Estimation of Quality-Adjusted Life Expectancy in Patients Under Prolonged Mechanical Ventilation

Mei-Chuan Hung, MPH a, Yuan-Horng Yan, MD, MSc b, Po-Sheng Fan, MD b, Ming-Shian Lin, MD b, Cheng-Ren Chen, MD b, Lu-Cheng Kuo, MD c, Chong-Jen Yu, MD, PhD c, Jung-Der Wang, MD, ScD a,d,*

a Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei, Taiwan
b Department of Internal Medicine, Chia-Yi Christian Hospital, Chiayi, Taiwan
c Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan
d Department of Public Health, National Cheng Kung University College of Medicine, Tainan, Taiwan

Keywords:
Health gap
Life expectancy
Quality-adjusted life expectancy (QALE)
Quality-adjusted life years (QALY)

ABSTRACT

Objectives: The purpose of this study was to estimate the quality-adjusted life expectancy (QALE) and the expected lifetime utility loss of patients with prolonged mechanical ventilation (PMV).

Methods: PMV was defined as more than 21 days of mechanical ventilation. A total of 633 patients fulfilled this definition and were followed for 9 years (1998–2007) to obtain their survival status. Quality of life of 142 patients was measured with the EuroQol five-dimensional (EQ-5D) questionnaire during the period 2008 to 2009. The survival probabilities for each time point were adjusted with a utility measurement of quality of life and then extrapolated to 300 months to obtain the QALE. We compared the age-, gender-matched reference populations to calculate the expected lifetime utility loss.

Results: The average age of subjects was 76 years old. The life expectancy and loss of life expectancy were 1.95 years and 8.48 years, respectively. The QALE of 55 patients with partial cognitive ability and the ability to respond was 0.58 quality-adjusted life years (QALY), whereas the QALEs of 87 patients with poor consciousness were 0.28 and 0.29 QALY for the EQ-5D measured by family caregivers and nurses, respectively. The loss of QALE for PMV patients was 9.87 to 10.17 QALY, corresponding to a health gap of 94% to 97%.

Conclusions: Theses results of poor prognosis would provide stakeholders evidence for communication to facilitate clinical decisions. The estimation may be used in future studies to facilitate the cost-effectiveness and reduction of the health gap.

Copyright © 2011, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

Funding: Supported, in part, by the National Science Council (Grant 98-2341-B-002-129), National Health Research Institutes (Grant 97A1-HDPP01-014 and 98A1-PHAPHD-014), and Chia-Yi Christian Hospital (Grant R97-9 and R98-3) in Taiwan. The authors declare that there is no potential conflict of interest.

* Address correspondence to: Jung-Der Wang, Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Rm. 719, No 17, Xuhzou Road, Taipei, Taiwan, 10055.
E-mail: jdwang@ntu.edu.tw.
Introduction
The number of patients requiring prolonged mechanical ventilation (PMV) is rapidly increasing, because the improved quality of care in ICUs (intensive care units) has resulted in the long-term survival of many patients [1–3]. However, these patients often continually require respiratory care after transfer to a rehabilitation facility, skilled nursing facility, or home care, and this creates a tremendous financial burden for the insurance system and/or their families [2,3]. The financial impact is particularly heavy for countries with a national health insurance system with universal coverage of their citizens and is aggravated by the innovation of new technologies and an aging population [4]. Most of these countries have adopted economic analyses to improve overall cost-effectiveness and contain costs [5–7]. Evaluation of the cost per quality-adjusted life year (QALY) gained from different healthcare services will ensure the most cost-effective policy decision for health care.

The National Health Insurance (NHI) of Taiwan adopts a system of comprehensive coverage for various health-care services, including maintenance hemodialysis and chronic respiratory care. It was first established in 1995 and has been extended to cover more than 99% of the citizens of Taiwan [8,9]. The NHI established a Pilot Program of Ventilator Dependent Managed Care in 2002 to provide subsequent and long-term care for patients using PMV who are overcrowding the ICU. The program intended to cover medical services in the acute stage in the ICU, during weaning trials in the respiratory care center, dispatch to the respiratory care ward if weaning trials failed, and respiratory therapy in home care. Because the expense of chronic care for patients under PMV at home is generally too profound for most families, many try to keep their loved ones at the respiratory care ward for as long as possible. Thus, the reimbursement has resulted in a large financial burden for the NHI. During 2005, the total number of PMV patients who required respiratory care in the NHI of Taiwan reached 30,000 and accounted for 7.5% of the total NHI health-care expenditures, and this has now become one of the major threats to the sustainability of the NHI [10,11].

