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# Survival of patients on Home Mechanical Ventilation. A Nationwide Prospective Study.

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**Summary**

Home mechanical ventilation is increasingly used as a therapeutic option to patients with symptomatic chronic hypoventilation. There is, however, a paucity of solid data on factors that could affect prognosis in patients on home ventilation. In the present study our aim was to study several factors in these patients with potential influence on survival.

We examined 1526 adult patients from a nationwide home mechanical ventilation register to which data had been reported prospectively for ten years. The patients constituted a broad diagnostic spectrum and the primary outcome in this study was death.

We found by far the poorest survival rate in the ALS patients with only five percent alive after five years. Among the other patient groups the survival pattern was more uniform and the scoliosis, polio and Pickwick patients presented the best survival rate, after 5 years being around 75%. No factors were associated with a greater hazard for death in the ALS patients; in the non-ALS patients, however, negative predictors for survival were age, concomitant use of oxygen therapy, tracheostomy ventilation and start of ventilatory support in an acute clinical setting. Centre size or county specific home ventilation treatment prevalence did not affect survival.

In conclusion, in a large material of patients on home mechanical ventilation we found by far the poorest survival in the ALS patients. In the non-ALS patients a number of patient related factors affected survival, while the size of the treating centre or the regional treatment prevalence did not.

## Introduction

One important outcome of home mechanical ventilation (HMV) is survival. It has been suggested that HMV can prolong survival and improve quality of life in neuromuscular and chest wall disorders (1-5), whereas it may reduce symptoms of nocturnal hypoventilation and breathlessness in other situations (6). A consensus that HMV should be offered as a therapeutic option to patients with symptomatic chronic hypoventilation appears to prevail in the field although there are few randomized controlled trials to support this.

Some guidance regarding the usefulness of HMV can be derived from studies comparing survival with respect to diagnosis (7-10). There are however but a few studies comparing survival as regards patient related factors such as physiological and clinical data (3, 9). The impact of caregiver related factors such as centre size and regional treatment prevalence has only scarcely been addressed in previous studies (9, 11).

We wished to examine the relationship between survival (with diagnosis, age and gender taken into consideration) on the one hand and clinical features and method of receiving HMV on the other. We also asked if the size of the treating centre and the HMV treatment prevalence in the county did impact survival as a possible evidence of differences in caregiver experience. We hypothesized that larger centre size and/or higher treatment prevalence would be associated with longer survival.

## Methods

Our database was the Swedish Home Mechanical Ventilation Register (12, 13). Inclusion criteria: all Swedish patients prescribed long-term ventilation for domiciliary use. Patients using only CPAP for any purpose or ventilators for physiotherapy only were not included. For patients starting therapy after January 1st 1996 we prospectively register data on inter alia blood gases, concomitant oxygen therapy, ventilator interface, mode and daily duration of therapy, and acute vs. elective initiation of HMV. The register continuously obtains data on vital status and the dates of death from the Swedish Population Register.

In this study we analyzed only patients over the age of 18 years when starting HMV (N=1526) during the 10-year period 1996-2005. The primary outcome in this study was death (before March 15th 2006).

In the preliminary analysis of survival we divided the patients according to the underlying diagnoses into eight groups: 1. Pickwickian (in the register defined as sleep apnea syndrome with respiratory insufficiency), 2. Pulmonary disease (66% COPD patients), 3. Neurological disease other than amyotrophic lateral sclerosis (ALS), *i.e.* mainly patients with progressive neuromuscular disease (88%), 4. ALS, 5. Post-poliomyelitis syndrome, 6. Scoliosis, 7. Tuberculosis sequelae (TBC) and finally 8. Other diseases, a group consisting of patients with high cervical lesions, central hypoventilation and a medley of other diagnoses. In view of the pronounced difference in survival between the ALS and non-ALS patients and the small differences within the latter group, we joined the non-ALS patients as one group for further analyses.

Among the nearly 50 clinics that manage the treatment of HMV patients, we arbitrarily label as “big centres” those six clinics who reported more than 100 patients starting HMV during the almost ten years inclusion period. These centres cared for 55 % of the HMV patients. For at least eight years from register start, four counties out of the 26 counties in Sweden, (henceforward referred to as “top counties”), consistently presented a much higher HMV treatment prevalence compared to the rest (13). In these counties lived 26 % of the HMV patients. At the time of this analysis the top counties had a treatment prevalence of 22 per 100.000 in contrast to 14 for the rest.

