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Factors associated with change in health-related quality of life among individuals treated with long-term mechanical ventilation, a 6-year follow-up study

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Abstract

Aims: To examine changes and explanatory variables for changes in health-related quality of life in patients treated with long-term mechanical ventilation over a 6-year period.

Background: Long-term mechanical ventilation is a treatment for individuals with chronic hypercapnic respiratory failure, primarily caused by neuromuscular diseases, obesity hypoventilation syndrome, chronic obstructive pulmonary and restrictive thoracic diseases. Studies on long-term outcome on health-related quality of life and factors influencing it are lacking.

Design: Prospective cohort study.

Methods: Data were collected from the Norwegian Long-Term-Mechanical-Ventilation Registry and from patient-reported questionnaire in 2008 and 2014. Health-related quality of life was measured by the Severe Respiratory Insufficiency questionnaire, containing 49 items and seven subdomains. Linear mixed effects models were used to measure changes and identify factors for changes.

Results: After 6 years, 60 patients were still participating, out of 127 at baseline. Health-related quality of life improved significantly in the total score and in four subdomains of the questionnaire. Satisfaction with training in long-term mechanical ventilation was an explanatory variable for improved 'psychological well-being' and follow-up for improvement of 'anxiety'. Side effects of the treatment like facial soreness were associated with the total score. High age and high forced vital capacity were related to lower 'physical function' and improved 'social functioning', respectively.

Conclusion: Long-term mechanical ventilation over 6 years improved health-related quality of life in most patients. Patient training, follow-up and reduction of side effects, largely delivered by trained nurses, contribute to achieve the main goal of the treatment—improved health-related quality of life.

KEYWORDS
long-term care, patient perspectives, quality of care, quality of life, respiratory nursing

1 | INTRODUCTION

Long-term mechanical ventilation (LTMV) is a treatment used for individuals with chronic hypercapnic respiratory failure (CHRF) primarily caused by neuromuscular diseases (NMD), obesity hypoventilation syndrome (OHS), chronic obstructive pulmonary disease (COPD) and restrictive thoracic disorders (RTD) (Windisch, 2008). LTMV is defined as non-invasive ventilation using a mask or mouthpiece, or invasive ventilation using a tracheostomy for a period of at least 3 months on a daily basis and the treatment is carried out mainly in the user's home or at a long-term care facility (Lloyd-Owen et al., 2005). The estimated prevalence of LTMV in Norway and Europe is 37 and 6.6 per 100,000 respectively (Norwegian LTMV Registry 2016, Lloyd-Owen et al., 2005).

Most individuals treated with LTMV have incurable and often chronically progressive diseases (Huttmann & Windisch, 2015; p. 277). Without LTMV, individuals with CHRF have severely impaired health-related quality of life (HRQoL) (Dellborg et al., 2002), but LTMV might have an impact on daily life (Brooks et al., 2004; Lindahl, Sandmann, & Rasmussen, 2005) and lifelong follow-up from the healthcare service is needed (Leasa & Elson, 2016). Improving or maintaining HRQoL is one of the main goals both in invasively ventilated (AARC, 2007) and in non-invasively ventilated individuals (McKim et al., 2011).

1.1 | Background

The knowledge about how LTMV has an impact on HRQoL, has increased, but is still patchy (MacIntyre, Asadi, Mckim, & Bagshaw, 2016; Simonds, 2016). Certain aspects of HRQoL are well documented while others are poorly investigated. Knowledge from qualitative studies found that LTMV gave more energy to cope with daily life (Ballangrud, Bogsti, & Johansson, 2009) and young men with Duchenne muscular dystrophy (DMD) reported that acquiring a ventilator enabled them to make a new positive start to life (Dreyer, Steffensen, & Pedersen, 2010).

In a discussion paper on quality of life, Moons, Budts, and De Geest (2006) found that quality of life was an umbrella term, covering different other concepts such as HRQoL, health status, symptoms and happiness (Moons et al., 2006). As a result, research under the heading of quality of life may cover similar, but still different concepts. In clinical research, the term HRQoL is widely used, but as this term also is lacking in conceptual clarity, previous research is based on many different measures. According to Windisch (2008), the concept of HRQoL has many components and covers aspects of self-reported physical health, psychological well-being, social relations and functional capacities. Following a comprehensive methodological process, including patients treated with LTMV, the Severe Respiratory Insufficiency (SRI) questionnaire was developed, specific for measuring HRQoL in LTMV patients (Windisch et al., 2003). Condition-specific questionnaires are more tailored and responsive than generic questionnaires towards problems of particular importance to the target group of patients (Fayers & Machin, 2016, p. 118). The

Why is this research/review needed?

- The main goal with long-term mechanical ventilation is to increase or maintain health-related quality of life. People suffering from chronic hypercapnic respiratory failure not treated with long-term mechanical ventilation have severely impaired health-related quality of life.
- The knowledge of how long-term mechanical ventilation has an impact on health-related quality of life is poor and there are even fewer studies on which factors influence changes in it over several years.
- Previous studies measuring health-related quality of life in patient treated with long-term mechanical ventilation have most often used questionnaires not specific for this group. The validated Severe Respiratory Insufficiency questionnaire has been developed for and together with this group of patients, but not yet used in a long-term follow-up study.

What are the key findings?

- Six-year follow-up study of patients treated with long-term mechanical ventilation found improved health-related quality of life measured by the specific and validated Severe Respiratory Insufficiency questionnaire.
- The improvements were in the total score of the questionnaire and in the domains reflecting anxiety related to breathing, contact and relationships with other people and the ability to cope with their condition and overall satisfaction with life.
- Patient-reported satisfaction with training and follow-up from healthcare professionals were factors that contributed to improved health-related quality of life in this group. Side effects from non-invasive ventilation interacted with change in the total SRI score. High forced vital capacity from lung function measurements was a factor for improvements in the social functioning domain and high age was an explanatory factor for reduced score the physical function domain.

How should the findings be used to influence policy/practice/research/education?

