



## Research article

# Home non-invasive ventilation: An observational study of aetiology, chronic respiratory failure of multiple aetiologies, survival and treatment adherence

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## ABSTRACT

Home non-invasive ventilation (NIV) is used to treat patients with chronic respiratory failure (CRF). However, knowledge on the prevalence and impact of multimorbid aetiology of CRF, patterns of NIV use, and survival of these patients is limited. Our aim was to analyse the multiple aetiologies of CRF, patterns of NIV use and the outcome of those patients.

We conducted a retrospective analysis of 1,281 patients treated with home-NIV between 2004 and 2014 in Turku University Hospital, Finland. The patients were divided into nine disease categories: obstructive airways disease (16 %); obesity hypoventilation syndrome (11 %); neuromuscular disease (10 %); chest wall diseases (4 %); sleep apnoea (26 %); interstitial lung diseases (3 %); malignancy (2 %); other (3 %) and acute (8 %), which refers to the patients who did not fulfil criteria of CRF. In addition, multiple aetiologies of CRF were found in 17 %. Mean adherence to home-NIV was  $6.0 \pm 4.4$  h/d and median treatment duration 410 (120–1021) days. Adherence, treatment duration or survival did not significantly differ between patients with either single or multiple causative diseases leading to CRF. Median survival was 4.5 years (95 % CI 3.6 to 5.4). The main reasons for discontinuing NIV were death (56 %) and lack of motivation (19 %).

We conclude that home-NIV is used in a variety of diseases. CRF of multiple aetiologies is prevalent and not limited to chronic obstructive lung disease and obstructive sleep apnoea overlap syndrome. However, the adherence to home-NIV or survival did not differ between patients with a single or multiple diseases causing CRF, but the survival of the home-NIV patients differed according to the underlying aetiology of CRF.

**Abbreviations:** NIV, non-invasive ventilation; CRF, chronic respiratory failure; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnoea; PAP, positive airway pressure; BMI, body mass index; OAD, obstructive airway disease; NMD, neuromuscular disease; CWD, chest wall disease; OHS, obesity hypoventilation syndrome; SA, sleep apnoea (including both obstructive and central sleep apnoea); ILD, interstitial lung disease; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; ASV, adaptive servo-ventilator; EEP, end expiratory pressure; ALS, amyotrophic lateral sclerosis.

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## Take home message

Home non-invasive ventilation (NIV) was used in a variety of diseases and one fifth of the patients had several diseases affecting initiation of home-NIV. Patients with multiple aetiologies of chronic respiratory failure (CRF) did not differ from the patients with a single aetiology of CRF in terms of adherence to the therapy or survival.

## 1. Introduction

Home non-invasive ventilation (NIV) is widely [1–3] and increasingly [4–7] used to treat chronic hypercapnic respiratory failure. Depending on the underlying aetiology of the chronic respiratory failure (CRF), long-term NIV has been shown to improve gas exchange, daytime sleepiness, health-related quality of life, survival, and hospitalization rates of patients with CRF [8–15]. Treatment guidelines for CRF have focused on distinct disease categories [9,16–18]. Data about the coexistence of the diseases leading to CRF are sparse and mainly limited to the overlap of chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) [19–21].

We hypothesized that patients with CRF of multiple aetiologies, i.e. those with more than one concomitant disease contributing to CRF, have a worse prognosis than those with a single disease causing CRF. The aim of this retrospective real-life study was to describe the clinical conditions leading to the initiation of home-NIV and compare the NIV settings, adherence, reasons for discontinuing NIV, and survival within each diagnostic category.

## 2. Materials and methods

### 2.1. Study subjects

Turku University Hospital maintains a database of all patients with positive airway pressure (PAP) devices in the hospital district. Patients who were implemented on home-NIV between January 2004 and July 2014 were included in the study, excluding 1) patients under 18 years of age ( $n = 5$ ) and 2) cases where NIV was restarted ( $n = 62$ ). The number of patients was 1,281. The study was approved by the Clinical Research Centre of the Turku University Hospital (approval code T05/014/21). The approval of ethical committee was not needed in registry studies according to prevailing Finnish legislation. The research was conducted according to the principles of the World Medical Association Declaration of Helsinki.