The Swedish Data Inspection Board has approved the register and the Medical Ethics Committee at the University of Lund has approved the study. For statistical analyses we used the software STATISTICA version 7.1 to generate descriptive data and compile regression models and graphs. Cox’s proportional hazards regression model was used to assess the effects of patient and caregiver related factors on survival. P values less than 0.05 were considered as significant.

**Results**

The majority (75%) of the patients was ventilated during night-time only, 22% were ventilated 8-24 hours per day and a small proportion (3%) was ventilated in day-time only. Ventilatory support was in all cases delivered by intermittent positive pressure ventilators. From therapy start HMV was provided as non-invasive ventilation (NIV) via a mask in 91% and as tracheostomy invasive ventilation (TIV) in 6% (some missing data). Still, in the patients starting HMV electively 2% only were tracheostomised while this was the case in

19% of the acute patients. Information on transition from NIV to TIV (or the opposite) does not with certainty reach the register.

Demographic information and the distribution of patient/caregiver related factors in the diagnostic groups are displayed in table 1. Although the Pickwick group is by far the biggest of the eight diagnostic groups the neurological patients including ALS patients make a total of almost the same quantity as the Pickwick patients.

The distribution of the patient related factors with respect to the two caregiver related factors are shown in table 2. It can be seen that acute start of HMV and the use of concomitant oxygen were more frequent in small centres and in the counties with low HMV prevalence. Counties with low prescription rates of HMV also had a higher proportion of tracheostomies.

The survival of the entire material is shown in a Kaplan-Meier plot in figure 1. The ALS patients are evidently different from all other groups by having the poorest survival rate at all times; that is a probability to survive after 2 years of 20% and after 5 years of just above 5%. The relative risk for death in the ALS patients compared to all other patients was 8.02 (CI 6.48-9.92, $p<0.001$).

Among the remaining groups the pattern is more uniform; still, mutual differences are present *e.g.* the TBC patients' relative risk for death compared to the scoliosis patients was 1.91 (95% CI: 1.25-2.90, $p<0.01$).

The relationship between survival and the singled out patient and caregiver related factors when starting HMV is shown in table 3 and 4. Table 3 displays the univariable analyses for each factor in the ALS and non-ALS groups. None of the factors significantly affected survival in the ALS patients, we, therefore, proceeded to multivariable analysis in the non-ALS patients only (table 4).

As seen age was a significant factor for survival while gender was not. Among the patient related factors we found that concomitant oxygen therapy, TIV and acute start of HMV were independently associated with worse survival. Concerning the two caregiver related factors we found no relationship to survival.

**Discussion**

From a large material of adult patients on HMV recorded prospectively in a national register we have in this report presented 10 years survival data. We have shown that patients suffering from ALS at all times distinctly had the poorest probability to survive. Among the remaining patient groups differences in survival could be pointed out, the best long-term survival rates being twice as good as the poorest, but the overall picture was relatively homogeneous. We have, therefore, with respect to impact factors on survival analysed them as one group. Although this may be an oversimplification, it enables us to perform these analyses in a much larger and more comprehensive material. We looked at a number of patient related factors when HMV was launched and in the non-ALS patients we found that use of concomitant oxygen, tracheostomy invasive ventilation and start in an acute clinical setting were factors which were associated with a greater hazard for death. Although there were differences in clinical practice between small and big centres and

between high and average prevalence counties, these differences seemed to have no effects on survival.

In ALS previous studies have stated varying survival rates. In an early series of 101 patients (14) survival rates were 69% at 2 years and 33% at 5 years. These are considerably higher rates compared with more recent smaller studies and our report. Part of an explanation of this may be that all patients were on TIV, whereas this only applies to 5% of our ALS patients (at therapy start). TIV may be preferable in patients with severe paralyses, especially of bulbar nature. We also speculate that caregivers and relatives may be more hesitant to withdraw TIV than NIV (15). In another study (16) including 122 patients, 38 used NIV more than 4 h/day and had a survival rate after 2 years just below 20%, which is very close to the findings in our study. In a control group consisting of 52 patients who renounced ventilatory support, none were alive after 2 years. In a recent study (3) one group of ALS patients showed a survival rate similar to our findings, while survival was better in another group that underwent early systematic respiratory evaluation (a caregiver related factor). In our study we were unable to demonstrate any factors affecting survival in the ALS patients, besides the diagnosis itself. This indicates that the rapid loss of motor neuron function in ALS overshadows the relatively strong prognostic factors in the non-ALS group.

