Monitoring the efficacy of home mechanical ventilation

PhD thesis

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INTRODUCTION

Home mechanical ventilation (HMV) is an established mode of treatment for patients with chronic respiratory failure, resulting in increased survival, reduced costs, infection rates, optimized medical care utilization and improved health-related quality of life (HRQL).

Use of HMV differs greatly in different parts of the world, with prevalence ranging from 2.9 to 12.9/100,000. Noninvasive techniques have been gaining ground even for the treatment of individuals who require 24-hour ventilation and now account for 72-97% of HMV cases.

Until recently, there has been no published data on HMV in Hungary, although the practice has been established since the 1990's. Extrapolation from the overall European prevalence of HMV would estimate about 650 patients.

HMV guidelines include evidence-based lists of indications and clearly defined, disease specific diagnostic algorithms, but treatment goals are less well established and practice varies greatly in different regions. There is a logical aim to develop evidence-based treatment goals and follow-up algorithms that are based on adequate

monitoring of efficacy of therapy. For this purpose, markers of efficacy of HMV have to be defined, but classic markers of ventilation and respiration, such as blood gas parameters, pulmonary function parameters and respiratory parameters have poor correlation with actual outcome and efficacy of therapy. On the other hand, HRQL improvement has been proven to be associated with outcome, hence it's a possible marker of efficacy and important tool for quality control and optimization of therapy.

OBJECTIVES

The aim of this thesis is to establish HRQL as a possible prospective marker for efficacy of HMV, by observing HRQL patterns after 6 months of optimal clinical care on a real-life HMV patient population. In order to conduct the study and interpret the results for a general HMV population, I first aimed to evaluate Hungarian HMV practice and validate the Hungarian version of the Severe Respiratory Insufficiency Questionnaire (SRIQ), the most widely used HRQL tool for chronic respiratory patients.

METHODS

For the first study we conducted a nationwide investigation in Hungary using an online survey focusing on HMV. Intensive care units, pulmonology centers and pediatric centers were invited, questions focused on HMV experience, number of patients treated and characteristics of practice.

For the second study, we created and validated the Hungarian version of the SRIQ, a self-administered HRQL tool with 7 scales (RC: respiratory complaints, PF: physical functioning, AS: attendant symptoms and sleep, SR: social relationships, AX: anxiety, WB: psychosocial well-being, SF: social functioning, SS: summary scale). The Hungarian version, created with the translation-backtranslation method, was tested for validity, viability and reliability in a large cohort of adult, stable chronic respiratory failure patients receiving HMV. Patients were recruited through the Semmelweis University Home Mechanical Ventilation Program, the Department of Pulmonology of Semmelweis University and the Department of Neurology of the Hungarian Army Medical

Center. Patients completed the Hungarian SRIQ and the 36 Item Short Form (SF-36) Questionnaires and repeated the SRIQ a week after enrollment to verify reproducibility. Viability was studied by time spent on the questionnaire, ability to self-administer the questionnaire and the missing item rate. Validity was determined by exploratory factor analysis of the 49 items in SRIQ, subsequent confirmatory factor analysis of subscales and by comparing the corresponding scales of the SRI with the Hungarian SF-36 already in use. Reliability was determined by testing the internal consistency using the Cronbach alpha coefficient. Reproducibility was assessed by correlation of the results of the questionnaires submitted by the same patient at different time points.

For the third, prospective observational follow-up study we evaluated HRQL change using the SRIQ six months after initiation of HMV in a real-life, large case mix population. We enrolled patients through the Semmelweis University Home Mechanical Ventilation Program, were HMV was initiated with patient tailored ventilation plans and equipment supply. Treatment goals were

normalization of p_aCO_2 and p_aO_2 levels and adequate respiratory secretion management. Optimal care was achieved by frequent physician follow-up.