The decision for the implementation of home-NIV was made by the attending senior pulmonologist, applying current guidelines [9,16,22–24]. Home-NIV was started at the respiratory ward of Turku University Hospital. NIV settings were optimized using overnight monitoring of oxyhaemoglobin saturation with pulse oximetry, transcutaneous carbon dioxide pressure with capnometry, or cardiorespiratory polygraphy, and morning arterial/capillary blood gas analyses. Patients had a follow-up visit at the respiratory ward 1–3 months after the implementation of home-NIV, and thereafter on a yearly basis at the outpatient clinic. They were followed until the 31<sup>st</sup> of July 2014, or until earlier death or discontinuation of NIV.

### 2.2. Clinical characteristics

The following data were collected from the electronic medical records: age at the implementation of home NIV, sex, smoking status, body mass index (BMI), and eventual oxygen supplementation at the beginning of the treatment and at the latest control visit. The indications for the implementation of home-NIV were re-evaluated using data from earlier lung function tests, blood gases and other laboratory results, imaging results, and the patient's performance status.

Patients were categorized into 9 groups based on the underlying aetiology of respiratory failure: obstructive airway disease (OAD), neuromuscular disease (NMD), chest wall disease (CWD), obesity hypoventilation syndrome (OHS), sleep apnoea (SA, including both obstructive and central sleep apnoea), interstitial lung disease (ILD), malignancy, other, and acute. The OAD group included patients with COPD, asthma and bronchiectasis. The malignancy group consisted of patients with primary or metastatic thoracic malignancy, where home NIV was used as a palliative therapy to alleviate severe dyspnoea. Acute group consisted of patients who were set up on home-NIV during an acute illness, but did not meet the criteria for CRF after the resolution of this acute illness, e.g. COPD patients with hypercapnia during an acute exacerbation but no evidence of hypercapnia after the resolution of the exacerbation. We decided to include this acute group in order to evaluate their adherence and other clinical features although not fulfilling the criteria for CRF. Patients with CRF of multiple aetiologies are referred to as multimorbid. By definition, the patients in the acute category are not included in multimorbid CRF. However, an acute illness like the exacerbation of COPD, congestive heart failure, pneumonia, pulmonary embolism, or stroke was recorded as a contributing factor for the implementation of home-NIV. A full list of underlying NMD diagnoses and diagnoses in category other can be found in the online supplementary material (Supplementary Tables A and B).

Reasons for discontinuation of home-NIV were analysed and classified as follows [1]: death [2]; lack of motivation [3]; not adapted [4]; NIV no longer required [5]; change to continuous positive airway pressure device (CPAP), or [6] other. The last group included patients with complications such as pneumothorax, patients with lung transplantation, transition to invasive mechanical ventilation, poor general health, or unknown reason for cessation of NIV. The causes for "NIV no longer required" were most often a significant weight loss, or the effect of chemotherapy or radiotherapy in the malignancy group.

Data on the ventilator settings and median daily usage hours were collected via the device memory card. Depending on the

ventilator type, inspiratory (IPAP) and expiratory pressure (EPAP), or in case of adaptive servo-ventilator (ASV), end expiratory pressure (EEP) were recorded. Data on ventilator settings were collected at implementation and at the last control visit. Patients with an average NIV use of  $\geq 4$  h per day were considered adherent.

When ventilator type was changed after thorough clinical evaluation (most commonly from bilevel NIV to ASV due to residual central apneas, after optimising treatment of baseline disorder), settings were recorded for both device types. In case of continuous home-NIV therapy, length of the treatment period was recorded from the date the first device was implemented to the date the last device was returned, to the date of death or, in the case of ongoing NIV therapy, to the 31st July in 2014.

