



The prognostic predictors of six-month mortality for residents with advanced dementia in long-term care facilities in Taiwan: A prospective cohort study

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ABSTRACT

Background: Although hospice or palliative care for patients with advanced dementia has been implemented for more than 30 years, few studies have investigated the prognostic predictors of 6-month mortality in these patients. Prognostication has been a major obstacle, and 6-month prognostic predictors for patients with advanced dementia are still considered elusive.

Objectives: To better understand the dying trajectories of patients with advanced dementia, we performed a longitudinal prospective cohort study to investigate the predictors of 6-month mortality for residents with advanced dementia in long-term care facilities in Taiwan.

Design: Prospective cohort study.

Setting: This study took place in 32 long-term care facilities selected from northern, central, and southern Taiwan.

Participants: The study included 320 residents with advanced dementia.

Measurements: Measurements were obtained after determining study eligibility; the participants underwent follow-up assessments once every 3 months for 6 months or died during follow-up. The assessments included demographic characteristics, health and medical status characteristics, and death-related information. The Kaplan-Meier survival function estimation and the Cox proportional hazards model were used to estimate the survival rate and predict the prognostic factors.

Results: Baseline data from 320 residents with advanced dementia in long-term care facilities were obtained. The mean age was 82.7 years and 61.6% were female. The 6-month survival rate was 78.1%. The major cause of death was multiple organ failure related to pneumonia. The 6-month prognostic predictors were pneumonia (adjusted hazard ratio, 5.56; 95% confidence interval, 2.46–12.6; p -value < .001), reduction in nutrient intake >25% (adjusted hazard ratio, 5.05; 95% confidence interval, 2.37–10.8; p -value < .001), oxygen dependency (adjusted hazard ratio, 2.58; 95% confidence interval, 1.51–4.39; p -value = .001), treatment for electrolyte abnormalities (adjusted hazard ratio, 2.14; 95% confidence interval, 1.10–4.14; p -value = .025), severe pressure injuries (adjusted hazard ratio, 2.04; 95% confidence interval, 1.13–3.67; p -value = .018), and long-term indwelling urinary catheters (adjusted hazard ratio, 1.80; 95% confidence interval, 1.09–2.96; p -value = .021).

Conclusion: Our results identified six prognostic predictors of 6-month mortality among residents with advanced dementia in Taiwan. These predictors may serve as risk assessment indicators for nursing staff who provide clinical care and can enable the identification of patients in recognized terminal decline, thereby allowing access to hospice palliative services.

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What is already known about the topic?

- Hospice or palliative care for patients with advanced dementia has been implemented for more than 30 years, but prognostication has been a major obstacle.
- The 6-month prognostic predictors in patients with advanced dementia identified two important dimensions: “change in nutrition and food intake status” and “infections”.

What this paper adds

- The probability of residents with advanced dementia surviving the next 6 months decreases over time. The 3-month and 6-month survival rates were 90% and 78.1%, respectively.
- Prognostic factors associated with 6-month mortality among residents with advanced dementia were pneumonia, reduction in nutrient intake >25%, oxygen dependency, treatment for electrolyte abnormalities, severe pressure injuries, and long-term indwelling urinary catheters (>30 days).

1. Background

Patients in the final stage of dementia have severe cognitive and physical impairments, and they depend on assistance to perform activities of daily living. However, comorbid diseases and ageing-related changes (such as multiple organ deterioration), can trigger events (such as fractures caused by a fall), immune-senescence resulting in a state of frailty, vulnerability to pathogenic infections, and low recovery ability in patients with advanced dementia (Holmes, 2006; Hussain et al., 2014). Therefore, such patients usually have recurrent complications (e.g., respiratory distress, infections, pain, skin problems, nutrition and hydration problems) that may even be life-threatening, requiring emergency room visits or hospitalizations (Harlos, 2010; Lussier et al., 2011; Ouldred and Bryant, 2008; Sabbagh et al., 2011). Accordingly, hospice or palliative care where the primary objective is to provide immediate symptom relief and comfort care is regarded to be ideal for patients with advanced dementia (van der Steen et al., 2013; World Health Organization, 2011).

There is some distinction between hospice and palliative care. The WHO (2011) defines palliative care as “an approach that improves the quality of life of patients and their families who are facing problems associated with life-threatening illness. It prevents and relieves suffering through the early identification, correct assessment, and treatment of pain and other problems, whether physical, psychosocial or spiritual”. The American Medical Association (2017) refers to hospice care as a specific type of palliative care for patients who are terminally ill with a life expectancy of 6 months or less if the illness runs its normal course. In 2000, Taiwan passed the Hospice Palliative Care Act, which was the first Natural Death Act in Asia. The Hospice Palliative Care Act guarantees terminally ill (initially focused on cancer) patients’ their request for medical treatment and protects their rights. These rights include signing a do-not-resuscitate order, refusing futile medical treatments, and receiving hospice palliative care at the end of their lives. Hospice palliative care refers to the mitigatory and supportive medical care given to relieve terminal illness patients from physical, mental, and spiritual pain in order to improve their quality of life. Taiwan’s National Health Insurance covers hospice palliative care for beneficiaries who are terminally ill and diagnosed with an incurable condition by two physicians and there is medical evidence showing that the prognosis will be fatal within the near future. Taiwan’s hospice palliative care is aligned with the spirit of hospice care. There are three levels of

hospice palliative care in Taiwan, including (1) inpatient hospice services (hospice wards/palliative care units); (2) hospice home care services (regular home visits or long-term care facility visits by nurses and interdisciplinary staff members); and (3) hospital-based hospice shared care services (providing hospice palliative care in acute hospital settings; the hospice palliative care team and the acute ward team work together to share the care responsibility). In September 2009, Taiwan’s National Health Insurance coverage for hospice palliative care was expanded from patients with terminal cancer and motor neuron disease to eight non-cancerous diseases, including advanced dementia (the eligibility criteria are shown in Supplementary Table 1) (Ministry of Health and Welfare of Taiwan, 2013).