- The findings add valuable new knowledge in the field of respiratory care and should be included in the current curriculum for healthcare professionals. The study outcomes are important to decision-making both at the individual level concerning treatment options and in terms of planning of healthcare services for patients treated with long-term mechanical ventilation.
- Nurses interact with long-term mechanical ventilation patients in the outpatient clinic, in hospital wards and through home care and are in a unique position to offer systematic patient training, prevent or reduce side effects of non-invasive ventilation and ensure that patients receive realistic information about possible side effects.
- We recommend further prospective international multicentre studies on the link between long-term mechanical ventilation and health-related quality of life aspects, including on intervention models for training and follow-up in this group of patients by including them as members of the multidisciplinary team and use of patient-reported and registry data to improve care and health-related quality of life.

scientific framework for the concept of HRQoL in the present study was therefore based on research that used the SRI questionnaire in patients treated with LTMV.

Applying the SRI questionnaire, a 1-year follow-up study found significant improvements amongst patients with CHRF in a mixed study population including NMD, OHS, RTD and COPD. HRQoL improved after 1 month of LTMV and the results remained stable at the elevated level during the following year (Windisch, 2008). Two randomized controlled trials (RCT) reported significant improvements in the SRI scores 1 year after initiating LTMV in patients with severe COPD (Köhnlein et al., 2014; Struik et al., 2014). Still, there is an ongoing discussion regarding the indication and benefit of LTMV in COPD patients (Simonds, 2016).

We have been unable to identify studies using a questionnaire specific to patients treated with LTMV in a follow-up study over more than 1 year, or studies focusing on the efficacy of ongoing LTMV over several years. However, some sociodemographic and clinical variables associated with HRQoL measured with the SRI questionnaire have been identified. Men had poorer HRQoL scores in the 'respiratory complaints' and 'anxiety' domains compared with women (López-Campos et al., 2008). The underlying disease was an explanatory variable for change in the single domains of the SRI, as significant improvements in 'physical function' were evident only in patients with COPD and RTD. The largest improvements were observed in NMD and OHS patients in the 'attendant symptoms and sleep' domain (Windisch, 2008). Co-morbidity was more prevalent in older patients with COPD, reducing their SRI score compared with younger patients with NMD (Huttmann, Windisch, & Storre, 2015). The physiological efficacy of the LTMV treatment is to decrease the work of breathing and support gas exchange (Georgopoulo, 2013). However, ventilation modes and additional long-term oxygen therapy were not associated with HRQoL (Budweiser et al., 2007) and ventilator settings in obese patients had no influence on change in HRQoL assessed by the SRI questionnaire (Murphy et al., 2012; Storre et al., 2006). Furthermore, the most common criteria generally used to examine the severity of CHRF are the physiological measurements, partial pressure of carbon dioxide ($pCO_{2)}$ and forced vital capacity (FVC) (Simonds, 2016).

These physiological measurements do not reflect the perceptions and subjective state of the patient, but correlations have been reported between these physical measurements and the physical aspects of HRQoL (Hahn et al., 2007). High ventilator pressure settings, aiming to reduce levels of pCO_2, were also proposed as the explanation for improved SRI scores in individuals with COPD (Köhnlein et al., 2014).

Some aspects of HRQoL in LTMV are well documented. However, there are certain areas especially relevant for nurses that have only been incompletely investigated. LTMV can be time-consuming and costly and may contribute to significant side effects. If LTMV increases the burden of disease without any positive effects on HRQoL, it would raise ethical concerns (Windisch, 2010 p. 582). Fex, Flensner, Ek, and Söderhamn (2012) recommended supplementary nursing support for people using advanced medical technology at home. Good HRQoL in individuals receiving LTMV depends on good care being provided by competent healthcare personnel (Brooks et al., 2004; Lindahl et al., 2005). However, shortcomings in the information and follow-up provided by healthcare staff have been reported. Access to better trained personnel has been requested by LTMV patients (Chang, Marsh, Smith, & Neill, 2010), who suffer from severe conditions requiring information, support and long-term care to enjoy the best quality of life available (Leasa & Elson, 2016). There is limited knowledge of how indicators like side effects of the treatment, satisfaction with LTMV training and follow-up might influence changes in HRQoL.

2 | THE STUDY

2.1 | Aims

The objectives of the present study were as follows:

- to examine changes in HRQoL in patients treated with LTMV from 2008-2014.
- To examine sociodemographic, clinical and patient-reported explanatory variables associated with changes in HRQoL in this group.

2.2 | Design

The research design was a prospective cohort study.

2.3 | Participants

In 2008, all patients aged ≥18 years in the Norwegian national LTMV registry in Western Norway were invited to participate in the study. The inclusion criteria were patients treated with non-invasive or invasive LTMV for at least 3 months who were mentally able to answer questions. Those who agreed to participate were followed until 2014.

2.4 | Data collection

Data collection included clinical variables from the LTMV registry as well as patient-reported clinical information from questionnaires at the start of the study in 2008 and at its end in 2014. At the start, an information letter, the baseline questionnaires and a stamped return envelope were sent by mail. The follow-up (2014) questionnaires were completed when the patients attended their regular consultation in the outpatient clinic at the two university hospitals in Western Norway.

2.4.1 | Norwegian registry for LTMV

The LTMV registry was established in 2002 and formally approved as a national medical quality registry 10 years later. The main purpose of the registry is monitoring LTMV to promote geographic equality, quality assurance, professional development, research and resource planning. Patients permanently dependent on non-invasive

or invasive LTMV during all or part of the day are included. There is a written consent to participate in the registry and it is possible for individuals to withdraw from the register. The national coverage ratio in the registry was 72% in 2016 (Norwegian LTMV Registry 2016). Data collected to the present study from the LTMV registry were sociodemographic data, the date and main diagnosis when starting LTMV, the type of connection to the ventilator, blood gas analyses and spirometry values.

2.4.2 | Explanatory variable for changes in HRQoL

Changes in HRQoL were examined according to baseline characteristics measured in 2008. The background variables used were: sex; age; education; marital status and disease. The potential explanatory variable for changes in HRQoL included: number of years treated with LTMV; pCO_2 and FVC. Patient-reported explanatory variable for changes in HRQoL included hours a day on LTMV, a yes/no question regarding whether they experienced any side effects, with further follow-up questions on which side effects, where they were given the following options: air leakage from the mask; soreness caused by mask pressure; condensation inside the mask; and an option to describe other side effects in their own words. Dependency on daily assistance with using the ventilator was measured by one yes/no question. Patient satisfaction with the follow-up from specialist healthcare professionals consisted of one statement ("Received adequate follow-up") as did patient satisfaction with training in the use of LTMV ("Received adequate training in LTMV"), both of which had five response categories ranging from "Strongly disagree"—"Strongly agree".