Demographic data, treatment characteristics, arterial blood gas values and lung function tests were collected at baseline, ventilator settings and blood gas values (if feasible) were collected at 6 months. HRQL was assessed at baseline and 6 months after initiation of HMV.

Data are represented as median (interquartile range) and n (%) for the first study and mean (±standard deviation) and n (%) for the following studies. Analysis was done using the Chi-squared test, the paired Student t-test, the analysis of variance (ANOVA) test and Pearson correlation. Factor analysis was performed, using the principal component method with a varimax rotation, using an eigenvalue >1 for extraction.

RESULTS

Home mechanical ventilation in Hungary

Out of 117 potential sites, 33.3% (39 sites) responded. 17 sites reported a total of 384 patients, corresponding to an

overall prevalence of 3.9/100,000 for HMV in Hungary. 10.4% (40) of patients received invasive, while 89.6% (344) received noninvasive ventilation. 93.2% of patients were treated by four sites that had a patient number of >50. When comparing sites, we found that sites with a substantial case number were more likely to be pulmonology affiliated (p=0.003), use predominantly noninvasive ventilation (p=0.001), with their most common diagnosis being central hypopnea (62.3%). Sites with a limited patient number were more likely to be intensive care unit affiliated (p=0.003), ventilating invasively (p<0.001) (Figure 1).

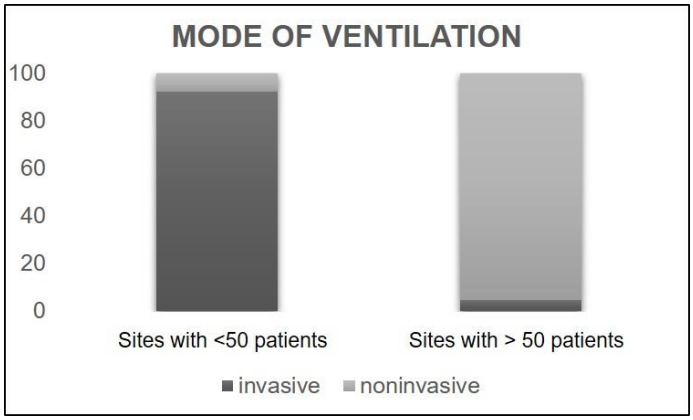

Figure 1. Distribution of mode of ventilation: *Y axis shows percentage of patients. First column shows data from sites that care for less than 50 patients, the second column shows data from units that care for more than 50 patients. Dark shading shows patients ventilated invasively, lighter shading shows patients ventilated noninvasively.*

Prevalence for different indications is shown on Figure 2.

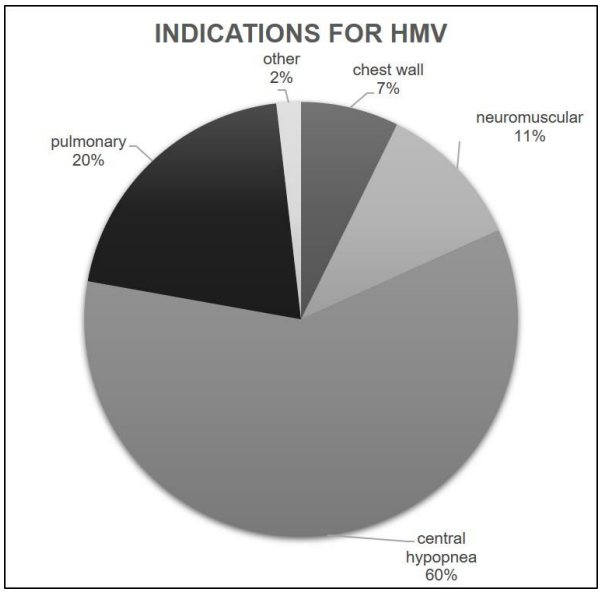

Figure 2. Pie chart of prevalence of indications for HMV

Daily ventilation need was less than 8 hours in 74.2% of reported patients, higher ventilation need (>16 hours/day) was more common in patients treated by a site with limited case numbers (80% vs. 5.6%, $p<0.001$). Duration of HMV was most commonly 1-5 years (50.1%), follow-up was ambulatory in 86.6% of cases, but home visits were more frequent at sites with limited case number compared to sites with a substantial case numbers (96.2% vs. 7.2%, $p<0.001$).