### 2.3. Statistical analyses

Continuous data are presented as mean and standard deviation (SD) if normally distributed and as median and interquartile range (IQR) if non-normally distributed. Categorical data are presented as frequency counts and percentages. Comparisons between groups were performed with *t*-test, Kruskal–Wallis test, analysis of variance, or Mann–Whitney test, as appropriate. The Kaplan–Meier method, log-rank test and Cox regression were used for analysis of survival. Patients who discontinued their home-NIV during follow-up were censored at the point of treatment cessation. In all statistical tests the *p*-value  $< 0.05$  was considered significant. Analyses were performed with IBM SPSS (Armonk, NY, USA: IBM Corp) version 27.01.

## 3. Results

### 3.1. NIV setups

Home-NIV was implemented on 1,281 patients. For 58 patients (4.5 %) NIV was restarted once and 4 patients went through three NIV setups. The device type was changed in 66 patients with novel set up on NIV, for some more than once. Yearly NIV setups increased during the study period: from 43 in year 2004 to 186 during the last year of the study (data not shown).

### 3.2. Patients and diagnostic groups

Majority of the patients were males, on average 68 years of age at onset. Most of the patients were overweight or obese and had a history of tobacco smoking (Table 1). Long term oxygen therapy was used in 193 (15 %) of the patients at the time of NIV setup. Twenty eight percent ( $N = 361$ ) of all patients had an acute contributing factor at the implementation of home-NIV. Twenty three percent ( $N = 75$ ) of these were SA patients. The most common causes for acute deterioration at the time of NIV setup were acute exacerbation of COPD, deterioration of cardiac insufficiency or pneumonia.

Most prevalent diseases causing CRF were SA (26 %), OAD (16 %), OHS (11 %) and NMD (10 %) (Fig. 1). Ninety five percent of the patients in the OAD group had COPD, while asthma and bronchiectasis accounted for the remaining 5 %. Amyotrophic lateral sclerosis (ALS) accounted for 50 % of the NMD group, and 38 % of all neuromuscular diagnoses, when multimorbid patients were taken into account (Supplementary Table A). Multiple aetiologies for CRF were found in 219 (17 %) patients, of which 177 (81 %) had SA. Combinations of OAD-SA and NMD-SA were the most frequent (Table 2). OAD coexisting with another cause of CRF was the most common of the diagnostic combinations without SA.

### 3.3. Ventilator settings

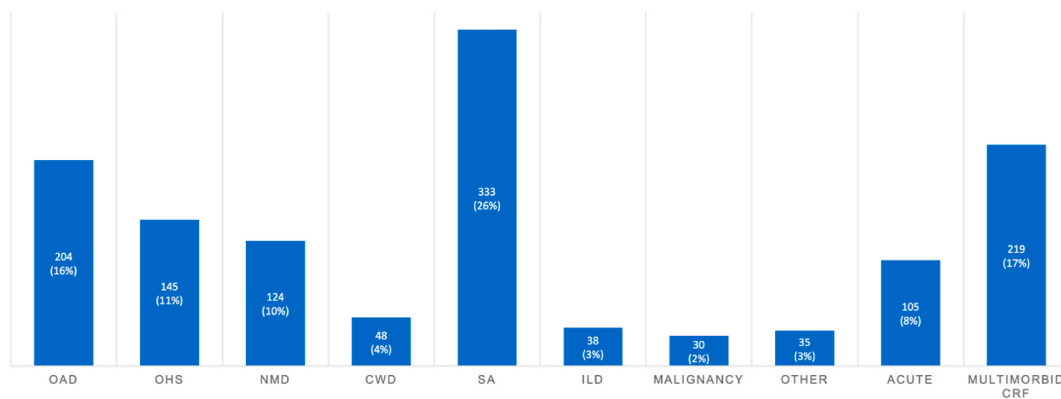
Mean IPAP for bilevel NIV slightly increased from  $15 \pm 4$  cmH<sub>2</sub>O at setup to  $16 \pm 4$  cmH<sub>2</sub>O at the time of the last control visit ( $p < 0.001$ ). Mean EPAP was  $7 \pm 2$  cmH<sub>2</sub>O at setup and  $7 \pm 3$  cmH<sub>2</sub>O at the last control ( $p < 0.001$ ). IPAP and EPAP pressures were