2.4.3 | Study setting: Clinical follow-up from healthcare professionals

Clinical follow-up for LTMV patients is organized through a national multi and interdisciplinary competence network. The network is coordinated by a physician and includes specially trained nurses and physiotherapists, specialists in neurology and general practitioners. It also includes a liaison nurse who plays an important role when the patient is transferred from hospital to their home with a ventilator, both in terms of educating the caregiver team and promoting contact with relatives and caregivers in the community. Follow-up visits take place 1 to 4 times a year depending on individual circumstances such as medical condition and psychosocial factors.

2.4.4 | Outcome variable of the study

The outcome variable in the present study was HRQoL, measured by the SRI questionnaire at baseline (2008) and follow-up (2014). This is a specific, multidimensional questionnaire covering physical, psychological and social functioning and was originally developed for and together with patients receiving LTMV to obtain subjective descriptions of issues that were important in their daily lives. The questionnaire contains 49 items and is divided into seven subdomains. High summary scale values (range 0–100) indicate a better HRQoL and the subscales are as follows:

SRI-Respiratory Complaints contains eight items relating to dyspnoea at rest and during physical activity. It covers how often breathlessness occurs and the degree of waking up with breathlessness at night. Breathlessness during speaking, eating and problems with coughing or mucus in the airways are included in this subdomain.

SRI-Physical Function consists of six items and includes the patient's ability to execute everyday physical activities, such as getting dressed, walking stairs and doing housework. Participation in physical leisure activities and how breathing problems have an impact on activities are covered by this subdomain.

SRI-Attendant Symptoms and Sleep contains seven items addressing the quality of sleep, measured by patient-reported waking up during the night, problems with falling asleep and general interruptions of sleep. Daytime tiredness, dizziness and headaches are also covered by this subdomain.

SRI-Anxiety consists of five items including experiences of feeling anxious about having attacks of dyspnoea and about suffering dyspnoea at night. Avoiding situations that are stressful due to breathing difficulties and being worried that the disease will get worse are also included in this subdomain.

SRI-Social Relationships contains six items including having friends and feeling comfortable in the company of other people or feeling lonely and isolated. The disease burden on family life is also covered in the subscore.

SRI-Social Functioning consists of eight items including the degree of broken contact with friends and acquaintances. Limited leisure opportunities, ability to attend social events and the impact of the disease on marriage or relationships are covered by this subdomain.

SRI-Psychological Well-Being includes nine items covering the patient's ability to cope with the disease. The degree of sadness and overall satisfaction with life are included. Each item belongs to only one subscale and all items are rated on a five-point Likert scale from "strongly agree" to "strongly disagree".

Questions refer to the patient's health status during the previous week. The summary scale was obtained by calculating the mean of the values of each scale (Windisch et al., 2003). However, the minimal clinically important difference of the SRI questionnaire has not been defined.

2.5 | Ethical considerations

The study was approved by the Norwegian Committee of Ethics in Medicine, Region III and by the Norwegian Centre for Research Data (project number 16001). In the Information letter, to the patients in 2008 it was informed that the data were stored for 10 years for a possible follow-up study and returning the questionnaires by mail were considered consent to participate in the study. One reminder letter was sent (Markussen, Lehmann, Nilsen, & Natvig, 2015). Prior to the follow-up study in 2014, the patients received a new information letter about the follow-up study. There was a written consent to participate in the follow-up study. It was possible for the patients

to decline from participation in the study, but still be a part in the register.

2.6 | Data analysis

All statistical analyses were carried out using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and Stata *SE* 14 (StataCorp LP, College Station, TX, USA) for Windows. Descriptive statistics were used to quantify sample characteristics. The items in the SRI were recoded and summarized following the guidelines of the original SRI questionnaire (Windisch et al., 2003). All statistical tests were two-tailed and *p* values lower than.05 were considered as statistically significant.

To estimate changes in the seven SRI domains from the start of the study in 2008 to its end in 2014, we used linear mixed effects models. All models defined the time-period as a fixed effect, whereas a random intercept for the individual was specified to account for correlated observations of the same individual (an exchangeable correlation structure was assumed). Further, to identify explanatory variables associated with change in the seven SRI domains from 2008 - 2014, we extended the abovementioned models to include the relevant explanatory variables and the product between the explanatory variable and time-period (i.e. an explanatory variable-by-time interaction) as model terms.

Estimated mean changes in the SRI domains from 2008 to 2014 in categories of explanatory variables were reported using regression model coefficients (β) with 95% confidence intervals (CIs) and *p* values. To obtain *p* values for explanatory variables associated with SRI change, we used the likelihood ratio test, i.e. comparing the log-likelihood between models with and without the explanatory variables - by-time interaction term. Analyses were adjusted for the following background variables: sex; age; education; marital status; years on LTMV and disease.

2.7 | Validity, reliability and rigour

Validity and reliability in quality of life research has been discussed (Macduff, 2000; Moons et al., 2006). Good validity and international relevance of this study is provided by using the SRI questionnaire, that has shown very good psychometric qualities and has been professionally adapted and translated into several languages (Duiverman, Wempe, Bladder, Kerstjens, & Wijkstra, 2008; Ghosh, Rzehak, Elliott,