This study has considered both long-term survival and quality of life (QOL) together for PMV patients. Such a lack of prognostic data plus the families’ unreasonably optimistic expectations often complicates the family-physician interaction [12], and makes it difficult to communicate among patients, their families, and health-care workers for clinical decision making before and throughout the course of installing mechanical ventilation. Therefore, the purpose of this study was to estimate the QOL utility, lifetime survival, quality-adjusted life expectancy (QALE), and expected utility loss for patients using PMV.

Methods
The cohort and survival of PMV patients
We recruited all patients who were admitted to the intensive care unit and later received care at a respiratory care center and respiratory care ward in a teaching hospital in southern Taiwan between 1998 and 2007. The recruitment criterion for PMV patients was the need for mechanical ventilation support for more than 6 hours per day for 21 days [13]. Each patient was followed from the 22nd day that he or she received PMV until they died or were censored on December 31, 2007. The Kaplan-Meier method was applied to estimate the survival function.

In general, when the patients are unable to have a normal respiration function, mechanical ventilation is installed for the support of life. It is commonly established in the intensive or critical care unit, and usually a tracheotomy is performed to provide a consistently patent airway. Even under the ventilator support, such patients did not survive for more than 1 to 3 years, but occasionally there were patients with a longer survival. Thus, lifetime survival of PMV patients (up to 300 months) was obtained using a linear extrapolation of a logit-transformed curve of the survival ratio between the PMV and an age-, gender-matched reference population generated by the Monte Carlo method from the life table of the general population of Taiwan. The detailed method and the mathematical proof under the assumption of constant excess hazard can be found in our previous reports [14–18] and are briefly summarized below. Because the collection period of PMV patients ranged from 1998 to 2007, we chose the life table of the middle year (2002) for the Monte Carlo simulation.

Survival function of the age-, gender-matched hypothetical reference population
The life tables for the general population were obtained from the vital statistics published by the Department of Statistics, Ministry of the Interior, Executive Yuan, Taiwan [19]. Because the individual survival time of the subjects in a hypothetical cohort cannot be directly derived from the life table of the general population, we used the Monte Carlo method to generate the simulated survival time of age- and gender-matched hypothetical reference subjects for each patient in the PMV cohorts. The total collection of hypothetical subjects was used as the reference population. Then, the survival curve of the reference population was obtained by applying the Kaplan-Meier method to the simulated survival times.

Cross-sectional sample of PMV patients for utility measurements of QOL
To estimate the QOL utility function for these patients, we recruited a cross-sectional sample of PMV subjects [18] who, after 21 days, continued to receive care from five institutions in Taiwan. Informed consent was obtained from every patient and/or his/her family caregiver, and the study commenced after the approval of the Institutional Review Boards (IRBs) of Chia-Yi Christian Hospital and National Taiwan University Hospital. The three local hospitals also approved the study after reviewing the approval documents of the above two major IRBs.

The utility value of the QOL for PMV patients was measured using the EuroQol five-dimensional (EQ-5D) questionnaire. It is a preference-based, generic instrument [20,21] and has been extensively used in many critically ill patients based on multi-attribute utility theory [22–24]. The five dimensions assessed by the EQ-5D are mobility, self-care, usual activities, pain/discom-
fort, and anxiety/depression, each with three levels of severity (no problems, some/moderate problems, and severe/extreme problems). This provides a utility value that ranges from 0 to 1 based on the five-dimensional health state classification; 0 represents the worst health status and 1 represents perfect health. For subjects with basic cognition who communicated their responses and achieved a score of more than 15 on a mini-mental state examination (MMSE) [25,26], we conducted QOL measurements with the EQ-5D via direct face-to-face interview. Each individual patient was cross-sectionally measured one time on EQ-5D. When the patient’s consciousness was too poor to communicate with the interviewer, family caregivers and nurses were used as proxies [27–30]. We have summarized the detailed methods of validating measurements in another study [31]. Briefly, we invited both family caregivers and nurses who directly took care of the patient to also evaluate the five dimensions of EQ-5D on the patient’s behalf based on his/her understanding. The results were directly compared with the patient’s own rating, which is considered the gold standard. The duration-to-date for each measurement is defined from the 22nd day after PMV to the date of the interview by the researcher. A cross-sectional sample of patients with PMV was obtained and the kernel-type smoothing method (moving average of the nearby 10%) was performed to calculate the mean QOL throughout the follow-up time period of 9 years [17,18]. The QOL value after 9 years was assumed to be the same as the end of follow-up time. We compared our results with the value systems of the United States and the United Kingdom. [21,32].

