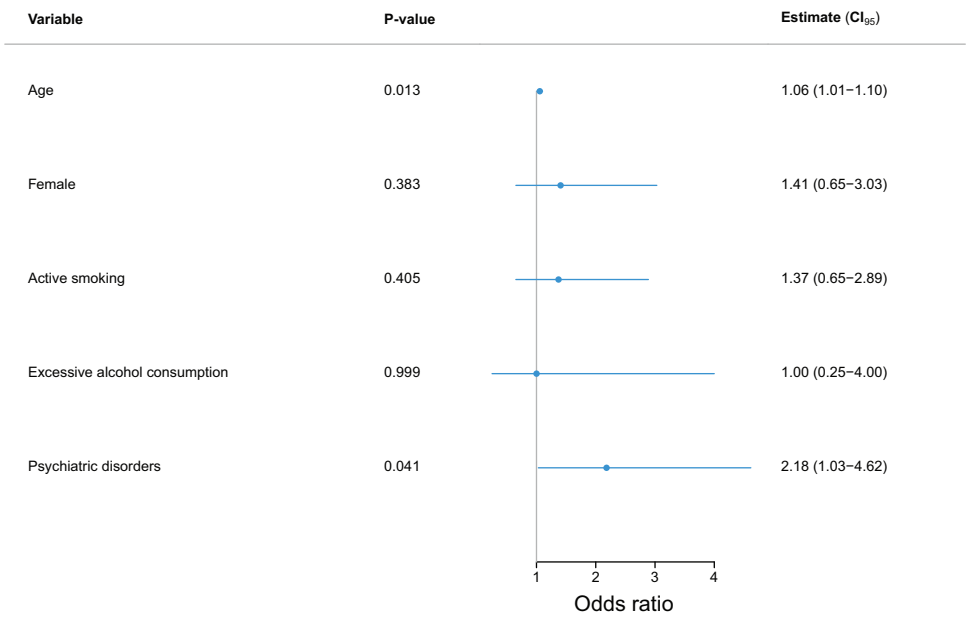

Figure 2. Multiple regression model describing the association between selected variables and risk of patient-initiated premature termination of NIV. X-axis shows odds ratio with 95% confidence interval.

Table 2. Sedation given during non-invasive ventilation treatment in proportion of total population.

	Total	Fulfilment of NIV treatment (Group A)	Premature termination of NIV, patient initiated (Group B)	Premature termination of NIV, physician initiated (treatment failure) (Group C)	P-value
Any sedation given	38.1%	34.4%	34.1%	21.4%	0.12
Opioids	18.5%	19.8%	17.1%	10.7%	0.72
Antihistamines	0.5%	0.8%	0%	0%	0.79
Narcoleptics	12.3%	13.7%	14.6%	3.6%	0.16
Benzodiazepines	10.8%	11.5%	12.2%	7.1%	0.57
Hypnotics	4.6%	4.6%	7.3%	0%	0.41

Discussion

Patients with psychiatric disorders and older patients had a significantly higher risk of patient-initiated premature termination of NIV treatment. Patient-initiated termination was associated with a significant increase in mortality rate. No significant differences were found in the use of sedation during NIV treatment between the outcome groups. This is consistent with a previous study showing that mentally vulnerable patients have a harder time adhering to medical treatments [15–17]. Previous studies have shown that treatment with NIV might lead to anxiety and feelings of being trapped, which might lead to refusal of treatment [8], which could explain the connection between mental disorders and NIV denial.

To the best of our knowledge, adherence to acute NIV treatment in patients with psychiatric disorders has not been investigated previously. However, in patients with anxiety and depression, as well as sleep apnoea, adherence to home continuous positive airway pressure therapy (CPAP) is comparable to patients without mental disorders [27]. This inconsistency might be explained by the different amounts of stress associated with home and acute settings. Although the indications from our study need confirmation, it is pertinent to investigate how patients with mental disorders can be helped to accept NIV treatment.

Older patients had a significantly higher risk of treatment failure. Results from previous studies are consistent with this finding, showing a higher degree of referral to palliative care in older patients with terminal COPD, especially those prescribed a treatment ceiling [28]. Thus, clinicians might be more susceptible to accepting refusal and initiating palliation in older and more fragile patients.

No significant associations were found between active smoking, excessive alcohol consumption, sex, and premature termination. This is consistent with the baseline results, which showed no significant differences between the groups regarding these variables. No other studies have investigated whether substance

abuse affects adherence to NIV. Alcohol consumption and smoking were not quantified or frequency with regard to the number of units or amount of tobacco per day, as this information was not available in most cases. A quantification between very heavy users and slight overconsumption might have shown other results. However, our results should be interpreted with caution because of the low numbers, and substance abuse should be included as a covariate in future larger studies in this area.