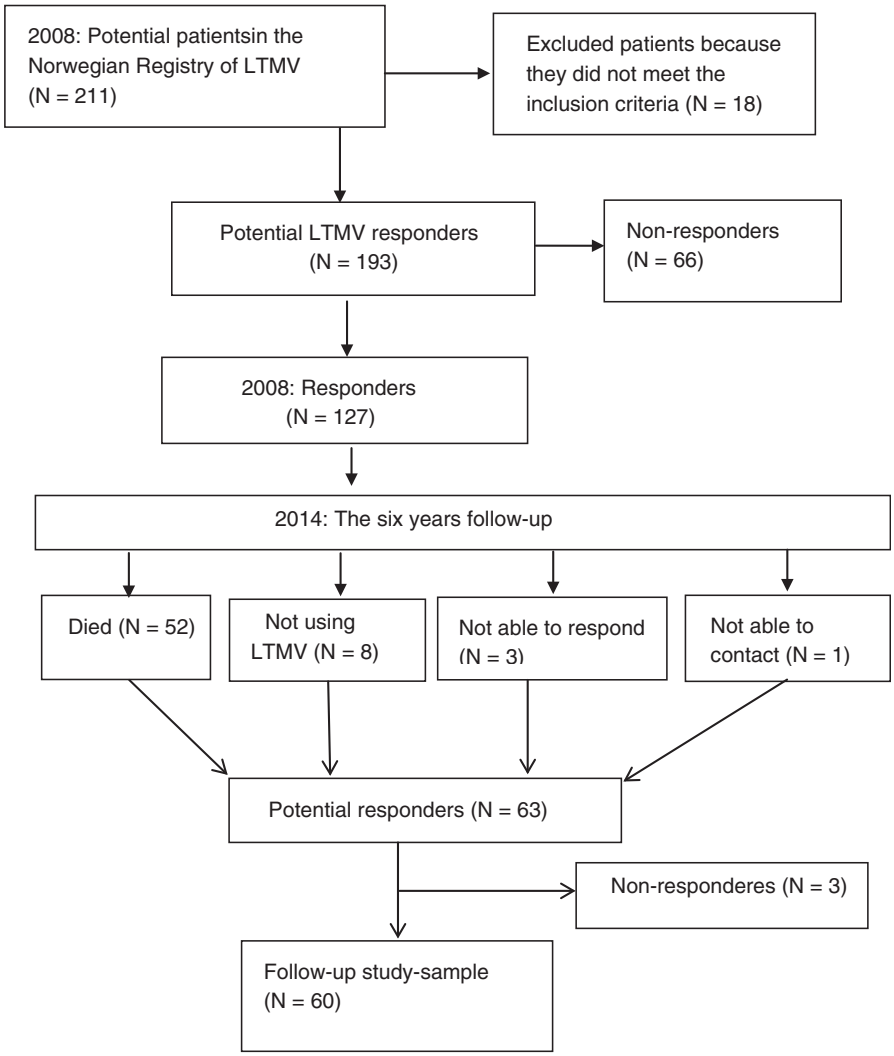

FIGURE 1 Flow diagram of the long-term mechanical ventilation (LTMV) patients from 2008 to 2014

& Windisch, 2012; Huttmann et al., 2015, p. 280; López-Campos et al., 2008; MacIntyre et al., 2016; Markussen et al., 2015; Oga et al., 2017; Ribeiro, Ferreira, Conde, Oliveira, & Windisch, 2017; Struik et al., 2013; Windisch, 2008; Windisch et al., 2003). Reliability and rigour are provided through high-quality clinical data from the LTMV registry.

3 | RESULTS

3.1 | Study population

Of 193 potential responders in the LTMV registry, 127 (65.8%) patients agreed to participate and completed the SRI questionnaire at baseline in 2008 (Figure 1). Of the 127 individuals eligible for follow-up in 2014, 52 had died during the 6-year period. Additionally, 15 patients were excluded for the following reasons: dementia or unable to answer the questionnaire ($N = 3$); stopped using LTMV ($N = 8$); unable to make contact ($N = 1$); and did not want to participate in follow-up study ($N = 3$). These exclusions related to the disease groups NMD ($N = 6$), COPD ($N = 2$), OHS ($N = 6$) and RTD ($N = 1$), leaving a final study sample of 60 (95%) patients (Figure 1), ranged in age from 18 to 85 years at inclusion in 2008. The majority of the patients lived in their own home, only five of the patients lived in nursing homes.

3.2 | Clinical characteristics

Before LTMV treatment (at least 3 months before the start of the study), the mean blood value of daytime carbon dioxide ($PaCO_2$ $kP_{a)}$ and oxygen (PaO_2 kP_a) was 6.7 (standard deviation [*SD*] 1.9) and 9.1 (*SD* 1.7), respectively. In 2008, the mean respirator inspiratory positive airway pressure (IPAP) was 15.5 cmH_2O (*SD* 2.8) and the expiratory pressure (EPAP) was 6.9 cmH_2O (*SD* 2.7) ($N = 45$). Non-invasive ventilation (NIV) was the main ventilation mode, only 2 of the surviving patients in 2014 had tracheostomy interface. No patients used a mouthpiece or helmet as an interface for LTMV. Side effects from the non-invasive LTMV were reported by 29 individuals (Table 1). The most common side effects were air leakage between the face and the mask ($N = 21$) and soreness caused by mask pressure ($N = 10$). Other patient-reported side effects were condensation inside the mask ($N = 5$), dry nose and mouth ($N = 2$), eye irritation, ventilator noise and patient-ventilator synchronization problem ($N = 1$). Three people reported three different kind of side effects, five individuals reported two different side effects, while most individuals reported one single side effect ($N = 21$).

3.3 | Change in HRQoL from 2008 to 2014

There were statistically significant improvements in the total SRI score at mean 4.74 ($p = .005$) and in four subdomains: SRI-Anxiety, SRI-Social Functioning, SRI-Social Relationships and SRI-Psychological Well-Being. The largest improvement was observed for the Social Relationships domain, with an improvement of 8.47 ($p = .001$) (Table 2) (Table S5). The improvements in the total score of SRI were seen in all disease groups, except in patients with COPD (Table 3), who also had a reduction in five of seven SRI subdomains (Table 4) (Table S1–S4).

TABLE 1 Baseline characteristic of the surviving individuals treated with LTMV in the longitudinal study

Characteristic	*N*	Baseline 2008
Background		
Sex, male (*n*, %)	60	32 (53.3)
Age, years (*M*, *SD*)	60	58.0 (15.5)
Education (*n*, %)		
Primary school	60	18 (30.0)
High school	60	23 (38.3)
College/University	60	19 (31.7)
Marital status (*n*, %)		
Married/cohabiting	60	34 (56.7)
Single/divorced/widowed	60	26 (43.3)
Years of LTMV (*M*, *SD*)	60	5.23 (4.0)
Disease (*n*, %)		
NMD[a]	60	26 (43.3)
COPD	60	6 (10.0)
OHS	60	22 (36.7)
RTD	60	6 (10.0)
Treatment		
LTMV h/day (*n*, %)[b]		
5–8	58	33 (56.9)
8–24	58	25 (43.1)
Dependency of daily assistance (*n*, %)	59	16 (27.1)
Side effects of non-invasive LTMV (*n*, %)	58	29 (50.9)
Satisfactions with LTMV training (*n*, %)[c]		
Some satisfaction	59	9 (15.5)
Quite satisfied	59	18 (30.5)
Very satisfied	59	32 (54.2)
Satisfactions with follow-up (*n*, %)[c]		
Some satisfaction	49	8 (16.3)
Quite satisfied	49	13 (26.5)
Very satisfied	49	28 (57.1)
Respiratory		
FVC (litre) (*M*, *SD*)	47	2.09 (1.07)
$PaCO_2$ kP_a daytime (*M*, *SD*)	47	5.66 (0.86)
PaO_2, kP_a daytime (*M*, *SD*)	44	10.3 (1.63)

SD, standard deviation; LTMV, long-term mechanical ventilation; NMD, neuro muscular disease; COPD, chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; RTD, restrictive thoracic disorders; FVC, forced vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.