Validation of the Hungarian version of the Severe Respiratory Questionnaire

104 patients completed the study. Mean age was 54.5 (±16.2) years, 77 (74.0%) patients were male. Indication for HMV was chronic obstructive pulmonary disease (COPD) in 20 (19.2%), restrictive chest wall disease (RCWD) in 6 (5.8%), obstructive sleep apnea or obesity hypoventilation syndrome (OSA/OHS) in 45 (43.3%) and neuromuscular disease (NMD) in 31 (29.8%) patients, while two patients (1.9%) suffered from other causes. 14 patients (13.5%) were ventilated through a tracheostomy. Patients received HMV for a mean of 9 (±4.8) hours per day, and they had been using HMV for 26.2 (±32.7) months. O_2 supplementation was used in 46 (44.2%) cases. The time to complete the SRI was the same as the time for the SF-36 (p=0.587). 72 (69.2%) questionnaires were self-administered. Overall missing items were 0.2 (±0.6), all questions were answered by 96-100% of patients.

Exploratory factor analysis explained 73.8% of the variance of the questionnaire, but it resulted in 13 scales. Confirmatory factor analysis for the 7 subscales showed

one component for one, two components for five and three components for one of the subscales, with components showing significant correlations. Correlation between corresponding SRIQ and SF-36 scales was significant.

The Cronbach alpha coefficient was 0.928 for the summary scale of the Hungarian SRI Questionnaire.

Reproducibility was high for most scales, resulting in a high overall correlation for the summary score (0.877, $p<0.001$).

Monitoring the efficacy of home mechanical ventilation through quality of life change

Out of the 75 patients enrolled, 66 completed the study. Mean age was 51.5 (±18.1), 69.7% were male, 21.2% were ventilated invasively, while 78.8% received noninvasive ventilation. Initiation of ventilation was after an acute episode in 60.6%, the rest were started on HMV electively.

Invasively ventilated patients had higher daily ventilation need (17.9 (±6.5) vs. 11.1 (±5.8) hours, $p<0.001$), lower FVC% (31.5 (±23.3) vs. 51.1 (±20.3), $p=0.004$) and PEF% (23.9 (±20.9) vs. 39.6 (±19.4), $p=0.013$) values, but had

corrected blood gas parameters (pO_2: 78.4 (±16.8) vs. 67.4 (±12.7) mmHg, p=0.016; pCO_2: 36.2 (±7.3) vs 53.2 (±17.7) mmHg, p=0.001) compared to noninvasively ventilated patients at baseline. Patients initiated after acute hospitalization had no significant differences in baseline clinical measurements compared to those enrolled electively.

Compliance remained stable during the study duration (>80% daily required ventilation use in 100% of patients), with slightly diminishing daily ventilator use at six months (12.6 (±6.6) vs 11.2 (±6.6) hours, p<0.001). Blood gas parameters showed improvement from baseline values (pO_2: 69.7 (±14.2) vs 73.7 (±14.3) mmHg, p=0.011; pCO_2: 49.7 (±17.5) vs 45.1 (±11.4) mmHg, p=0.005; HCO_3: 28.0 (±5.2) vs 26.9 (±3.3) mmol/L, p=0.038), despite decrease in O_2 supplement use (1.8 (±2.8) vs 1.3 (±2.2) L/min, p=0.011).

Overall SRI score was 57.7 (±14.4) and several subscales showed values under 60, corresponding to limited HRQL (Figure 3). Baseline SRI-AS and -AX subscales were significantly associated with initial diagnosis (p=0.048 and

p=0.018 respectively). The SRI-AS scores were the lowest in OHS and ALS patients, while SRI-AX scores were the lowest in COPD and ALS patients (Figure 3).