**Table 1**  
Baseline demographics of the study population.

	N = 1,281
Age, Median (IQR) (years)	68 (60–76)
<b>Gender</b>	
Male, n (%)	774 (60.4)
Female, n (%)	507 (39.6)
<b>Body mass index, Mean (SD) (kg/m<sup>2</sup>)<sup>a</sup></b>	32.8 ( $\pm 9.9$ )
<25, n (%)	200 (23.4)
25 - 35, n (%)	337 (39.5)
>35, n (%)	317 (37.1)
<b>Smoking status, n (%)</b>	
Never smoker	348 (27.1)
Ex-smoker	500 (39.0)
Current smoker	311 (24.3)
Not known	122 (9.5)

Continuous variables are presented as mean  $\pm$  SD or median and IQR.

<sup>a</sup> Data missing from 427 subjects at baseline.



**Fig. 1.** Number of patients in the study cohort starting home non-invasive ventilation (NIV) per diagnostic category (total N = 1,281), and the number of multimorbid CRF patients in the entire cohort. OAD, obstructive airway disease; OHS, obesity hypoventilation syndrome; NMD, neuromuscular diseases; CWD, chest wall diseases; SA, sleep apnoea; ILD, interstitial lung disease; Malignancy, palliative NIV for patients with thoracic malignancy; Other, another disease leading to CRF; Acute, NIV because of acute illness; Multimorbid CRF, CRF of multiple aetiologies.

**Table 2**  
CRF of multiple aetiologies.

Diagnostic combinations	N = 219 (%)
OAD-SA	57 [26]
NMD-SA	55 [25]
CWD-SA	23 [11]
ILD-SA	18 [8]
OAD-ILD	14 [6]
Other-SA	8 [4]
OAD-Malignancy	7 [3]
SA-OAD-ILD	6 [3]
OAD-CWD	5 [2]
ILD-CWD	4 [2]
Malignancy-SA	4 [2]
OAD-Other	4 [2]
Other rare diagnostic combinations	14 [6]

significantly increased between the setup and the last control in groups OAD, OHS, CWD, SA, other and multimorbid CRF ( $P < 0.05$ ) (Supplementary Fig. 1).

### 3.4. Adherence and duration of NIV treatment

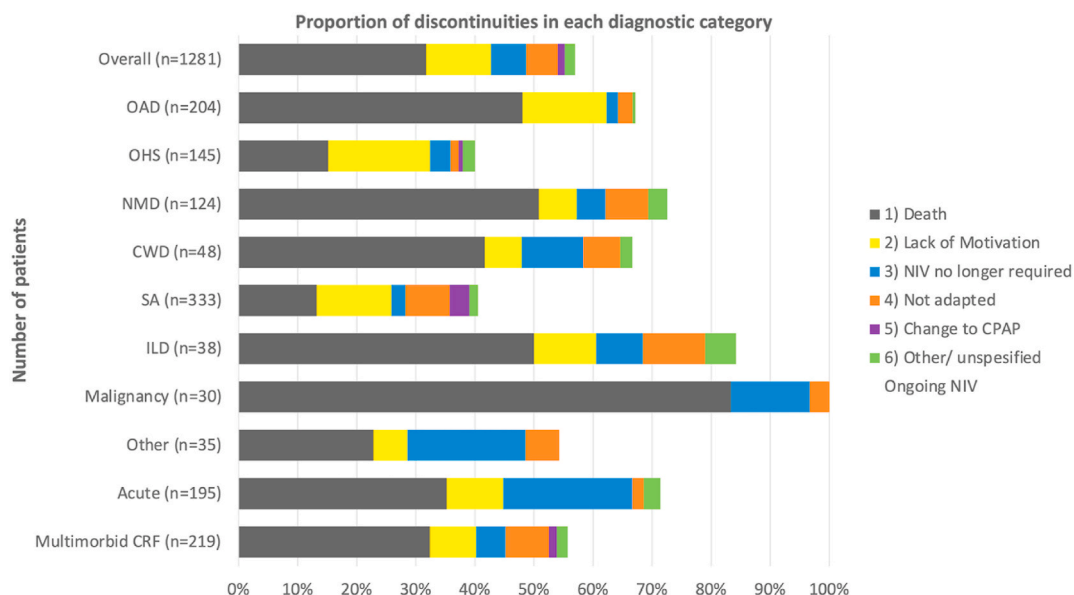
Data of daily NIV use was available for 1,037 patients (81.0 %). The overall NIV adherence was  $6.0 \pm 4.4$  h/d, and 66 % of the study population were classified as adherent, i.e. using NIV  $\geq 4$  h/d. Adherence varied according to the diagnostic category and the p-value for the differences across groups were  $<0.001$  for both mean and median daily NIV usage. Patients in the NMD, CWD, OAD and multimorbid CRF categories had best adherence, and acute the lowest. Median duration of the NIV treatment was 410 (120–1021) days and mean  $688 \pm 754$  days. OHS and SA groups had the longest treatment periods. Patients in the malignancy group had the shortest median treatment period of 46 days. There was a significant difference in the median duration of NIV treatment across the diagnostic categories ( $P < 0.001$ ) (Supplementary Table C). However, no significant differences were found in adherence or NIV treatment duration between patients with a single or multiple aetiologies of CRF.