[a]None with amyotrophic lateral sclerosis (ALS).

[b]Because of low numbers, the 8–12 and 12–24 categories of this variable were grouped together.

[c]Because of low numbers, the three lowest categories of this variable were grouped together.

TABLE 2 Changes in HRQoL from 2008 to 2014 measured by The Severe Respiratory Insufficiency (SRI) questionnaire in the individuals treated with long-term mechanical ventilation

SRI	N	2008 M (SD)	N	2014 M (SD)	Change[a] mean	95% CI	p
Respiratory complaints	59	61.0 (22.4)	60	62.8 (20.8)	1.86	(−3.19, 6.91)	.46
Physical functioning	59	45.9 (23.0)	60	46.7 (23.4)	0.67	(−4.07, 5.42)	.78
Attendant symptoms and sleep	59	53.3 (20.1)	60	55.7 (21.6)	2.48	(−2.14, 7.11)	.29
Social relationships	59	70.7 (24.4)	60	79.1 (19.5)	8.47	(3.48, 13.5)	.001
Anxieties	59	64.2 (27.5)	60	72.1 (22.9)	7.94	(2.42, 13.5)	.006
Well-being	59	66.1 (22.0)	60	74.2 (17.0)	7.66	(3.28, 12.0)	.001
Social functioning	59	56.5 (24.9)	60	62.4 (25.7)	5.89	(0.91, 10.9)	.02
SUM score	59	60.0 (18.5)	60	64.8 (16.8)	4.74	(1.49, 8.00)	.005

HRQoL, health-related quality of life; *SD*, standard deviation; CI, confidence interval.
[a]Change in SRI is estimated by linear mixed effects model with random intercept.

TABLE 3 Change in the Severe Respiratory Insufficiency (SRI) sum score according to baseline characteristics

Characteristic	SRI-SS 2008 M (SD)	SRI-SS 2014 M (SD)	Estimated change in means[a]	95% CI	p for change	p for interaction
Background						
Sex						.88
Female	57.8 (16.1)	62.3 (15.0)	5.06	(0.30, 9.80)	.04	
Male	61.8 (20.0)	66.4 (18.0)	4.57	(0.21, 8.94)	.04	
Age						.79
≤60	61.7 (16.2)	66.9(15.1)	5.25	(0.40, 10.1)	.03	
>60	58.7 (20.0)	62.7 (17.6)	4.37	(0.08, 8.66)	.05	
Education						
Primary school	56.2 (20.8)	61.2 (19.1)	5.01	(−0.74, 10.8)	.09	.71
High school	56.0 (15.5)	61.7 (14.1)	6.16	(0.86, 11.4)	.02	
College/University	68.7 (16.8)	70.8 (15.9)	2.98	(−2.76, 8.72)	.30	
Marital status						.74
Married/cohabiting	59.9 (18.1)	64.9 (16.5)	5.25	(1.03, 9.48)	.01	
Single/divorced/widowed	60.2 (19.0)	64.0 (17.1)	4.17	(−0.76, 9.11)	.10	
Years on LTMV						.56
≤ 4	57.7(18.7)	63.0 (16.0)	5.65	(1.30, 9.99)	.01	
> 4	62.9 (17.8)	66.2 (17.5)	3.75	(−1.00, 8.49)	.12	
Disease						
NMD	62.8 (13.2)	65.2 (10.6)	3.2	(−1.61, 8.00)	.19	.14
COPD	51.1 (25.7)	48.5 (21.0)	−2.6	(−12.3, 7.06)	.60	
OHS	60.1 (20.2)	69.0 (18.5)	9.00	(3.85, 14.1)	.001	
RTD	57.8 (22.9)	61.6 (20.8)	3.83	(−5.83, 13.5)	.44	
Treatment						
LTMV h/day[b]						.88
5–8	61.0 (18.2	64.9(14.4)	4.51	(0.24, 8.77)	.04	
8–24	59.2 (19.6)	63.1(19.7)	4.02	(−0.82, 8.88)	.10	
Dependency of daily assistance						.76
No	60.9 (19.1)	65.4 (18.1)	4.56	(0.81, 8.31)	.02	
Yes	57.5 (16.2)	62.8 (12.4)	5.72	(−0.54, 11.9)	.07	
Side effects of non-invasive LTMV						.02

(Continues)

TABLE 3 (Continued)

Characteristic	SRI-SS 2008 *M* (*SD*)	SRI-SS 2014 *M* (*SD*)	Estimated change in means[a]	95% CI	*p* for change	*p* for interaction
No	63.9 (20.1)	64.7 (18.8)	1.07	(−3.38, 5.52)	.64	
Yes	56.2 (16.1)	65.1 (15.4)	8.89	(4.66, 13.1)	<.001	
Satisfactions with LTMV training[c]						.09
Some satisfaction[b]	51.1 (15.2)	60.7 (16.2)	9.56	(1.69, 17.4)	.02	
Quite satisfied	55.2 (18.2)	62.7 (17.4)	8.06	(2.35, 13.8)	.006	
Very satisfied	65.1 (18.0)	67.0 (16.6)	1.80	(−2.43, 6.03)	.40	
Satisfactions with follow-up[c]						
Some satisfaction	57.0 (27.4)	63.8 (16.9	9.87	(0.13,19.6)	.05	.24
Quite satisfied	53.1 (14.8)	60.0 (12.1)	6.90	(0.20, 13.6)	.04	
Very satisfied	66.4 (16.5)	68.5 (17.7)	2.01	(−2.63, 6.65)	.39	
Respiratory[d]						
FVC (litre)						
Per 1 unit increase			2.26			.17
$PaCO_2$ kP_a daytime						
Per 1 unit increase			−1.04			.62
PaO_2, kP_a daytime						
Per 1 unit increase			−1.67			.15

SRI-SS, severe respiratory insufficiency sum score; *SD*, standard deviation; CI, confidence interval; LTMV, long-term mechanical ventilation; NMD, neuro muscular disease; COPD, chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; RTD, restrictive thoracic disorders; FVC, forced vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.