Hypoxia as well as need of concomitant oxygen have previously been depicted as factors that were related to poor survival in HMV (9, 17). We could not confirm that hypoxia is a significant factor probably because hypoxia in many cases is corrected by HMV (18). On the other hand we could confirm that the use of concomitant oxygen was associated with

worse prognosis indicating that these two factors are not equivalent. The use of concomitant oxygen may reflect a component of pulmonary parenchymal disease (with worse prognosis). However, the interpretation that it reflects suboptimal ventilator therapy remains a possibility. Smaller centres with less experience may be more prone to correct hypoxemia with oxygen than to adjust the ventilator settings to achieve the desired therapy goal. Furthermore, launch of HMV in an acute clinical setting involved a greater risk for death, a fact Duiverman et. al. (10) found in a miscellaneous group of 20 mainly tuberculosis sequelae patients as well.

An explanation of why acute start of HMV, use of concomitant oxygen and TIV were more frequent in small centres and in the counties with low HMV prevalence may be that clinical procedures and follow up prior to HMV start were less extensive compared to that in big centres or top counties. This may result in more patients embarking on ventilatory support in an emergent situation and in turn entailing more patients starting this as TIV. Need of concomitant oxygen at HMV start may be related to this scenario or may reflect suboptimal ventilator therapy as discussed above.

Most studies of to day report outcome of HMV delivered as NIV. In this study 98 patients (6%) from start were embarked upon TIV and this was coupled with a greater risk for death which may not be surprising as one might claim that the disease severity was more profound in these patients. On the other hand, as we discussed above in the ALS patients, tracheostomy per se should not necessarily imply shorter survival and in some patients TIV is more feasible compared to NIV. Post polio and scoliosis patients on TIV have, furthermore, been reported to perceive better health compared to NIV for these diagnoses

(19). It is, however, a weakness of our study that the register contain no certain documentation on transition from NIV to TIV, yet our assumption is that this was performed in less than 10% of all patients and most often in the neurological patients.

One could expect that treatment in big centres with a much greater patient flow or in centres with more consistent follow up procedures resulted in a better outcome, but in our report this was not the case. One study has shown a possible connection to consistent procedures (9) as the survival was better in the patients (primarily on LTOT) with complete data of respiratory function. On the other hand if the patient selection in the centres is biased according to local expertise and tradition, most of the centres, small or big, might have worked up a somewhat uniform quality of care for the patients once HMV has been started. We have, furthermore, previously shown (13) that with regard to elective patients the counties with high treatment prevalence had as strict indications to launch HMV as all other counties, demonstrating that disease severity at HMV launch is quite homogeneous in Sweden. As regards centre size and treatment prevalence our hypothesis was that “big is better”, a notion we can turn down and recast to “size doesn’t matter”.

In conclusion, in a large material of adult HMV patients, the ALS group had by far the poorest survival rate. Survival was roughly in line with that in previous studies and predictors of increased risk for death in non-ALS patients were greater age, use of supplemental oxygen treatment, tracheostomy ventilation and launch of HMV in an emergent clinical setting. The relative risk for death was not affected by the size of the treating centre and the treatment prevalence in the county.

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**Table 1**

Primary data in 1526 adults starting HMV.