Although hospice or palliative care for patients with advanced dementia has been implemented for more than 30 years, few studies have investigated the prognostic predictors of 6-month mortality in these patients; such prognostication has been a major obstacle (Mitchell et al., 2012; van der Steen et al., 2017). Holloway et al. (2014) reported that accurately estimating the prognosis and effectively communicating it to patients and their family caregivers is beneficial for medical decision-making. At present, predicting the prognosis of diseases is mainly based on existing prediction models or on the clinicians’ experience. However, the prognostic predictors of 6-month mortality in patients with advanced dementia are still unclear. Previous empirical studies have identified two important dimensions: “changes in nutrition and food intake status (<25% food eaten, malnutrition, decreased appetite, anorexia, cachexia, weight change, trouble swallowing)” and “infections (pneumonia, pressure injuries \geq stage 3)” (Aminoff and Adunsky, 2006; Aminoff, 2008; Hicks et al., 2010; Luchins et al., 1997; Mitchell et al., 2004, 2009, 2010; Schonwetter et al., 2003). However, prior research has shown that prognostic indicators of 6-month mortality lack large sample sizes in prospective follow-up cohorts (subjects in most studies numbered less than 200), focus on Caucasians, and include data from western countries and health insurance systems with limited data in the minimum data set regarding nursing home resident assessment and care screening. Therefore, different ethnic groups and medical insurance systems need to be included in future studies. To better understand the dying trajectories of patients with advanced dementia, we performed a longitudinal prospective cohort study to investigate the prognostic predictors of 6-month mortality for residents with advanced dementia in long-term care facilities in Taiwan.

2. Methods

2.1. Study design

This was a prospective cohort study. The participants underwent follow-up assessments once every 3 months for 6 months or died during follow-up. We recorded their survival status and relevant demographic characteristics, health and medical status, and death-related information.

2.2. Setting and participants

Sixty-one long-term care facilities with at least 60 beds in northern, central, and southern Taiwan were contacted, of which 32 agreed to participate, including 21 nursing homes (providing assistance with activities of daily living and full-time skilled nursing care), 10 residential care facilities (providing supervision and personal care services; residents move in when they are not dependent on nursing care), and one dementia special care unit (caring for patients who have been diagnosed with dementia, providing supervision and assistance with activities of daily living,

along with medical and nursing care). All of the facilities provide hospice palliative care liaison services to residents with advanced dementia. The inclusion criteria for the residents were a diagnosis of dementia made by a physician, a Functional Assessment Staging (FAST) score stage seven C or greater, and being institutionalized for >30 days.

Fig. 1 displays the cohort development. We screened 355 residents with advanced dementia who met the inclusion criteria. The family caregivers of 35 residents refused to participate (these family caregivers did not permit residents to enroll, and six family caregivers could not be contacted), resulting in a refusal rate of 9.9%. The remaining 320 residents participated in this study; with 12 being lost to follow-up during the study period (attrition rate of 3.8%). The numbers and reasons included for attrition at 3 and 6 months are shown in Fig. 1). The mean follow-up time was 156.2 ± 49.7 days, ranging from 3 to 180 days. The data analysis included all available data up to the time of loss to follow-up, withdrawal, death or the end of the study.

2.3. Data collection and measurement

This project was reviewed and approved by the Institutional Review Board of National Yang-Ming University (Number: YM104090F). A researcher personally explained the study and its purpose to institutional agents and family caregivers and obtained their written informed consent prior to performing any study-related procedures. After the institutions identified research subjects who met the inclusion criteria, we reviewed their medical records to collect data at baseline (Time 0/ Day 1), 3 months (Time 1/ Day 90) and 6 months (Time 2/ Day 180). The baseline data also included data related to health and medical status from the 6 months prior to study initiation. For the residents living in long-term care facilities for less than 6 months, we collected their data from the entirety of their stay in the institution. For subjects who died during follow-up, death-related information was collected (Fig. 1).