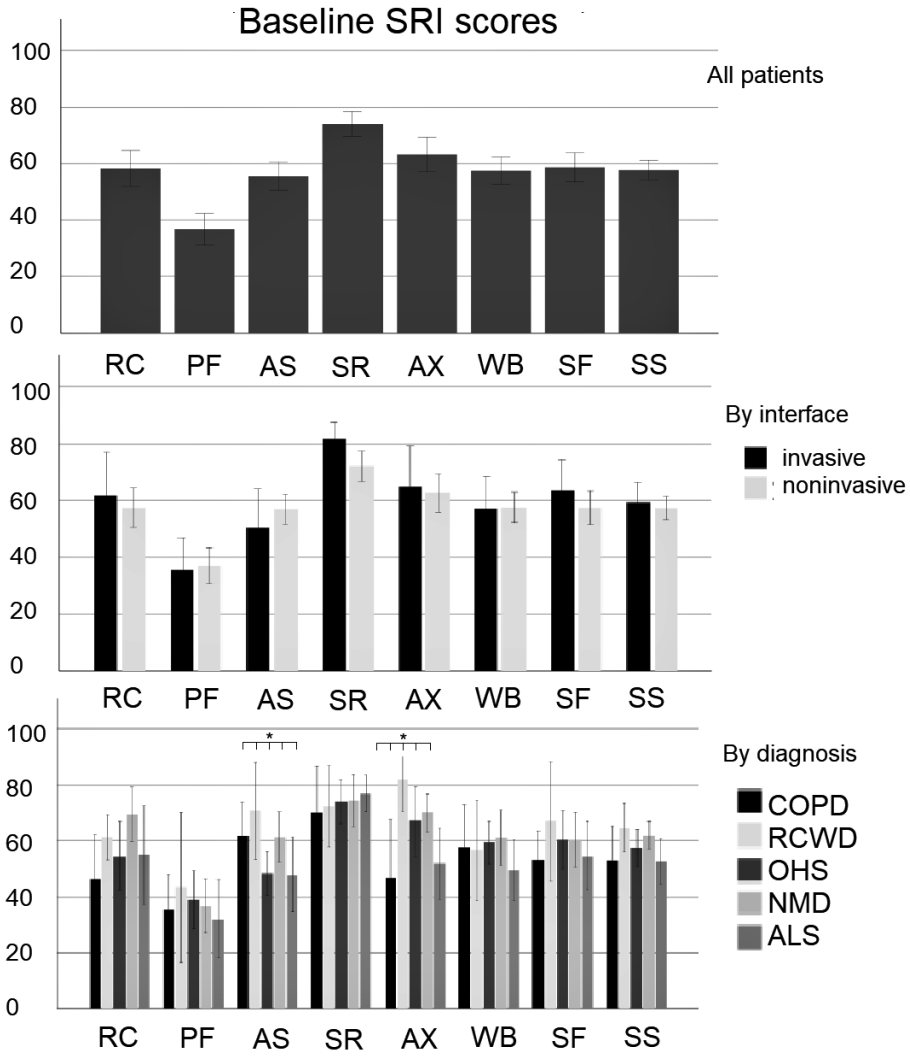

Figure 3. Bar graphs of baseline scores of the SRI subscales for the whole study group, by interface and by diagnosis: *Boxes represent means, error bars represent standard error. Significant differences are marked with asterisk. COPD - chronic obstructive pulmonary disease, RCWD - restrictive chest wall disease, OHS - obesity hypoventilation syndrome, NMD - neuromuscular disease, ALS - amyotrophic lateral sclerosis, RC - Respiratory complaints, PF - Physical functioning, AS - Attendant symptoms and sleep, SR - Social relationships,*

AX - Anxiety WB - Psychological well-being, SF - Social functioning, SS - Summary Score

There was no difference in baseline SRI scores in patients initiated acutely compared to those initiated electively. There was an 10.5% overall improvement of SRI summary scores from baseline to six-months [57.7 (±14.4) vs. 68.2 (±15.8), $p<0.001$]. All SRI subscales showed significant improvement after initiation of HMV.