[a]Estimated by mixed effects models, adjusted for background variables: sex, age, education, marital status, years on LTMV and disease.

[b]Because of low numbers, the 8–12 and 12–24 categories of this variable were grouped together.

[c]Because of low numbers, the three lowest categories of this variable were grouped together.

[d]For continuous respiratory variables, data are presented as estimated change in SRI-SS for one unit increase (in the respiratory variables) and the corresponding *p* for interaction.

3.4 | Explanatory variables associated with change in HRQoL

Of 13 baseline characteristics evaluated as potential explanatory variables for change in HRQoL from 2008 to 2014, five variables were identified as significant factors for change in HRQoL. Side effects of the non-invasive LTMV were significantly associated with the total SRI score (Table 3) and SRI-Physical function (Table S1). Satisfaction with LTMV training was associated with an improved SRI-Psychological Well-Being score (Table 4). Satisfaction with follow-up from healthcare professionals in the specialist health care service was one explanatory variable for improvement in the SRI-Anxiety score (Table 5). High age was one explanatory variable for a lower SRI-Physical Function score (Table S1) and high FVC was correlated with improved HRQoL in the SRI- Social Functioning score (Table S2).

4 | DISCUSSION

This study adds valuable new knowledge by being the first study to examine the impact of 6 years of LTMV on HRQoL using the specific SRI questionnaire developed together with and for people treated with LTMV. HRQoL improved both as measured by the total score and by four of the seven SRI subdomains. The improvements occurred in the clinically important domains 'anxiety', 'social functioning', 'social relationships' and 'psychological well-being'.

This study is also unique in that it identified explanatory variables possible for nurses to intervene on, aiming to achieve the main goal of LTMV, which is to improve HRQoL. These results were based on self-reported measures and as in most research on HRQoL, the results may partly be explained by a better adaptation to living with a chronic illness. However, a meta-analysis examining the clinical significance of such an explanation, could not confirm this when examining studies based on measures of response shift (Schwartz et al., 2006).

4.1 | Patient evaluation of LTMV training and follow-up as factors associated with changes in HRQoL

The positive relationship between patient satisfaction with training in the use of LTMV and improvement in the SRI-Psychological Well-Being score is clinically important. It indicates that thorough basic training in use of the ventilator and interfaces are vital success factors for a better satisfaction with life after 6 years.

TABLE 4 Change severe respiratory insufficiency (SRI)-well-being (WB) score according to baseline characteristics

Characteristics	SRI-WB 2008 *M* (*SD*)	SRI-WB 2014 *M* (*SD*)	Estimated change in means[a]	95% CI	*p* for change	*p* for interaction
Background						
Sex						.92
Female	65.8 (22.7)	73.4 (18.2)	7.91	(1.52, 14.3)	.01	
Male	66.6 (21.8)	74.5 (16.0)	7.44	(1.57, 13.3)	.01	
Age						.96
≤60	66.8(21.7)	75.1(17.1)	7.73	(1.19, 14.2)	.02	
>60	65.8(22.6)	73.1 (17.0)	7.51	(1.74, 13.3)	.01	
Education						.87
Primary school	60.3 (24.4)	69.4 (18.2)	9.18	(1.41, 16.9)	.02	
High school	62.9 (19.2)	70.4 (17.1)	7.49	(0.36, 14.6)	.04	
College/University	76.2 (20.2)	82.3 (12.6)	6.32	(−1.42, 14.0)	.11	
Marital status						.24
Married/cohabiting	65.1 (19.3)	75.1 (15.4)	9.85	(4.23, 15.5)	.001	
Single/divorce widowed	67.7 (25.4)	72.4 (19.0)	4.66	(−1.90, 11.2)	.16	
Years on LTMV						.43
≤4	63.4 (23.3)	73.2 (17,7)	9.21	(3.38, 15.0)	.002	
>4	69.7 (20.1)	74.9 (16.2)	5.72	(−0.66, 12.1)	.08	
Disease						.18
NMD	71.2 (16.6)	76.0 (13.0)	5.33	(−1.18, 11.8)	.12	
COPD	62.0 (33.5)	60.6 (23.8)	−1.39	(−14.5, 11.7)	.83	
OHS	61.5 (23.7)	75.0 (18.8)	13.0	(6.07, 20.0)	<.001	
RTD	67.9 (23.0)	75.0 (16.1)	7.06	(−6.03, 20.1)	.29	
Treatment						
LTMV h/day[b]						.77
5–8	69.2 (21.8)	75.5 (15.9	6.65	(0.87, 12.4)	.02	
8–24	63.7 (22.7)	72.2 (18.8)	7.98	(1.39, 14.6)	.02	
Dependency of daily assistance						.94
No	65.9, 22.3)	74.0 (18.4)	7.40	(−1.02, 15.8)	.08	
Yes	67.2 (21.7)	73.6 (13.3)	7.76	(2.71, 12.8)	.003	
Side effects of non-invasive LTMV						.15
No	67.2 (23.2)	72.1 (20.6)	11.2	(5.35, 17.1)	<.001	
Yes	64.6 (21.5)	75.9 (13.7)	4.87	(−1.31, 11.0)	.12	
Satisfactions with LTMV training[c]						.01
Some satisfaction	61.0 (16.0)	74.4 (11.8)	13.4	(3.13, 23.6)	.01	
Quite satisfied	58.5 (21.1)	72.5 (16.2)	14.8	(7.45, 22.2)	<.001	
Very satisfied	71.8 (22.8)	74.5 (19.1)	2.14	(−3.35, 7.62)	.45	
Satisfactions with follow-up[c]						.06
Some satisfaction	62.0 (27.2)	67.7 (14.3)	6.25	(−6.23, 18.7)	.32	
Quite satisfied	60.0 (21.6)	74.6 (15.1)	14.5	(5.93, 23.1)	.001	
Very satisfied	74.2 (21.0)	76.7 (18.8)	1.78	(−4.17, 7.74)	.56	
Respiratory[d]						
FVC (litre)						
Per 1 unit increase			2.61			.27
$PaCO_2$ kP_a daytime						
Per 1 unit increase			1.93			.52

(Continues)

TABLE 4 (Continued)

Characteristics	SRI-WB 2008 *M* (*SD*)	SRI-WB 2014 *M* (*SD*)	Estimated change in means[a]	95% CI	*p* for change	*p* for interaction
PaO_2, kP_a daytime						
Per 1 unit increase			−2.93			.07

SRI-SS, severe respiratory insufficiency sum score; *SD*, standard deviation; CI, confidence interval; LTMV, long-term mechanical ventilation; NMD, neuro muscular disease; COPD, chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; RTD, restrictive thoracic disorders; FVC, forced vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.