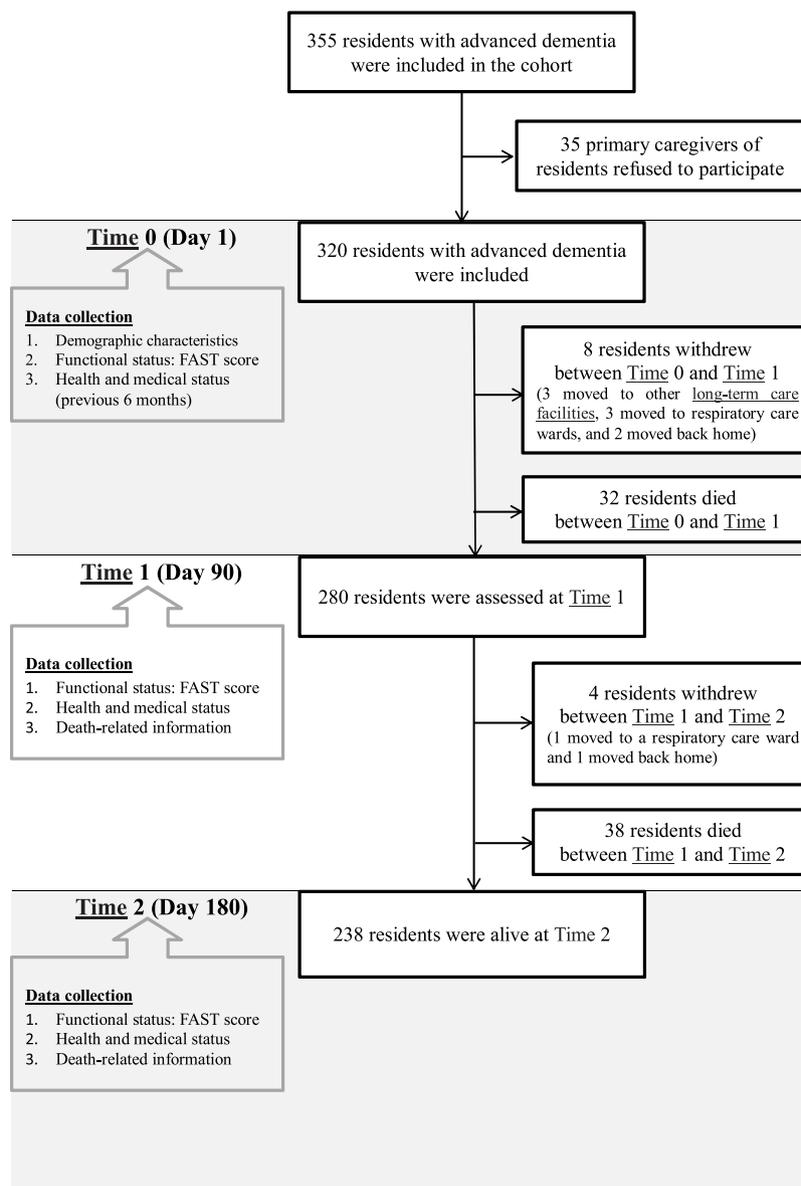


Fig. 1. Flow chart of cohort development and data collection.

2.4. Instruments

2.4.1. Screening instrument

The FAST score developed by Reisberg was used to confirm that the residents met the inclusion criteria. The FAST score classifies dementia disease progression into seven main stages and subdivides stage 6 and stage 7 into 5 and 6 sub-stages, respectively, to confirm disease severity. Concurrent validity values of FAST scores with those of the Mini-Mental State Examination, Global Deterioration Scale, and Ordinal Scales of Psychological Development scales were 0.80, 0.90, and -0.79 ($p < .001$), respectively. The rater consistency (fixed effect intra-class correlation) was 0.86, and the rater agreement (random effect intra-class correlation coefficient) was 0.87 (Sclan and Reisberg, 1992). We obtained consent from the original authors before initiating this study. The FAST score included 16 items. First, the traditional Chinese version of the FAST score was created by translating the instrument from English to traditional Chinese, and then translating it back. We then invited five experts (three neurologists, one clinical psychologist of neuroscience, and one supervisor of a dementia special care unit) to assess the validity of the content. A 4-point rating scale (1 = not clear/relevant, 2 = somewhat clear/relevant, 3 = quite clear/relevant, and 4 = highly clear/relevant) was then used to determine the agreement of these experts. The averages of the item scores (meaningfulness, fluency, comprehensibility, and succinctness) ranged from 0.94 to 0.97. Inter-rater reliability was subsequently assessed. Two nurses with over 10 years of experience in dementia care tested the reliability of the traditional Chinese version of the FAST score by sampling 35 residents with dementia from a dementia special care unit in November 2015. The inter-rater reliability showed an intra-class correlation coefficient of 0.83. The traditional Chinese version of the FAST score was therefore considered to be useful in a clinical setting for people with advanced dementia.

2.4.2. Questionnaire and chart review

The questionnaire used was constructed based on a systematic review of relevant prognostic factors for 6-month mortality in patients with advanced dementia, the eligibility criteria for hospice palliative care in Taiwan, and the researchers' clinical experience (Aminoff and Adunsky, 2006; Aminoff, 2008; Hicks et al., 2010; Luchins et al., 1997; Ministry of Health and Welfare of Taiwan, 2013; Mitchell et al., 2004; Mitchell et al., 2009; Mitchell et al., 2010; Schonwetter et al., 2003). A chart review included the following three components:

- 1 *Demographic characteristics*, including location of institution, facility type, age, gender, and length of institutionalization (months);
- 2 *Health and medical status characteristics*, including (1) comorbid diseases and medications used (monthly); (2) dementia severity: type and duration of dementia [at the time of diagnosis (from medical records) and severity of dementia (FAST score rated by a researcher) at the three time points of follow-up]; (3) advance directives and received hospice palliative care, such as a do-not-resuscitate order or a do-not-hospitalize order; (4) nutrition status and eating problems: body weight (monthly), body mass index (monthly), intake of nutrients and water (monthly), nutritional markers, such as serum albumin level, weight loss >10%, and reduction in nutrient intake >25%; (5) infections and antimicrobial therapy such as aspiration pneumonia, skin problems and treatment (monthly) and type of antimicrobial drugs used, duration and routes of administration; (6) acute medical conditions, such as emergency room visits, hospitalizations (diagnosis, time and duration of hospitalization), supplemental oxygen therapy (frequency and type of

oxygen therapy), and electrolyte abnormalities and treatment; and (7) life-sustaining treatment as described in detail in our study (using government documents of Taiwan), such as cardiopulmonary resuscitation, endotracheal intubation, use of mechanical ventilation (invasive ventilation or non-invasive ventilation), defibrillation, and drugs. Additionally, based on literature reviews also included were specialized treatments such as use of a nasogastric tube, surgery, long-term indwelling urinary catheters (>30 days), or other invasive procedures.