Interface did not affect change in SRI subscales ($p=0.660$). Changes in SRI-RC, -PF, -SF and -SS subscales were significantly influenced by initial diagnosis ($p=0.025$, $p<0.001$, $p=0.002$ and $p=0.025$ respectively) (Figure 4). When further analyzing HRQL changes within diagnostic groups, we found that different diagnostic groups had different HRQL change patterns, which is visualized in the bubble chart depicting relative changes in different patient groups (Figure 5).

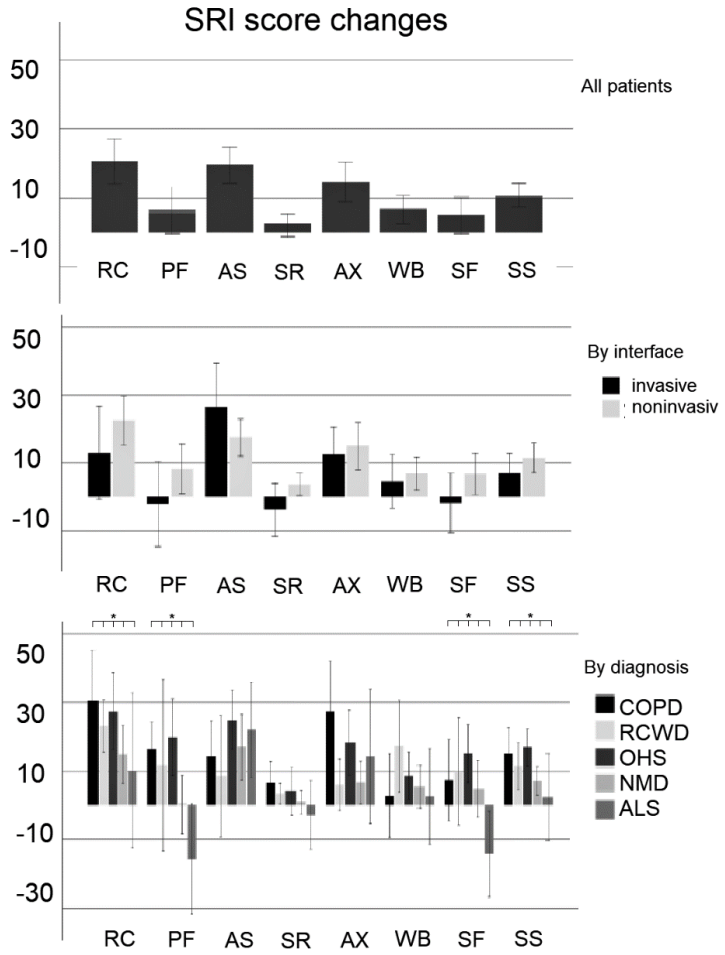

Figure 4. Bar graphs of changes in the scores of SRI subscales at the 6-month follow-up in the whole study group, by interface and by diagnostic groups: *Boxes represent means, error bars represent standard error. Significant differences are marked with asterisk. COPD - chronic obstructive pulmonary disease, RCWD - restrictive chest wall disease, OHS - obesity hypoventilation syndrome, NMD - neuromuscular disease, ALS - amyotrophic lateral sclerosis, RC - Respiratory complaints, PF - Physical functioning, AS - Attendant symptoms and sleep, SR - Social relationships, AX - Anxiety WB - Psychological well-being, SF - Social functioning, SS - Summary Score*