The overall in-hospital mortality of 19.5% is consistent with the mortality of 16–27% previously found [5–7]. A significantly higher mortality was observed in Group B and, not surprisingly, also seen in Group C. Group C also included a significantly larger proportion of patients who were intubated. These findings are largely consistent with previous findings, as it is well established that NIV treatment significantly increases survival in patients with type 2 respiratory failure [3,4]. These findings underline the effect of NIV treatment and highlight the importance a personalized approach to support patients in fulfilling treatment.

There was no significant difference in the proportion of patients who stayed at a teaching hospital among the outcome groups. This was inconsistent with a previous study that reported a higher mortality rate in non-teaching hospitals [29]. In this study, all included hospitals included had an ICU available. As the pattern of admission to ICU and teaching hospital did not differ between Group A and Group B, this did not explain the differences in outcome and mortality.

The termination rate is 32% in group B and C combined. This is consistent with the discontinuation rate of 30% reported in previous studies [9,10]. In this study, patient-initiated termination (Group B) was performed in 21.0% of cases, indicating that it was, actually, more common than pure treatment failure (Group C). To the best of our knowledge, this finding cannot be compared to previous findings, as it has not been previously investigated.

No significant differences were found in the sedation patterns during NIV treatment. As the pattern of sedative drug use did not differ between Group A and B, this does not explain the differences in mortality and outcome. On the one hand, this could suggest that those with patient-initiated termination might have a greater need for sedative drugs, to prevent premature termination. However, there is a possibility of differences regarding the timing and dosage of medication, as this was not available from the medical records. A previous study found that 20–25% of patients received sedation during NIV, but variations between geographic regions have been found [12]. Heavy sedatives, such as Propofol and Dexmedetomidine, have been reported to be more commonly used in other countries, but were not observed in any of the cases in this study [12]. While hand restraints were commonly used in some countries, they were not used on any patients in this study, which might explain the higher rate of drug use [12].

While this study shows a higher risk of patient-initiated premature termination of NIV treatment and thus a higher mortality in patients with psychiatric disorders, future research should reveal how these patients can be helped. A previous review underlined the importance of the relationship between patients and medical personnel to achieve adherence to treatment of any kind [30]. Awareness of the staff of vulnerable groups and education in handling these patients could potentially improve adherence to treatment. Further studies should examine how staffing and the time available for staff to support patients during treatment affect adherence. Medication may not be the solution to this problem, but as previous studies have shown conflicting results, further studies could be needed [10,13]. Though, a comparison of the safety, patterns of use, and effectiveness of sedative drug use does not necessarily have useful external validity across the world.

Limitations

A relatively high number of patients had missing spirometric results. However, these patients were not excluded from the study. This is because studies have shown that approximately 14% of patients, especially those with several comorbidities, are not diagnosed with COPD before their first admission with AECOPD [31]. It is also common for patients with COPD in Denmark to be diagnosed in primary care, in which case the spirometry results would not be available [32]. As one-fifth of patients died during admission, a significant number would be excluded, as they would not be able to participate in spirometry after discharge. This could lead to missing information about patients with the highest risk of patient-initiated termination, leading to exclusion bias. To avoid this, and because of the acute setting, recent spirometry was not considered an inclusion criterion in this study, although missing spirometry introduces a risk of misclassification bias. Over and underdiagnosing of COPD could both lead to sample bias, especially if the wrongfully excluded or included patients share similar traits. The analysis could be affected by this, both leading to interpretation of patterns, which are not there in real life or blurring associations As this is the first and only study investigating adherence to

acute NIV treatment and its association with psychiatric disorders, the data still contribute important information, which might form the basis for future studies on this subject.

There is a risk of confounding by disease severity and disease burden, both regarding mortality and risk of premature termination. Due to missing data regarding FEV1, there is a possibility of significant differences among the outcome groups, even though no significant differences are seen with the available data. Disease burden could be assessed with e.g. Modified Medical Research Dyspnea Scale or BODE Index, and both of these would require interviewing the patient about daily symptoms [33].

A higher number of patients would yield a higher power of the study, making it possible to substantiate the results and include more variables in the regression model without the risk of overfitting.