- 3 *Death-related information*, including the date, cause, and location of death

2.5. Statistical analyses

SPSS for Windows version 20.0 was used for all statistical analysis, and the statistical significance level was set at $p < .05$. The following data analyses were performed: (1) descriptive statistics, (2) survival analysis using (i) the Kaplan-Meier survival function estimation to evaluate the survival time, (ii) bivariate analysis: using the log-rank test and univariate Cox proportional hazards model to compare of survival functions and the ratio of hazard functions between the two groups; the predictor variables reaching significance in the crude analysis were included in collinearity diagnosis, and (iii) Cox proportional hazards model: the results of bivariate analysis guided the selection of predictor variables for inclusion in a multivariate Cox proportional hazards model. Age and gender were forced in, and a forward stepwise regression was used to determine the appropriate model. After the final Cox proportional hazards model had been derived, the bootstrap method was used to verify the stability of model and Harrell's C-statistic was used to assess the discrimination ability of the model.

3. Results

3.1. Characteristics of participants

Table 1 shows the detailed characteristics obtained at baseline (Day 1), Day 90, and Day 180 from the 320 institutionalized residents with advanced dementia. At baseline, the mean age was 82.7 years (standard deviation [SD]: 8.8), 61.6% were female, 76.6% were living in a nursing home, and the most common type of dementia was senile dementia (75%). At the 6-month follow-up, death trends appeared to be increasing in terms of age (older age), gender (male), dementia severity (stage 7f of FAST score), more comorbid diseases, long-term indwelling urinary catheters, oxygen dependency (>20 days/month), treatment for electrolyte abnormalities, diagnosed with pneumonia, and using of life-sustaining treatment.

Table 2 presents the vital status distributions and the results from the log-rank test. The residents experienced some eating problems and changes in nutritional status, with a high proportion (91.9%) using feeding tubes, 15 of whom had a first feeding tube insertion, 11 (3.6%) had a reduction in nutrient intake >25%, 10 were fed via feeding tubes; and 51 (16.6%) had malnutrition (albumin level <2.5 g/dl or weight loss >10%). There were some acute medical conditions: 168 residents (54.5%) underwent a hospitalization, 8 were diagnosed with cardio-cerebrovascular diseases and 6 received aggressive treatments (e.g., use of life-sustaining treatment or surgical procedures). The following factors were associated with an increased risk of 6-month mortality: age (crude hazard ratio [HR]: 1.06, 95% confidence interval [CI]: 1.03–1.09, 1.03–1.09, p -value [p] < .001), duration of antimicrobial therapy (crude HR: 1.02, 95% CI: 1.01–1.02, $p < .001$), use of feeding tubes ($\chi^2 = 4.78$, degree of freedom

Table 1
Characteristics of participants at three time points within the 6-month follow-up (n = 320).