[a]Estimated by mixed effects models, adjusted for background variables: sex, age, education, marital status, years on LTMV and disease.

[b]Because of low numbers, the 8–12 and 12–24 categories of this variable were grouped together.

[c]Because of low numbers, the three lowest categories of this variable were grouped together.

[d]For continuous respiratory variables, data are presented as estimated change in SRI-SS for one unit increase (in the respiratory variables) and the corresponding *p* for interaction.

Patient satisfaction is related to the extent to which general healthcare needs and condition-specific needs are met (Guldvog, 1999). The importance of giving proper training to a ventilator-assisted individual is recognized as fundamental for good HRQoL. However, it has not previously been well documented (Norregaard & Escarrabill, 2010; p.172). According to Escarrabill (2015, p.282), the competencies of the LTMV patient are directly related to the clinical outcome. To our knowledge, no studies have focused on patient training or education in patients receiving LTMV with HRQoL as a primary outcome. A Cochrane review also concluded that there was a small improvement in quality of life in COPD patients without LTMV treatment who received a short patient training program compared with those receiving usual care (Howcroft, Walters, Wood-Baker, & Walters, 2016).

The SRI-Anxiety score was considerably improved both in the overall analysis and in subanalysis of the different disease categories, in line with the outcomes of other studies (Köhnlein et al., 2014; Struik et al., 2014; Windisch, 2008). The findings implicate that follow-up from healthcare professionals might contribute to improve the HRQoL of individuals receiving LTMV related to anxiety for breathlessness. Furthermore, it might indicate that they feel safer in situations where breathlessness may occur. According to Gibson, Brooks, DeMatteo, and King (2009), it is especially important for LTMV patients to have control over their day-to-day schedules, the assistance provided and how it is carried out.

One of the challenges in clinical practice is to identify and target the patients' genuine needs (Leasa & Elson, 2016). There are different approaches to follow-up. The setting for patient training and follow-up in this study was a 'real-world' setting, including a multi and interdisciplinary network model that shares and disseminates professional knowledge and skills in the field of LTMV. An evaluation of management of DMD emphasizes the importance of multidisciplinary care for these patients (Bushby et al., 2010). Escarbilrabill and Norregaard (2010, p.179), also highlight the benefits of network models, such as professional development and continuing education. An important element of patient education and follow-up in ongoing LTMV is the contact between patient and healthcare professionals over several years, where patients and professionals identify and discuss problems caused by, or related to, the LTMV. The patient is thus involved in the care process. This partnership might affect the evaluation of and satisfaction with, the healthcare service. However, the role of patient-reported outcomes measure (PROM) in facilitating communication between healthcare professionals in the multidisciplinary team and the patient as a team member is yet to be explored (Norekvaal, Faalun, & Fridlund, 2016).

4.2 | Patient-reported side effects as factors associated with changes in HRQoL

Patient-reported side effects of non-invasive LTMV were significantly associated with the total SRI score and the SRI-Physical function domain. To our knowledge, this study was the first to identify side effects, such as soreness caused by mask pressure or air leakage between the mask and face, were associated with a lower total SRI score at baseline compared with those reporting no side effects. According to Elliott (2004), some air leakage is an unavoidable consequence of non-invasive LTMV. However, frequent side effects can clearly worsen HRQoL or counteract the HRQoL benefits gained from LTMV (Windisch, 2010, p. 585).

4.3 | Clinical data from the LTMV registry as explanatory variables associated with changes in HRQoL

High FVC was one explanatory variable for improved HRQoL in terms of SRI-Social Functioning, a key domain because it indicates improved leisure opportunities, including the ability to go out in the evening and attend social events (Windisch et al., 2003). An explanation of high FVC as clinically important factor might be that the patients with higher FVC have more physical strength to carry out the social functioning. Interaction between high FVC and improved HRQoL are rarely reported. However, a weak but significant positive association between pulmonary variables and HRQoL was also found in patients with cystic fibrosis who were not treated with LTMV (Hahn et al., 2007).

High age was an explanatory variable for a lower score for SRI-Physical Function. This is in line with Huttmann et al. (2015), who found reduced HRQoL in individuals receiving LTMV of higher age and with chronic lung diseases, compared with younger patients with NMD. Tissot et al. (2015) also found that patients treated with non-

TABLE 5 Change in the severe respiratory insufficiency (SRI)-Anxiety (AX) score according to baseline characteristics