**Statistical analysis**

*Integration of survival and QOL functions, QALE, lifetime utility loss, and health gap*

The lifetime survival probabilities along the duration-to-dates (or time after beginning PMV) were multiplied (or adjusted) with the QOL values measured from EQ-5D to obtain a quality-adjusted survival curve, of which the sum of the total area under this curve was the QALE with QALY as the common unit [18]. The expected lifetime utility loss for PMV patients was calculated by assuming a uniform utility of one for the age- and gender-matched reference subjects and subtracting the QALE of PMV patients [14,16,18]. In other words, based on the hazard function or vital statistics of Taiwan, we simulated survival functions of ten reference people of the same age and gender for every PMV patient and assumed that the utility of their QOL is one that would have been the QALE of each PMV patient had they not developed the condition. The health gap, usually considered an indicator of health inequality, was defined and calculated as the proportion of expected loss of lifetime utility of patients with PMV in comparison with age- and gender-matched hypothetical referents simulated from vital statistics of Taiwan [33]. To facilitate the computation, we used the MC-QAS software program built on the R statistical package for quality adjusted survival estimation and 300-month extrapolation, designed by Dr. Jing-Shiang Hwang, Institute of Statistical Science, Academia Sinica, Taipei, Taiwan which can be downloaded for free from the following website: [http://www.stat.sinica.edu.tw/jshwang](http://www.stat.sinica.edu.tw/jshwang).

**Results**

The medical records of 633 patients who fulfilled the definition of PMV were abstracted and linked to the National...
Mortality Registry of Taiwan in 2007 to obtain their survival status. Many suffered from multiple co-morbidities, including hypertension (about half), diabetes mellitus (about two-fifths), stroke, and chronic obstructive pulmonary disease (COPD), among others, as summarized in Table 1. More than half required mechanical ventilation because of ventilation failure resulting from the above multiple co-morbidities or from cardiopulmonary resuscitation, whereas about one-seventh needed such services because of chronic lung conditions, including COPD. The overall 1-year survival rate was 33%.

From 2008 to 2009 we also screened 177 patients from five institutions and enrolled 142 patients with PMV (response rate of 80%); 55 patients provided their EQ-5D ratings directly and 87 were assessed only through either family caregivers and/or nurses. The demographic and clinical characteristics of the above two groups of PMV subjects are summarized in Table 1.

The life expectancy was 1.95 years and is depicted as the area under the survival curve of PMV patients in Figure 1. The average loss of life expectancy of these patients was 8.48 years, whereas the difference between the survival curve of age- and gender-matched referents and that of PMV patients is shown by the shaded area in Figure 1. After adjustment for QOL utility values directly measured on 55 patients who were able to respond, the QALE was 0.58 QALY, whereas QALE of patients with poor consciousness were 0.28 and 0.29 QALY for EQ-5D measured by family caregivers and nurses, respectively. Assuming that the utility value of each referent was one throughout their lifetime, the loss of QALE for PMV patients was 9.87 QALY (upper panel of Fig. 2), whereas the results for 87 patients with poor cognition and inability to respond (MMSE<15) were 10.17 and 10.16 QALY for utility values measured by family caregivers and nurses, respectively. The sensitivity analysis of substituting the utility values of the United States with those from the United Kingdom did not show a significant difference in QALE between patients and their proxies and is summarized in Table 2. The health gap was 94% and 97% for patients with a partial cognition and poor cognition, respectively.