| Variables | Time 0 (Day 1 data) (n = 320) n (%) /M ± SD | Time 1 (Day 90 data) (n = 280) n (%) /M ± SD | Time 2 (Day 180 data) (n = 238) n (%) /M ± SD |
|---|--|---|--|
| <i>Demographic characteristics</i> | | | |
| Location of institution | | | |
| Northern Taiwan | 113 (35.3) | 103 (36.8) | 90 (37.8) |
| Central Taiwan | 88 (27.5) | 76 (27.1) | 60 (25.2) |
| Southern Taiwan | 119 (37.2) | 101 (36.1) | 88 (37.0) |
| Facility type (n = 32) | | | |
| Nursing home (n = 21) | 245 (76.6) | 206 (73.6) | 176 (73.9) |
| Residential care facility (n = 10) | 24 (7.5) | 24 (8.6) | 19 (8.0) |
| Dementia special care unit (n = 1) | 51 (15.9) | 50 (17.9) | 43 (18.1) |
| Age (years) | 82.7 ± 8.8 | 82.4 ± 9.1 | 81.6 ± 8.7 |
| Length of institution stay (months) | 58.4 ± 55.6 | 61.7 ± 55.8 | 61.5 ± 50.5 |
| Gender | | | |
| Female | 197 (61.6) | 175 (62.5) | 156 (65.5) |
| Male | 123 (38.4) | 105 (37.5) | 82 (34.5) |
| <i>Functional status</i> | | | |
| Stage of Functional Assessment Staging score | | | |
| Stage 7c | 4 (1.3) | 4 (1.4) | 4 (1.7) |
| Stage 7d | 66 (20.6) | 62 (22.1) | 57 (23.9) |
| Stage 7e | 143 (44.7) | 130 (46.4) | 109 (45.8) |
| Stage 7f | 107 (33.4) | 84 (30.0) | 68 (28.6) |
| <i>Health and medical status characteristics</i> | | | |
| Types of dementia | | | |
| Degenerative | 272 (85.0) | 235 (83.9) | 200 (84.0) |
| Senile dementia (type not specified) ^a | 240 (75.0) | 207 (73.9) | 178 (74.8) |
| Alzheimer's disease | 32 (10.0) | 28 (10.0) | 22 (9.2) |
| Non-degenerative (vascular dementia) | 48 (15.0) | 45 (16.1) | 38 (16.0) |
| Duration of dementia (years) | 7.5 ± 4.0 | 7.5 ± 4.0 | 7.5 ± 4.0 |
| Number of comorbid diseases | 7.4 ± 2.5 | 7.3 ± 2.5 | 7.1 ± 2.4 |
| Hypertension | 265 (82.8) | 231 (82.5) | 194 (81.5) |
| Chronic obstructive pulmonary disease | 210 (65.6) | 177 (63.2) | 140 (58.8) |
| Peptic or gastric ulcers | 166 (51.9) | 143 (51.1) | 113 (47.5) |
| Advance directives | | | |
| Has a do-not- resuscitate order | | | |
| Yes | 156 (48.8) | 134 (41.9) | 109 (45.8) |
| No | 164 (51.3) | 146 (45.6) | 129 (54.2) |
| Has a do-not-hospitalize order | | | |
| Yes | 3 (0.9) | 6 (2.1) | 2 (0.8) |
| No | 317 (99.1) | 274 (97.9) | 236 (99.2) |
| Use of feeding tubes | | | |
| Yes | 279 (87.2) | 248 (88.6) | 214 (89.9) |
| No | 41 (12.8) | 32 (11.4) | 24 (10.1) |
| Long-term indwelling urinary catheters (>30 days) | | | |
| Yes | 101 (31.6) | 78 (27.9) | 59 (24.8) |
| No | 219 (68.4) | 202 (72.1) | 179 (75.2) |
| Oxygen dependency (>20 days/month) | | | |
| Yes | 76 (23.8) | 64 (23.2) | 44 (18.5) |
| No | 244 (76.3) | 216 (76.8) | 194 (81.5) |
| Weight loss >10% | | | |
| Yes | – | 9 (3.2) | 17 (7.1) |
| No | 320 (100) | 271 (96.8) | 221 (92.9) |
| Reduction in nutrient intake >25% | | | |
| Yes | – | 1 (0.4) | 1 (0.4) |
| No | 320 (100) | 279 (99.6) | 237 (99.6) |
| Severe pressure injuries (≥stage III) | | | |
| Yes | 20 (6.3) | 18 (6.4) | 18 (7.6) |
| No | 300 (93.8) | 262 (93.6) | 220 (92.4) |
| Emergency room visit | | | |
| Yes | – | 8 (2.9) | 8 (3.4) |
| No | 320 (100) | 272 (97.1) | 230 (96.6) |
| Diagnosis with cardio-cerebrovascular diseases ^b | | | |
| Yes | – | 1 (0.4) | 2 (0.8) |
| No | 320 (100) | 279 (99.6) | 236 (99.2) |
| Treatment for electrolyte abnormalities ^c | | | |
| Yes | – | 75 (26.8) | 62 (26.1) |
| No | 320 (100) | 205 (73.2) | 176 (73.9) |
| Hospitalization | | | |
| Yes | – | 84 (30.0) | 102 (42.9) |
| No | 320 (100) | 196 (70.0) | 136 (57.1) |
| Pneumonia | | | |
| Yes | – | 95 (33.9) | 75 (31.5) |
| No | 320 (100) | 185 (66.1) | 163 (68.5) |
| Use of life-sustaining treatment ^d | | | |
| Yes | – | 24 (8.6) | 13 (5.5) |

Table 1 (Continued)

| Variables | Time 0 (Day 1 data) (n = 320) n (%) /M ± SD | Time 1 (Day 90 data) (n = 280) n (%) /M ± SD | Time 2 (Day 180 data) (n = 238) n (%) /M ± SD |
|---|--|---|--|
| No | 320 (100) | 256 (91.4) | 225 (94.5) |
| Antimicrobial therapy | | | |
| Yes | 104 (32.5) | 194 (69.3) | 192 (80.7) |
| No | 216 (67.5) | 86 (30.7) | 46 (19.3) |
| Serum albumin level (g/dl) | – | 3.3 ± 0.5 | 3.3 ± 0.5 |
| Days of hospitalization (n = 168) | – | 19.4 ± 14.6 | 21.0 ± 17.9 |
| Days of antimicrobial therapy (n = 260) | – | 30.0 ± 20.5 | 37.0 ± 30.0 |

n: numbers; M: mean; SD: standard deviation.

^a Senile dementia, uncomplicated: the diagnostic code was 290.0/F03.90 by the International Statistical Classification of Disease and Related Health Problems, Nine/Tenth Revision.

^b Cardio-cerebrovascular diseases include cardiovascular disease (acute myocardial infarction or deep vein thrombosis) and cerebrovascular accident (ischemic/hemorrhagic stroke, or subarachnoid hemorrhage).

^c Medications used to correct electrolyte abnormalities.

^d Life-sustaining treatment, i.e., cardiopulmonary resuscitation, endotracheal intubation, use of mechanical ventilation, defibrillation, and drugs.