Characteristics	SRI-AX 2008 *M* (*SD*)	SRI-AX 2014 *M* (*SD*)	Estimated change in means[a]	95% CI	*p* for change	*p* for interaction
Background						
Sex						.53
Female	63.9 (25.4)	73.6 (23.0)	9.9	(1.87, 17.9)	.02	
Male	64.4 (29.5)	70.7 (23.0)	6.3	(−1.07, 13.7)	.09	
Age						.96
≤60	63.9 (27.2)	71.7 (23.2)	7.79	(−0.45, 16.0)	.06	
>60	64.4 (28.0)	72.3 (22.9)	8.05	(0.76, 15.3)	.03	
Education						.22
Primary school	58.3 (27.0)	72.8 (24.6)	14.4	(4.70, 24.2)	.004	
High school	59.8 (27.3)	66.9 (23.7)	7.17	(−1.61, 15.9)	.11	
College/University	74.9 (26.4)	77.6 (19.6)	2.76	(−6.71, 12.2)	.57	
Marital status						.53
Married/cohabiting	62.7 (29.1)	72.2 (21.9)	9.48	(2.31, 16.7)	.01	
Single/divorced/widowed	66.2 (25.5)	71.9 (24.5)	5.92	(−2.42, 14.3)	.16	
Years on LTMV						.59
≤4	60.7 (28.5)	70.0 (19.5)	9.28	(1.99, 16.6)	.01	
>4	68.6 (26.0)	74.6 (26.5)	6.26	(−1.93, 14.4)	.13	
Disease						.94
NMD	67.9 (24.0)	75.4 (16.0)	7.85	(−0.63, 16.3)	.07	
COPD	48.3 (32.3)	52.5 (24.6)	4.17	(−13.2, 21.5)	.64	
OHS	66.6 (27.4)	76.3 (25.8)	9.71	(0.63, 18.8)	.04	
RTD	55.8 (36.2)	61.7 (27.5)	5.83	(−11.5, 23.2)	.51	
Treatment						
LTMV h/day[b]						.40
5–8	64.5 (28.1)	73.5 (21.2)	9.28	(1.99, 16.6)	.01	
8–24	65.0 (27.8)	69.5 (25.5)	4.55	(−1.93, 14.4)	.27	
Dependency of daily assistance						.44
No	66.5 (26.7)	72.2 (24.2)	5.67	(−0.19, 11.5)	.06	
Yes	61.4 (26.6)	71.2 (20.0)	10.2	(02.3, 20.1)	.04	
Side effects of non-invasive LTMV						.15
No	69.8 28.1)	71.6 (25.1)	1.91	(−5.07, 8.90)	1.92	
Yes	62.3 (25.1)	71.4 (25.8)	9.09	(2.34, 15.8)	.008	
Satisfactions with LTMV training[c]						.29
Some satisfaction	53.3 (26.2)	68.8 (23.4)	15.5	(2.83, 28.3)	.02	
Quite satisfied	61.8 (24.9)	68.9 (23.4)	7.35	(−1.87, 16.6)	.12	
Very satisfied	70.3 (27.0)	74.5 (23.1)	4.18	(−2.57, 10.9)	.22	
Satisfactions with follow-up[c]						.009
Some satisfaction	49.5 (37.1)	75.0 (23.3)	26.9	(11.8, 41.9)	<.001	
Quite satisfied	53.1 (23.2)	66.5 (22.6)	13.5	(2.32, 24.6)	.02	
Very satisfied	73.6 (24.6)	75.3 (21.0)	1.69	(−5.90, 9.29)	.66	
Respiratory[d]						
FVC (litre)						
Per 1 unit increase			−1.54			.60
$PaCO_2$ kP_a daytime						
Per 1 unit increase			−1.19			.75

(Continues)

TABLE 5 (Continued)

Characteristics	SRI-AX 2008 *M* (*SD*)	SRI-AX 2014 *M* (*SD*)	Estimated change in means[a]	95% CI	*p* for change	*p* for interaction
PaO_2, kP_a daytime						
Per 1 unit increase			−2.18			.28

SRI-SS, severe respiratory insufficiency sum score; *SD*, standard deviation; CI, confidence interval; LTMV, long-term mechanical ventilation; NMD, neuro muscular disease; COPD, chronic obstructive pulmonary disease; OHS, obesity hypoventilation syndrome; RTD, restrictive thoracic disorders; FVC, forced vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.
[a]Estimated by mixed effects models, adjusted for background variables: sex, age, education, marital status, years on LTMV and disease.
[b]Because of low numbers, the 8–12 and 12–24 categories of this variable were grouped together.
[c]Because of low numbers, the three lowest categories of this variable were grouped together.
[d]For continuous respiratory variables, data are presented as estimated change in SRI-SS for one unit increase (in the respiratory variables) and the corresponding *p* for interaction.

invasive LTMV >75 years had a significantly lower HRQoL measured with SF-36 than patients <75 years.

Previous research has found improvements in the SRI scores 1 year after initiating LTMV in patients with severe COPD (Köhnlein et al., 2014; Struik et al., 2014). One explanation of these differences might be the progressive nature of some of the disease categories might influence HRQoL more clearly in a 6-year study than in a 1-year follow-up. The severity of COPD (GOLD 2017) is also reflected in this study with a reduction in the total SRI score and in five of seven SRI subdomains in the few surviving COPD patients after 6 years in this study population. Huttmann et al. (2015), also found reduced HRQoL in individuals receiving LTMV with chronic lung diseases, compared with those with NMD. However, the ventilator pressure settings for these 60 patients were lower compared with some of the other studies (Windisch, 2008; Köhnlein et al. (2014). Nevertheless, in this study we observed significant reductions in carbon dioxide from before starting LTMV to baseline in 2008, indicating good physiologic effect of the LTMV treatment.

4.4 | Limitations of this study

The study has some limitations. Firstly, the study sample is relatively small and heterogeneous in terms of the diagnoses leading to LTMV, which means that the sample size is insufficient to perform subgroup analyses, such as interaction studies between explanatory variables and HRQoL for the specific subgroups, NMD, OHS, COPD or RTD. Secondly, non-responders in 2008 had lower FVC than those who attended, suggesting more severe disease and a lower HRQoL in the non-participating group, which might influence the representativeness of the sample and generalizability of the result. However, information about the physiological variables of non-participating LTMV patients is a strength for the study. Recruiting patients from the national registry also contributes to strengthen the representativeness of the sample and the generalizability of the result, even if the coverage ratio in the registry was not 100%. Thirdly, there was no control group in this study. Nonetheless, a RCT evaluation of HRQoL in patients receiving LTMV vs. a non-ventilated control group of patients would obviously be considered unethical. Despite the design was unable to examine causal relationships, the study revealed clinical important explanatory variables for improved HRQoL.

5 | CONCLUSION

This study adds important new knowledge by being the first study to examine the impact of 6 years of ongoing LTMV on HRQoL using the specific SRI questionnaire developed for and together with this patient group. The total SRI score and the scores in four of the seven subdomains improved in the majority of the patients treated with LTMV. This study pointed out that patient training, follow-up and reduction of side effects, a healthcare service largely delivered by trained nurses, contribute to achieve the main goal of LTMV treatment- improved HRQoL.

We recommend further prospective studies on HRQoL aspects in LTMV, including standardized intervention models to minimize side effects and to improve training, involvement and follow-up of the patients. LTMV is an expensive treatment for few patients in the community; to assure larger sample size we recommend international cooperation and multicentre studies using the SRI questionnaire.

AUTHOR CONTRIBUTIONS

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE [http://www.icmje.org/recommendations/]):

- substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
- drafting the article or revising it critically for important intellectual content.

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CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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