### 3.5. Reasons for NIV discontinuation

NIV was discontinued in 730 cases during the follow-up period. Discontinuation rate at one year was 47 %. The most common reason for NIV cessation was death (56 %), followed by lack of motivation (19 %), NIV no longer required (10 %), not adapted to NIV (10 %), change to CPAP (2 %) and other reasons (3 %). Reasons for NIV cessations varied according to the underlying aetiology of CRF (Fig. 2).

### 3.6. Survival

After the implementation of NIV, median overall survival was 4.5 (95 % CI 3.6 to 5.4) years (Fig. 3). Survival analysis was also



**Fig. 2.** Reasons for discontinuing home NIV in the different diagnostic categories. OAD, obstructive airway disease; OHS, obesity hypoventilation syndrome; NMD, neuromuscular diseases; CWD, chest wall diseases; SA, sleep apnoea; ILD, interstitial lung disease; Malignancy, palliative NIV for patients with thoracic malignancy; Other, another disease leading to CRF; Acute, NIV because of acute illness; Multimorbid CRF, CRF of multiple aetiologies; CPAP, continuous positive airway pressure device.

performed excluding the malignancy and acute groups, since these groups were expected to bias survival of the study population. For this subgroup median survival was 5.4 (95 % CI 3.6 to 6.5) years.

Survival rate at 1 year was 79 % and at 5 years 49 %. There was a considerable difference in survival between the diagnostic groups ( $p < 0.001$ ) (Fig. 3A). SA and OHS groups had the best survival and median survival was not reached in these groups. Survival rate at 1 year and 5 years was 90 % and 75 % in SA, and 91 % and 68 % in OHS, respectively. Median survival for the OAD category was 2.7 (95 % CI 2.1 to 3.3) years and for the CWD category 2.2 (95 % CI 1.1 to 3.3) years. Median survival in the NMD category was 2.0 (95 % CI 1.3 to 2.6) years and in a subgroup analysis the survival of the ALS patients 1.0 (95 % CI 0.6 to 1.4) years and 7.2 (95 % CI 3.4 to 11.0) years for those with other NMD (data not shown).

Neither NIV adherence  $\geq 4$  h/d versus less ( $p = 0.427$ ) (Fig. 3B), nor the number of diseases contributing to CRF ( $p = 0.138$ ) (Fig. 3C) had an influence on survival. Kaplan-Meier survival analysis was even performed using a cut of value of adherence  $\geq 5$  h/d and excluding ILD, malignancy, other and acute groups, but no significant differences were seen in survival according to adherence. Cox regression analysis was conducted (with the variables of age  $>60$  years or  $\leq 60$  years, gender, BMI  $>30$  or  $\leq 30$  kg/m<sup>2</sup>, smoking, adherence and one or more causative diseases for CRF), but only age over 60 years (hazard ratio (HR) 3.2, 95 % CI 2.0–5.0,  $p < 0.001$ ) and BMI over 30 kg/m<sup>2</sup> (HR 0.4, 95 % CI 0.3–0.5,  $p < 0.001$ ) were associated with better survival.