In this study, psychiatric disorders were defined by the use of psycholeptics and opioid drops, which leads to certain limitations and risk of bias. Opioid drops and some antidepressants could be used for pain relieve [34,35]. Certain sedative antihistamines can be used to treat travel sickness or allergies [36]. Mental disorders are underdiagnosed in patients with COPD [37], and there is a risk of misclassification bias in this case. Misclassification is also common as symptoms of mental disorders might mimic physical disorders (e.g. loss of appetite, weight loss, and tiredness) [38], and studies have shown that antidepressants and anxiolytics might be prescribed to patients not meeting the criteria for psychiatric disorders [39]. However, a prospective study with a depression or anxiety scale during admission or after discharge would not eliminate this risk because of high mortality. Thus, the definition of mental illness used in this study was deemed the most appropriate.

As some variables were patient reported (smoking, alcohol use, etc.), there is always a risk of recall bias. There is also a risk of errors in the medical records made by clinicians during admission. There is always a risk of unknown confounders.

Internal validity was assessed to be high because very few patients were excluded. This also reduces the risk of exclusion bias. As there are no international recommendations concerning the use of sedative drugs and the possible use of force during NIV treatment, external validity might vary greatly across countries with traditions and national regulations [11]. Studies have also shown that the use of psychopharmaceuticals varies across countries [40] and access to NIV varies markedly across the world [41]. However, external validity is probably high in Danish or similar settings.

Conclusion

A significant association was found between older age, psychiatric disorders, and patient-initiated premature termination of NIV. There were no significant associations with sex, excessive alcohol use, or active smoking. Significantly higher in-hospital mortality was observed in patients with patient-initiated termination. No significant differences in the patterns of sedative drug use were found among the different outcome groups in this study.

Disclosure statement

No potential conflict of interest was reported by the author (s).

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Approval of final manuscript

All authors have approved of the final manuscript.

Author contributions

Ulla Møller Weinreich – Conceptualization, Data curation, Funding Acquisition, Methodology, Investigation, Writing – Review and editing. **Peter Ascanius Jacobsen** – Data curation, Formal analysis, Investigation, Methodology, Visualisation, Writing – Review and editing. **Mia Solholt Godthaab Brath** – Conceptualization, Data Curation, Methodology, Writing – Review and editing.

Data availability statement

Data will not be made publicly available as it contains confidential patient information.

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Appendix

Table A1. A Comparison between 'fulfilment of treatment' and 'Premature termination of NIV, physician initiated (Rapid improvement)'.

	Premature termination of NIV, physician initiated (Rapid improvement)	Fulfilment of NIV treatment >72 hours
Number	28	103
Age (years)	71 (9.4)	71.3 (9.6)
Sex, male	39.3%	46.6%
BMI	26.2 (9.9)	31.2 (9.7)
FEV1%	33% (15.1)	33.7% (14.1)
In-hospital mortality	0%	6.8%
Mortality, 30 days	0%	11.7%
Readmission, 30 days	64.3%	70.8%
Length of hospital stay (Days)	6.4 (3.8)	10 (8.7)
Intubation	0%	2.9%
Stay at ICU	71.4%	36.9%
Stay at university hospital	42.9%	54.4%
Daily use of psycholeptics (Psychiatric disorder)	42.9%	52.4%
Daily use of inhaled medications	96.4%	90.3%
Active smoker	60.7%	39.8%
Excessive use of alcohol	7.1%	11.7%
PH before NIV	7.25 (0.1)	7.24 (0.1)
Standard Bicarbonate before NIV (mmol/L)	26.4 (7.7)	28.1 (5.0)
$PaCO_2$ before NIV (kPa)	9.6 (2.0)	11.1 (3.6)
Living alone	53.6%	46.6%
Receiving home care	53.6%	61.2%

Table B1. Daily use of psycholeptics, extended version.

	Total population	Fulfilment of NIV treatment Group A	Premature termination of NIV, patient initiated Group B	Premature termination of NIV, physician initiated (treatment failure) Group C	P-value
Daily use of psychopharmaceuticals	49.2%	50.4%	61.0%	21.7%	**<0.01**
Antidepressants	30.8%	34.4%	34.1%	4.3%	**<0.05**
Benzodiazepines	10.8%	9.9%	17.1%	4.3%	0.25
Neuroleptics	15.4%	13.7%	19.5%	8.7%	0.16
Hypnotics	10.8%	8.4%	14.6%	17.4%	0.30
Oramorph	7.2%	9.2%	4.9%	0%	0.24
Other	4.6%	3.8%	7.3%	0%	0.36

Values in percentage of whole outcome group using the specific drug. P-values obtained from ANOVA across all outcome groups.