[df] = 1, $p = .03$), long-term indwelling urinary catheters ($\chi^2 = 31.3$, $df = 1$, $p < .001$), oxygen dependency ($\chi^2 = 71.0$, $df = 1$, $p < .001$), albumin level < 2.5 g/dl or weight loss $> 10\%$ ($\chi^2 = 26.6$, $df = 1$, $p < .001$), reduction in nutrient intake $> 25\%$ ($\chi^2 = 55.0$, $df = 1$, $p < .001$), severe pressure injuries ($\chi^2 = 16.9$, $df = 1$, $p < .001$),

diagnosis with cardio-cerebrovascular diseases ($\chi^2 = 23.0$, $df = 1$, $p < .001$), treatment for electrolyte abnormalities ($\chi^2 = 71.1$, $df = 1$, $p < .001$), hospitalization ($\chi^2 = 56.7$, $df = 1$, $p < .001$), pneumonia ($\chi^2 = 74.0$, $df = 1$, $p < .001$), and use of life-sustaining treatment ($\chi^2 = 54.8$, $df = 1$, $p < .001$).

Table 2

Distribution of vital status, according to demographic, health, and medical variables of the residents with advanced dementia within the 6-month follow-up period (n = 320).

| Variables | Number of cases | Proportion (%) | Survivors (n = 238) n (%) /M ± SD | Deceased (n = 70) n (%) /M ± SD | Log-rank test p-value |
|--|--------------------------|----------------|--------------------------------------|------------------------------------|--------------------------|
| <i>Demographic characteristics</i> | | | | | |
| Age (years) | 82.6 ± 8.9 ^a | | 81.6 ± 8.7 ^a | 86.2 ± 8.6 ^a | – |
| Gender | | | | | .07 |
| Female | 193 | 62.7 | 156 (80.8) | 37 (19.2) | |
| Male | 115 | 37.3 | 82 (71.3) | 33 (28.7) | |
| <i>Health and medical status</i> | | | | | |
| Use of feeding tubes | | | | | .03 |
| Yes | 283 | 91.9 | 214 (75.6) | 69 (24.4) | |
| No | 25 | 8.1 | 24 (96.0) | 1 (4.0) | |
| Long-term indwelling urinary catheters | | | | | < .001 |
| Yes | 100 | 32.5 | 59 (59.0) | 41 (41.0) | |
| No | 208 | 67.5 | 179 (86.1) | 29 (13.9) | |
| Oxygen dependency | | | | | < .001 |
| Yes | 92 | 29.9 | 44 (47.8) | 48 (52.2) | |
| No | 216 | 70.1 | 194 (89.8) | 22 (10.2) | |
| Albumin level < 2.5 g/dl or weight loss $> 10\%$ | | | | | < .001 |
| Yes | 51 | 16.6 | 26 (51.0) | 25 (49.0) | |
| No | 257 | 83.4 | 212 (82.5) | 45 (17.5) | |
| Reduction in nutrient intake $> 25\%$ | | | | | < .001 |
| Yes | 11 | 3.6 | 1 (9.1) | 10 (90.9) | |
| No | 297 | 96.4 | 237 (79.8) | 60 (20.2) | |
| Severe pressure injuries (\geq stage III) | | | | | < .001 |
| Yes | 35 | 11.4 | 18 (51.4) | 17 (48.6) | |
| No | 273 | 88.6 | 220 (80.6) | 53 (19.4) | |
| Diagnosis with cardio-cerebrovascular diseases | | | | | < .001 |
| Yes | 8 | 2.6 | 2 (25.0) | 6 (75.0) | |
| No | 300 | 97.4 | 236 (78.7) | 64 (21.3) | |
| Treatment for electrolyte abnormalities | | | | | < .001 |
| Yes | 117 | 38.0 | 62 (53.0) | 55 (47.0) | |
| No | 191 | 62.0 | 176 (92.1) | 15 (7.9) | |
| Hospitalization | | | | | < .001 |
| Yes | 168 | 54.5 | 102 (60.7) | 66 (39.3) | |
| No | 140 | 45.5 | 136 (97.1) | 4 (2.9) | |
| Pneumonia | | | | | < .001 |
| Yes | 137 | 44.5 | 75 (54.7) | 62 (45.3) | |
| No | 171 | 55.5 | 163 (95.3) | 8 (4.7) | |
| Use of life-sustaining treatment | | | | | < .001 |
| Yes | 38 | 12.3 | 13(34.2) | 25(65.8) | |
| No | 270 | 87.7 | 225(83.3) | 45(16.7) | |
| Days of antimicrobial therapy (n = 260) | 42.6 ± 31.7 ^a | – | 37.0 ± 30.0 ^a | 58.6 ± 31.1 ^a | |

n: numbers.

^a Represents mean and standard deviation.

Table 3

Univariate and multivariate Cox regression analysis of prognostic factors associated with 6-month mortality for residents with advanced dementia in long-term care facilities (n = 320).