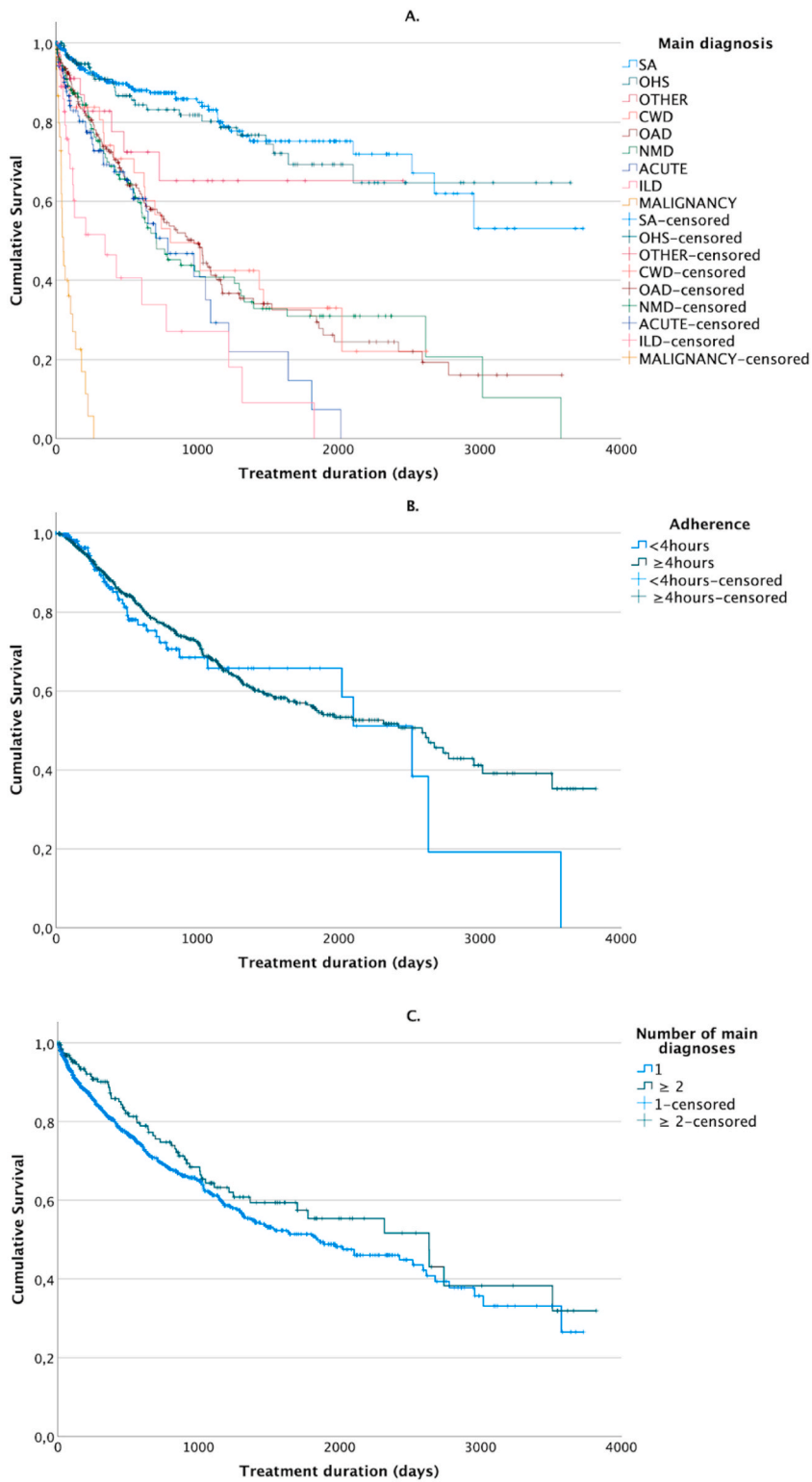
#### 4. Discussion

The present study is one of the largest long-term follow-up studies on CRF patients treated with home-NIV. To the best of our knowledge, it is the first to evaluate the effect of multiple aetiologies of CRF on the course of NIV treatment. In our study, 17 % of the patients had multiple aetiologies contributing to CRF. However, they did not significantly differ in terms of adherence to NIV treatment from those with a single causative disease of CRF.