Discussion

This study estimates lifetime survival function and quality of life in PMV patients while simultaneously obtaining the quality-adjusted life expectancy and the expected lifetime utility loss, and providing empirical evidence to facilitate discussion on health policy decision among patients, their families, health-care workers, and the policy makers. We found that the life expectancy of patients using PMV was 1.95 life years, which is less than the 2.65 life years estimated by Cox et al. [34] through Markov model simulation. Moreover, the QALE estimated by this study was only 0.28 to 0.58 QALY, which is much less than the 1.77 QALY reported previously [34]. Although investigators would usually like to compare the results from ex ante prediction with those of ex post outcome evaluation, the two studies cannot be directly compared because of major differences in the recruited subjects and measurements. Our study has a much higher proportion of patients with poor consciousness (62% vs. 30%), the patients were on PMV more than 21 days, and the patients were on average 10 years older than theirs (mean ages 76 vs. 66 years) [34,35]. Thus, our subjects had a poorer quality of life and lower 1-year survival rate (33% vs. 42%) than others [23, 34–36]. Moreover, different types of utility measurements of QOL were applied in different studies, EQ-5D versus SF-36 or quality of well-being index. Hence, the estimated QALE in our patients under PMV were lower than those reported from previous studies. We therefore recommend that future research on patients with normal or better consciousness be conducted to determine the QALE more accurately for such patients with different age and gender strata.

Given the limited resources in health care, it is inevitable that most countries with a national health insurance system must consider the comparative cost-effectiveness of their decisions on resource allocation, and the common unit of QALY that simultaneously considers both mortality and morbidity (or, survival and quality of life) has become more widely used. The National Institute for Health and Clinical Excellence in the United Kingdom [37,38] is known worldwide for such practices. However, there are still controversial issues of distributive justice in bioethics concerning potential discrimination against the aged and disabled [39,40]. Daniels proposes in the
principle of distributive justice that everyone is entitled to obtain health care up to their “normal life span,” if possible [39], and this is adopted in the calculation of a health gap proposed in the summarization of the population health [33]. The health gap was 94% and 97% for patients with a partial cognition and poor cognition, respectively, indicating that these patients are more disadvantaged and deserve more resources based on the principle of justice. Therefore, we recommend that more efforts be implemented to improve the long-term survival and QOL for PMV patients with different underlying causes or co-morbidities to improve the efficacy of such a treatment if the cost is paid by the patients themselves or their private health insurances. If, however, the expense of PMV is paid by national health insurance, the results of this study can facilitate a more reasonable decision among all stakeholders according to the principles of equity and efficiency. For example, are we willing to spend more resources on PMV or child health, vaccinations, and preventive care, among others? Without the above data, the task of making health decisions is generally difficult.

In Asian countries (including Taiwan), where patients and their families are not accustomed to preparing their wills early in life or signing “do not resuscitate” documents before they are critically ill, the estimates of QALE for patients with PMV are relevant and can be the opening to begin a dialogue between all stakeholders and the public. The results provide the first evidence to sound the wake-up call for the public to contemplate and openly discuss the principles of health resources distribution for the national health insurance on PMV care.

Our study has the following limitations. First, the validity of the QOL measurement for critically ill patients with an impairment of cognition or even unconsciousness must be addressed. To resolve this difficulty, we conducted a survey of the patient’s proxies that included both family caregivers and nurses who directly took care of the patient, which was reported in other studies [27–29,34]. The results are summarized in a separate report directly comparing the EQ-5D values of 55 patients with those rated by their family caregivers and nurses [31]. Because EQ-5D contains only two dimensions that require subjective rating, namely, pain/discomfort and anxiety/depression, we found minor differences of the final EQ-5D values between the patient-caregiver pairs and patient-nurse pairs, −0.03±0.14, and 0.03±0.22, respectively. The results enabled us to stratify these patients according to the severity of their cognitive ability deficits and to calculate the quality-adjusted life expectancy as a sensitivity analysis, which showed that the difference between patients with good and poor consciousness is less than 0.30 QALY (Table 2). Although our sample size was too small for us to further stratify into more categories according to age and gender, it seemed that the difference might not be large for patients with poor consciousness. Second, we assumed a uniform utility of one for the age- and gender-matched reference subjects that over-estimated the lifetime utility of the general population and also the expected lifetime utility loss of PMV patients. However, because such an assumption is uniformly applied, the bias was minimized when we calculated the health gaps for different health conditions. Third, during the lifetime extrapolation of QOL function it was assumed that the patients remained at the same level of QOL near the end of follow-up. Such an assumption could have resulted in an overestimation because the actual QOL might gradually decline as the patient ages. Fourth, the accuracy of the estimation of QALE would have improved if we had obtained quality-of-life measurements during the follow-up of every patient in the PMV cohort. Unfortunately, we were unable to conduct this study prospectively. Thus, we simply took another consecutive, cross-sectional sample of 142 PMV patients with different duration-to-dates and applied a smoothing method for the estimation of lifelong QOL function. We have demonstrated through simulation that a random sample of more than 50 subjects would be adequate for the above estimation, or, the relative bias would be less than 5% [18]. In fact, the PMV cohort to estimate survival function was described as a very homogenous group. The results are summarized in Table 1. Fifth, we used the age- and gender-matched general population as the reference group to estimate the loss of QALE and health gap for PMV patients.