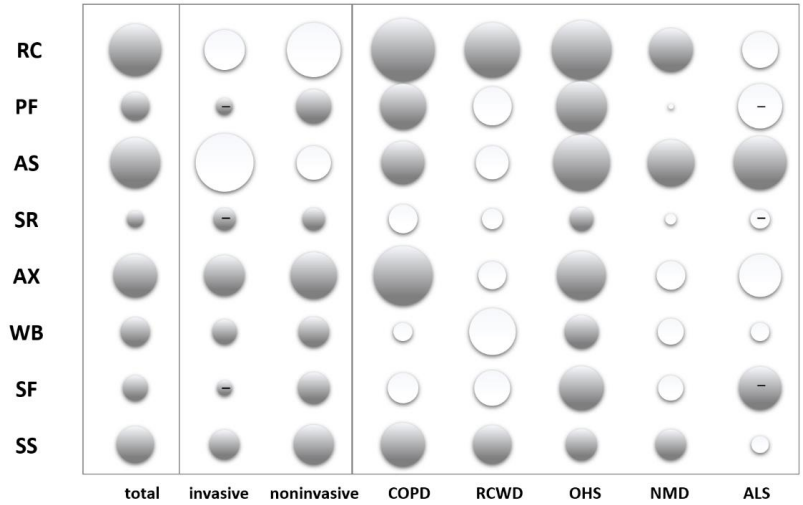

Figure 5. Bubble chart of SRI subscale changes for the whole study group and according to interface and diagnosis after 6 months of home mechanical ventilation:

Size corresponds to value of change from baseline. Significant changes are marked with gray shading. Negative changes are marked by negative sign pattern. COPD - chronic obstructive pulmonary disease, RCWD - restrictive chest wall disease, OHS - obesity hypoventilation syndrome, NMD - neuromuscular disease, ALS - amyotrophic lateral sclerosis, RC - Respiratory complaints, PF - Physical functioning, AS - Attendant symptoms and sleep, SR - Social relationships, AX - Anxiety WB - Psychological well-being, SF - Social functioning, SS - Summary Score

Overall SRI-SS scores improved in all patient groups except for ALS, the patients benefiting most were COPD patients, while OHS patients improved across the most SRI subscales. SRI-RC subscale improved in all groups but ALS patients, and most prominently in COPD and OHS patients.

HRQL improvement was higher in patients initiated acutely compared to patients initiated electively [12.3 (±16.8) vs. 7.4 (±9.4), p=0.029] and in patients using O_2 supplementation compared to patients that did not [12.0 (±15.6) vs. 9.0 (±13.8), p=0.006]. Patients with worse baseline scores improved more, most prominently seen for SRI-RC and SRI-AS scales (Figure 6).