| | Pickwick | Pulmonary | Neuromusc | ALS | Post-polio | Scoliosis | TBC | Other |
|---|---|---|---|---|---|---|---|---|
| N (% of all patients) | 422 (28) | 251 (16) | 224 (15) | 165 (11) | 141 (9) | 123 (8) | 98 (6) | 102 (7) |
| Start age (SD) | 61 (11.2) | 63 (11.5) | 49 (16.2) | 64 (10.5) | 67 (9.1) | 62 (13.2) | 73(6.0) | 56 (16.2) |
| Age > 75 years (%) | 7 | 11 | 3 | 13 | 18 | 18 | 41 | 12 |
| Male gender (%) | 56 | 37 | 58 | 68 | 48 | 36 | 41 | 58 |
| $PaCO_2$ (SD) | 7.1 (1.3) | 7.7 (1.6) | 7.3 (1.7) | 6.6 (1.4) | 7.1 (1.3) | 7.5 (1.3) | 7.6 (1.0) | 7.2 (1.6) |
| $PaO_2$ (SD) | 7.5 (1.5) | 7.4 (1.8) | 9.0 (2.0) | 9.7 (1.7) | 8.3 (1.4) | 7.7 (1.8) | 7.4 (1.3) | 8.0 (2.2) |
| $PaO_2$ < 7.4 kPa (%) | 49 | 53 | 22 | 8 | 22 | 42 | 49 | 37 |
| Acute start (%) | 31 | 33 | 32 | 17 | 19 | 27 | 19 | 39 |
| TIV (%) | 1 | 4 | 19 | 4 | 8 | 3 | 2 | 21 |
| Big centre (%) | 53 | 54 | 57 | 70 | 57 | 44 | 61 | 44 |
| Top county (%) | 33 | 31 | 25 | 10 | 12 | 24 | 43 | 19 |

Arterial blood gases were obtained in elective patients only. Big centre (%) is the fraction of the patients cared for by big centres. Top county (%) is the fraction of the patients living in one of the four high treatment prevalence counties.

TIV: tracheostomy invasive ventilation.

**Table 2**

Percentage distribution of patient related factors at HMV initiation with respect to the two caregiver related factors.

| | Big centre | | | Top county | | |
|---|---|---|---|---|---|---|
| | Yes | No | | Yes | No | |
| Age > 75 years | 12 | 12 | | 14 | 12 | |
| Male gender | 54 | 48 | | 53 | 51 | |
| Concomitant $O_2$ | 15 | 31 | *** | 15 | 25 | *** |
| $PaO_2$ < 7.4 kPa | 40 | 37 | | 43 | 37 | |
| Acute start | 22 | 37 | *** | 24 | 30 | * |
| TIV | 6 | 8 | | 3 | 8 | ** |

TIV: tracheostomy invasive ventilation.

* p<0.05, ** p<0.01, *** p<0.001.

Table 3

Univariable analyses of relative risk for death in the ALS and non-ALS patients.

| | **ALS** | **Non-ALS** |
|---|---|---|
| Age > 75 years | 1.30<br>0.77 – 2.21 | 2.05 ***<br>1.61 -2.62 |
| Male gender | 0,79<br>0,54 – 1,16 | 0.92<br>0.76 – 1.10 |
| Concomitant $O_2$ | 2,0<br>0.89 – 4.61 | 1.85 ***<br>1.52 – 2.25 |
| $PaO_2$ < 7.4 kPa | 0.78<br>0.31 – 1.98 | 1.27 *<br>1.04 – 1.56 |
| Acute start | 1.29<br>0.83 – 2.03 | 1.76 ***<br>1.45 – 2.13 |
| TIV | 0.70<br>0.28 – 1.71 | 1.51 **<br>1.12 – 2.03 |
| Big centre | 1.31<br>0.88 – 1.95 | 0.86<br>0.72 – 1.03 |
| Top county | 1.02<br>0.59 – 1.75 | 1.13<br>0.93 – 1.37 |

Each cell shows on top the Hazard Ratio and below the 95% confidence intervals.

TIV: tracheostomy invasive ventilation.

* p<0.05, ** p<0.01, *** p<0.001.

Table 4

Multivariable analyses of relative risk for death in the non-ALS patients

| | |
|---|---|
| Age > 75 years | 2.05 ***<br>1.55 – 2.70 |
| Male gender | 1.06<br>0.86 – 1.31 |
| Concomitant $O_2$ | 1.63 ***<br>1.27 – 2.10 |
| $PaO_2$ < 7.4 kPa | 1.04<br>0.83 – 1.30 |
| Acute start | 1.79 ***<br>1.19 – 2.70 |
| TIV | 1.79 **<br>1.19 – 2.68 |
| Big centre | 1.03<br>0.83 – 1.27 |
| Top county | 1.22<br>0.97 – 1.52 |

Legend as in table 3.

Legend to Figure 1

Probability to survive in 1526 adult patients after starting HMV.