| Variables | Univariate Cox regression analysis | | | Multivariate Cox regression analysis ^a | | |
|---|------------------------------------|-----------|---------|---|-----------|---------|
| | Crude HR | 95% CI | p-value | Adjusted HR | 95% CI | p-value |
| Age | 1.06 | 1.03–1.09 | < .001 | 1.02 | 0.99–1.05 | .214 |
| Gender (Female = 0) | 1.54 | 0.97–2.47 | .07 | 0.69 | 0.40–1.20 | .189 |
| Long-term indwelling urinary catheters (No = 0) | 3.57 | 2.22–5.74 | < .001 | 1.80 | 1.09–2.96 | .021 |
| Oxygen dependency (No = 0) | 6.61 | 3.98–11.0 | < .001 | 2.58 | 1.51–4.39 | .001 |
| Serum albumin <2.5 g/dl or weight loss >10% (No = 0) | 3.37 | 2.06–5.50 | < .001 | | | |
| Reduction in nutrient intake >25% (No = 0) | 8.47 | 4.30–16.7 | < .001 | 5.05 | 2.37–10.8 | < .001 |
| Severe pressure injuries (≥stage III) (No = 0) | 2.98 | 1.73–5.16 | < .001 | 2.04 | 1.13–3.67 | .018 |
| Diagnosis of cardio-cerebrovascular diseases (No = 0) | 6.08 | 2.62–14.1 | < .001 | | | |
| Treatment for electrolyte abnormalities (No = 0) | 8.28 | 4.60–14.9 | < .001 | 2.14 | 1.10–4.14 | .025 |
| Pneumonia (No = 0) | 12.4 | 5.95–26.0 | < .001 | 5.56 | 2.46–12.6 | < .001 |
| Use of life-sustaining treatment (No = 0) | 5.26 | 3.22–8.60 | < .001 | | | |
| Days of antimicrobial therapy | 1.02 | 1.01–1.02 | < .001 | | | |

n: numbers; HR: hazard ratio; CI: confidence interval.

^a Age and Gender were forced in. A stepwise forward regression model was used.

3.2. Survival time

70 residents (21.9%) residents died during follow-up, of whom 77.1% died in hospitals; the mean survival time was 92.9 days (SD: 54.4, range: 3–178). The major cause of death was multiple organ failure related to pneumonia (n=63, 90%). The Kaplan-Meier survival curve showed that the probability of residents with advanced dementia surviving for 6 months decreases over time. The 3-month and 6-month survival rates were 90% and 78.1%, respectively.

3.3. Prognostic factors of 6-month mortality

All significant predictors from the univariate analysis were included in the multivariate Cox proportional hazards model; the results are shown in Table 3. The prognostic factors of 6-month mortality in residents with advanced dementia were pneumonia (adjusted HR, 5.56; 95% CI, 2.46–12.6; $p < .001$), reduction in nutrient intake >25% (adjusted HR, 5.05; 95% CI, 2.37–10.8; $p < .001$), oxygen dependency (adjusted HR, 2.58; 95% CI, 1.51–4.39; $p = .001$), treatment for electrolyte abnormalities (adjusted HR, 2.14; 95% CI, 1.10–4.14; $p = .025$), severe pressure injuries (adjusted HR, 2.04; 95% CI, 1.13–3.67; $p = .018$), and long-term indwelling urinary catheters (adjusted HR, 1.80; 95% CI, 1.09–2.96; $p = .021$). The discriminative performance of the final model was assessed using Harrell's C-statistic. A value of $C = 0.86$ indicates that 86% of the subjects were correctly classified.

4. Discussion

This prospective cohort study included 6 months of follow-up data from 320 residents with advanced dementia in long-term care facilities. The 6-month survival rate was 78.1%. Six prognostic factors (pneumonia, reduction in nutrient intake >25%, oxygen dependency, severe pressure injuries, treatment for electrolyte abnormalities, and long-term indwelling urinary catheters) were associated with 6-month mortality. The prognosticators of pneumonia and severe pressure injuries (≥stage III) were involved in the dimension of “infections”; reduction in nutrient intake >25% is associated with the dimension of “change in nutrition and food intake status”, and others including oxygen dependency, treatment for electrolyte abnormalities, and long-term indwelling urinary catheters (>30 days) were related to the dimension of “physical condition changes”.

The 6-month mortality rate, and pneumonia being the major cause of death, was similar to the findings of previous prospective

studies (Mitchell et al., 2009, 2010; van der Steen et al., 2007). We also found that hospitalizations (mortality rate of 39.3%) and received hospice palliative care (7/9; mortality rate of 77.8%) were associated with significantly shorter survival times. These findings are consistent with previous studies (Aminoff and Adunsky, 2006; Hanrahan et al., 1999; Hicks et al., 2010; Luchins et al., 1997) and may be due to frailty, weakened immune systems, and a reduced recovery ability (Cintra et al., 2014; Morrison and Siu, 2000).

Pneumonia was both a prognostic predictor of 6-month mortality and a major cause of hospitalization in this study (137/168, 81.5%). We also found that the residents diagnosed with pneumonia had an increase in 6-month mortality from 4.7% to 45.3%. This finding may be associated with the frequent administration of aggressive treatments (e.g., antimicrobial therapy and intensive care unit referral) during hospitalization, the occurrence of other medical complications, increased frequency and days of hospitalization, and the short-term risk of mortality (Fulton et al., 2014; Hicks et al., 2010; Mitchell et al., 2012; Rexach, 2012).

With disease progression, patients with dementia experience atrophy of the mesial cortical surface, which causes poor appetite and low energy intake, potentially changing nutritional status and increasing morbidity and mortality (Candy et al., 2009; Hoffer, 2006). Previous studies on the prognosis of patients with advanced dementia have indicated that changes in food intake and nutritional status have significant effects on 6-month survival (Aminoff, 2008; Aminoff and Adunsky, 2006; Hanrahan et al., 1999; Hicks et al., 2010; Luchins et al., 1997; Mitchell et al., 2004, 2010). We also found that a reduction in nutrient intake >25% significantly increased the risk of 6-month mortality. In addition, Jaul et al., (2016) reported that changes in nutrient intake, nutritional status, and immobility resulted in skin problems, particularly pressure injuries, in 95% of their institutionalized residents with advanced dementia. Our results showed 2.04 times the risk of mortality for residents with severe pressure injuries (≥stage III). In addition, 20 of the 35 residents with severe pressure injuries underwent wound debridement surgery, and this aggressive treatment increased the risk of mortality for older patients.