Furthermore, against our hypothesis, patients with multiple aetiologies of CRF did not have a significantly different prognosis than the patients with only one disease causing CRF. This can reflect the overall poor prognosis of CRF as such, the effect of the NIV therapy, as well as the size and heterogeneity of the multimorbid patient group and sleep apnoea as the predominant comorbidity. Previously, CRF of multiple aetiologies has been identified mainly as the coexistence of OSA [25,26]. In our study SA was also the most common disease (81 %) contributing to the multimorbid CRF. Furthermore, NMD-SA was almost as frequent as OAD-SA. This is likely influenced by our categorization, as we were interested in the phenomenon of CRF of multiple aetiologies as a whole, and therefore did not generate a group of COPD-OSA overlap. Only advanced COPD with respiratory failure was included in our OAD group. Therefore, coexistence the OAD and SA in our study is not comparable to the general concept of COPD-OSA overlap, which may include also cases of less severe COPD.

Previous studies have also suggested high incidence of SA among NMD-patients treated with home-NIV [25]. Finally, the remaining 19 % of our multimorbid patients had another concomitant condition than SA leading to CRF. Therefore, CRF of multiple aetiologies is a clinically important finding beyond the COPD-OSA overlap.

The most common single causes of CRF were SA, OAD, OHS, and NMD. The distribution of the diagnostic categories is in line with



**Fig. 3.** Kaplan-Meier curve for survival in different diagnostic categories (A), according to NIV adherence (B) and according to the number of diseases causing CRF (C).

previous European studies [1,4,26,27] with the entity of SA being an exception. This could be explained by three major reasons. First, because of the retrospective setting of this study comprehensive information on all relevant variables, such as systematic baseline spirometry or blood gas in a stable phase of the underlying disease, was not available. Therefore, patients with SA were categorized as “SA only” even if airway obstruction or obesity might have substantially contributed to the respiratory failure. On the other hand, due to the classification method used, OAD and OHS groups are not likely to be biased because of hidden comorbidities. Second, our clinical practice is to offer a trial of NIV to SA patients with mild hypercapnia failing a CPAP trial. Third, the inclusion of patients treated with ASV probably increases the proportion of SA patients in our study, while ASV treatment option was not available [4] or patients treated with ASV were excluded [26] in previous studies. In our study population central apneas were most often caused by earlier stroke or heart failure. Use of opioids was not common.

Adherence to therapy differed by the underlying aetiology of CRF. Over 70 % of the patients were adherent in the categories of OAD, NMD, CWD, and multimorbid CRF. Overall adherence was comparable to the previous studies in Finland [27] and other European countries [4,26,28]. In ventilator settings IPAP and pressure support appeared slightly lower compared to the ones reported in the latest publications [26,28]. Moreover, the increase in treatment pressures seems minor, but it reflects our way of titrating pressure support until reversal of hypercapnia. However, lower treatment pressures could be one reason why we were not able to show improvement in survival for adherent patients, contrary to the findings of Patout and colleagues [26]. Other possible reasons are the heterogenic study population and the range of device types used during the long observation period. The choice of the 4 h daily NIV use as a cut off for good compliance can be debated. Evidence regarding survival in CRF is limited, but preliminary results refer to  $\geq 4$  h/d [26,29] or  $\geq 5$  h/d usage [30]. In our data, no survival benefit was observed for  $\geq 4$  or  $\geq 5$  h daily NIV usage.