Table 2 – QALE (in years) and expected lifetime loss of utility for patients under PMV based on different value systems of EQ-5D and patient’s cognition for sensitivity analysis.

<table>
<thead>
<tr>
<th>Categories</th>
<th>Country of value system for EQ-5D</th>
<th>QALE (SE)</th>
<th>Expected lifetime loss of utility (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with partial cognition and ability to respond (MMSE=15, n=55)</td>
<td>UK</td>
<td>US</td>
<td></td>
</tr>
<tr>
<td>QOL measured by patients (n=55)</td>
<td>0.74 (0.13)</td>
<td>0.58 (0.09)</td>
<td>9.73 (0.13)</td>
</tr>
<tr>
<td>QOL measured by family caregivers (n=44)</td>
<td>0.67 (0.15)</td>
<td>0.61 (0.18)</td>
<td>9.80 (0.16)</td>
</tr>
<tr>
<td>QOL measured by nurses (n=53)</td>
<td>0.70 (0.16)</td>
<td>0.64 (0.15)</td>
<td>9.77 (0.11)</td>
</tr>
<tr>
<td>Referents (age- and gender-matched)</td>
<td>10.47 (0.02)</td>
<td>10.45 (0.02)</td>
<td>—</td>
</tr>
<tr>
<td>Patients with poor cognition and inability to respond (MMSE&lt;15, n=87)</td>
<td>UK</td>
<td>US</td>
<td></td>
</tr>
<tr>
<td>QOL measured by family caregivers (n=81)</td>
<td>0.44 (0.09)</td>
<td>0.28 (0.05)</td>
<td>9.98 (0.13)</td>
</tr>
<tr>
<td>QOL measured by nurses (n=81)</td>
<td>0.43 (0.09)</td>
<td>0.29 (0.05)</td>
<td>9.99 (0.09)</td>
</tr>
<tr>
<td>Referents (age- and gender-matched)</td>
<td>10.42 (0.02)</td>
<td>10.45 (0.02)</td>
<td>—</td>
</tr>
</tbody>
</table>

MMSE, mini-mental state exam; PMV, prolonged mechanical ventilation; QALE, quality-adjusted life expectancy; QOL, quality of life; SE, standard error.
Because patients with PMV usually cannot survive for more than 1 day without ventilation support, it is almost impossible or extremely difficult to collect another group of patients under the same condition but without mechanical ventilation. However, future studies are planned that will collect more PMV cases and stratify them by different co-morbidities and/or underlined diseases to determine if their survival and QOL are different to further improve the cost-effectiveness for such care. Finally, because each country may have different quality of care, and hence, different survival and QOL functions, the generalization of the results from this study to other nations may be limited.

Conclusions

The life expectancy of an average 76-year-old patient under PMV was about 1.95 years in Taiwan, which amounts to 0.58 QALY (partial consciousness) and 0.28 QALY (poor consciousness) after an adjustment for quality of life measured by EQ-5D. The estimate is useful to facilitate discussions among patients, their families, and health-care workers for clinical decision making early and throughout the course of installing mechanical ventilation. Moreover, the results can also serve as a starting point for a public dialogue on resource allocation for the NHI on critical care, aging, and palliative care. Future studies should further integrate medical cost into the estimation of the cost per QALY gained together with consideration of reduction of the health gap to preserve health equality.

References


[38] Vergel YB, Sculpher M. Quality-adjusted life years. Pract Neurol 2008;8:175–82.