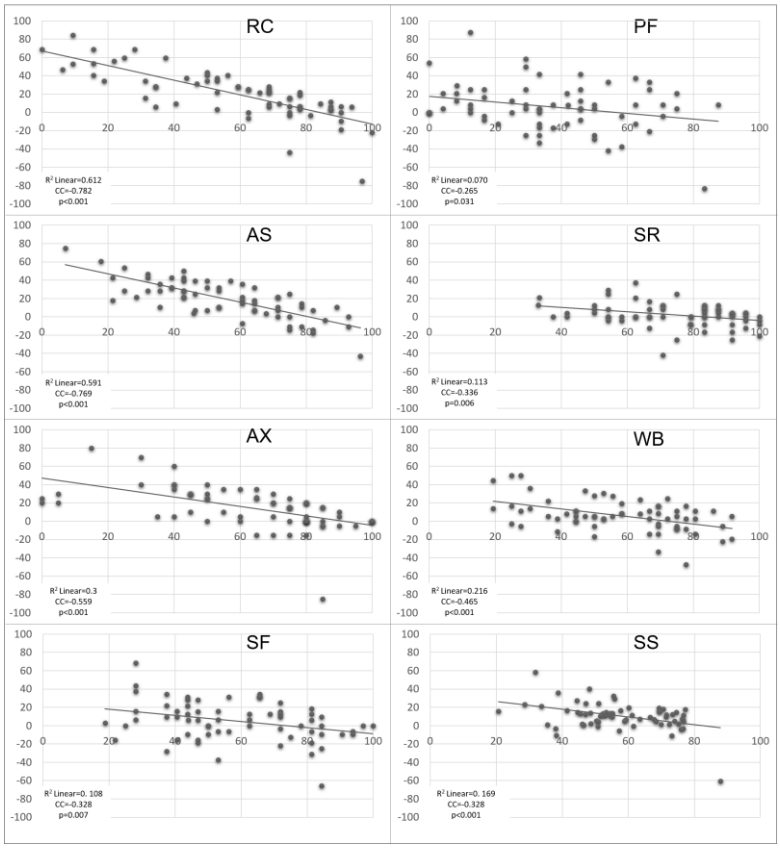

Figure 6. Subscale changes in relation to baseline subscales: *Scatterplot of SRI subscale changes according to initial SRI values. X axis shows change of SRI subscale. Y axis shows initial SRI subscale value. R^2Linear - coefficient of determination, CC - correlation coefficient, RC - Respiratory complaints, PF - Physical functioning, AS - Attendant symptoms and sleep, SR - Social relationships, AX - Anxiety WB - Psychological well-being, SF - Social functioning, SS - Summary Score*

CONCLUSION

1. Our results show a 3.9/100,000 prevalence of HMV in Hungary. Although a growing practice can be assumed, this is markedly reduced compared to previously reported international data.
2. We found that sites treating a substantial case number were pulmonology affiliated, using noninvasive techniques for less dependent patients, while sites treating a limited number of patients were intensive care units overseeing dependent, invasively ventilated patients.
3. We uncovered a possible gap in diagnosis and care for more dependent patients that could be managed with noninvasive techniques, possibly accounting for the relatively low prevalence.
4. We created the Hungarian version of the SRI Questionnaire, which was found to be a viable, valid, reliable and reproduceable HRQL tool applicable for Hungarian patients.
5. Regarding monitoring the efficacy of HMV in a real-life population, we found that initiation of treatment

is accompanied by improved HRQL in several patient groups suffering from chronic respiratory failure.

6. Our findings suggest that HRQL improvement is independent of classic markers of the severity of chronic respiratory failure or interface used for ventilation, but it is dependent on the type of disease causing the chronic respiratory failure, initiation type, initial HRQL and O_2 supplementation need.
7. Our results further suggest that acutely initiated, O_2 dependent COPD and OHS patients with low initial HRQL can expect the most benefit, while ALS patients can expect maintenance of overall HRQL despite ongoing neurological deterioration.
8. Finally, our results can provide a reference for expected HRQL change with optimal HMV management.

LIST OF PUBLICATIONS

Publications included in the thesis

1. **Valkó L**, Baglyas S, Gál J, Lorx A. (2018) National survey: current prevalence and characteristics of home mechanical ventilation in Hungary. BMC Pulm Med, 18: 190. **IF: 2.184**
2. **Valkó L**, Baglyas S, Kunos L, Terray-Horváth A, Lorx A, Gál J, Windisch W. (2020) Validation of the Hungarian version of the SRI Questionnaire. BMC Pulm Med, 20: 130. **IF: 2.813**
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4. **Valkó L**, Baglyas S, Gyarmathy VA, Gal J, Lorx A. (2020) Home mechanical ventilation: quality of life patterns after six months of treatment. BMC Pulm Med, 20: 221. **IF: 2.813**

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9. Csósza G, **Valkó L**, Baglyas S, Losonczy G, Lorx A, Gál J, Karlócai K. (2019). Mellkasdeformitás okozta pulmonalis hipertónia oki kezelése. Card Hung, 49(3): 184-18.