In line with previous studies, survival differed considerably according to diagnostic categories [4,26,31]. Differences in categorizing do not allow in-depth comparing of survival between the studies. However, in our data survival for OAD patients was 2.7 years, 1.0 year for ALS patients and the median survival of the groups SA, OHS and other-NMD was considerably longer resembling the findings in previous studies [26,27,32].

Two lifestyle-related phenomena were highlighted: 63 % of the patients were current or ex-smokers, and over 75 % of the patients were overweight or obese. A few smaller studies have reported the percentage of smokers in patients with CRF treated with NIV [25,27,33]. Percentage of current or ex-smokers was similar to the findings of Tan [25] and Rantala [27]. The mean BMI in our study was comparable to earlier studies [27,28,31]. Obesity seemed to have a favourable effect on the survival as in some previous studies [26,30,34]. This ‘obesity paradox’ has also been identified in patients with established cardiovascular diseases, overweight or obese patients having better survival than lean patients [35]. Improved survival in our study is explained by a high proportion of patients with SA and OHS, as these groups had the best prognosis.

The main cause for the discontinuation of NIV was death (56 %). This reflects not only the poor prognosis of CRF, but also the palliative nature of home-NIV therapy. However, the underlying aetiology of CRF affected the reasons for NIV discontinuation. Lack of motivation was highlighted as a cause in the OHS and SA groups, and problems in adaptation to NIV in SA patients, which was in line with previous studies [4,27]. The proportions of patients discontinuing NIV because of poor adherence or no longer requiring NIV were in concordance with the previous European study [26].

This large, unselected real-life cohort provides a view to the diversity of patients on home-NIV. Only the study by Patout and colleagues has reported results from a larger cohort [26]. Our follow-up period of ten years is exceptionally long. However, there are several possible biases in this single centre study, and our retrospective setting causes several limitations. First, because of the absence of a standardized data collection protocol at the time of NIV setup, complete data was not available for all patients. Indications for NIV implementation were re-evaluated, but the changes in blood gases were not systematically recorded. We do not have data on the interfaces. However, it is unlikely to explain the differences between the groups since interfaces were selected and fitted individually and not based on the underlying aetiology of CRF. None of the patients used mouth piece ventilation. Second, the acute category can be criticized, because no specific disease causing CRF could be identified. Despite this, 35 % of the acute category patients used home-NIV until death, and NIV was ongoing in 29 % at the end of the study period – a finding that suggests the existence of an unidentified cause of CRF (data not shown). Third, lack of information on comorbidities and causes of death may affect the interpretation of survival analyses. Fourth, treatment pressures might be considered low. However, it should be taken into account that the ventilator settings used reflect the clinical practice from the beginning of the 21st century, and there has been a shift towards more intense ventilator settings thereafter. The study period from 2004 to 2014 was chosen because our standard operating procedures to start NIV remained quite stable during this period. Fifth, unfortunately we were not able to systematically report mode, backup rates, or other parameters as the recordings especially from the beginning of the study period were limited to usage hours, AHI and IPAP/EPAP. S/T mode was used in most patients but we do not have exact data on this.

In conclusion, CRF of multiple aetiologies presented one fifth of all home-NIV patients and was not limited to COPD-OSA overlap. However, CRF of multiple aetiologies did not significantly differ in terms of NIV adherence or survival from those with a single disease causing CRF. Smoking and overweight were common features among CRF patients. The most common reason for discontinuing NIV was death, reflecting the severity of the underlying diseases.

#### Ethics declaration list

Review and/or approval by an ethics committee was not needed for this study because it was not needed in registry studies according to prevailing Finnish legislation. The patients were anonymized after inclusion to the registry. The study was approved by the Clinical Research Centre of the Turku University Hospital (approval code T05/014/21). The research was conducted according to the principles of the World Medical Association Declaration of Helsinki.

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## Data availability statement

All relevant data are within the paper and its supplementary files.

## CRediT authorship contribution statement

**Salla Fagerudd:** Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Aino Lammintausta:** Writing – review & editing, Supervision, Software, Formal analysis, Data curation. **Tarja Laitinen:** Writing – review & editing, Supervision. **Ulla Anttalainen:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization. **Tarja Saaresranta:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e32508>.

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