In the current study, a high proportion (91.9%) of the residents were fed via a feeding tube for an average of >3 years. This finding suggests that use of a feeding tube is the only option for dealing with eating difficulties or anorexia in Taiwan. These findings suggest that attention has not been given to the issues of medical decision-making, ethical considerations, dignity, and quality of life associated with tube feeding. Another important aspect is that Taiwan passed the Patient Autonomy Act in January 2016 and will

be implementing new regulations in January 2019. The act permits a patient with severe dementia to refuse life-sustaining treatment according to a letter of intent from the patient or an advanced directive, and in particular, this is not limited to the advanced stage. Moreover, decision-making with regards to types of life-sustaining treatment has been expanded to include issues of artificial nutrition and hydration. Along with disease progression, these indicate the need of clinicians and the nursing staff to be ready to discuss the efficacy, medical complications, ethical and legal considerations, and quality of life related to artificial nutrition and hydration with patients and family caregivers.

Our results are similar to those of Mitchell et al (2004) in that the residents with oxygen dependency had a higher risk of mortality. One reason for this may be that a high proportion of our subjects had pulmonary diseases, including pneumonia due to viral/bacterial infections, acute asthma exacerbation, and status asthmaticus requiring hospitalization. In addition, the 15 residents who had a chronic respiratory failure and were treated with non-invasive ventilation had a high mortality rate (73%; 11 of whom died during follow-up), possibly due to a high rate of adverse effects with non-invasive ventilation (respiratory infections and multiorgan failure) (Hernández et al., 2016).

Previous studies showing a relationship between long-term indwelling urinary catheters and mortality are controversial (Nicolle, 2014). In the present study, long-term catheterized residents with advanced dementia increased their likelihood of death (adjusted HR, 1.80; $p = .021$). This result is similar to the previous finding (Hanrahan et al., 1999).

Patients with advanced dementia who have electrolyte abnormalities are eligible for hospice palliative care in Taiwan. Previous studies have reported a prevalence rate of electrolyte abnormalities in older hospitalized patients of 10.6% and have noted that hypernatremia, hyperkalemia, and hypokalemia are predictors of immediate mortality. Furthermore, hypernatremia has been reported to be common in hospitalized patients with dementia, mainly due to dehydration from fever or cachexia (Auyeung and Lee, 2007; Schlanger et al., 2010). Our results also found that treatment for electrolyte abnormalities significantly affected the 6-month prognosis, possibly due to a higher rate of infections.

Our study revealed that residents with advanced dementia in Taiwan usually receive many aggressive treatments (12.3%, use of life-sustaining treatment; 4.9%, long-term use of non-invasive ventilation; 75%, diagnosed with cardio-cerebrovascular diseases to receive surgical treatment), with 6-month mortality rate ranging from 65.8% to 75%, even when they had an advanced stage of disease. On the other hand, Chen et al., (2018) determined the average rate of hospice palliative care coverage in patients with dementia to be 1.64% from 2009 to 2013; in our study, it was 0.97%. The reasons for the use of more aggressive treatments and the underutilization of hospice palliative care for patients with advanced dementia in Taiwan may include a limited understanding among family caregivers and healthcare staff concerning the poor prognosis and clinical course of advanced dementia and the lack of a designated area (equipment requirement and space) for hospice palliative care in long-term care facilities.

Despite the large sample size and high follow-up rate, there are several limitations to this study. The study mainly focused on factors predicting 6-month mortality in institutionalized residents with advanced dementia. Future studies should enroll community-dwelling patients with advanced dementia to extend the results to a wider patient population. We found that in the residents who had acute medical complications, 25 of 152 family caregivers changed their minds about previously established do-not-resuscitate orders and allowed the residents to receive life-sustaining treatment. We did not interview the family caregivers to gain a better

understanding of the decision-making process, and future studies should investigate this further. Ultimately, 12 subjects dropped out during the follow-up period, and we tested for homogeneity between those who were enrolled and those who dropped out. There were no statistically significant differences.

5. Conclusions

Understanding the factors that affect disease prognosis is beneficial for the development of policies and the provision of services that meet patient needs. Our results identified six prognostic predictors of 6-month mortality among residents with advanced dementia in Taiwan. These predictors may serve as risk assessment indicators for nursing staff who provide clinical care and can enable the identification of residents in terminal decline, thereby allowing access to hospice palliative care. Future studies should investigate the use of prognostic predictors as references for the development of hospice palliative care for residents with advanced dementia.

Authors' contributions

All authors have contributed significantly to the manuscript. Pei-Chi Hsieh, and Li-Chan Lin designed the study. Li-Chan Lin, Shiao-Chi Wu, Jong-Ling Fuh, and Ying-Wei Wang provided critical feedback and helped shape the research. Pei-Chi Hsieh, Shiao-Chi Wu, Jong-Ling Fuh, and Li-Chan Lin analysed and interpreted the data. Pei-Chi Hsieh wrote the original draft of the manuscript. Li-Chan Lin wrote reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

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Conflict of interest

No conflicts of interest have been declared by the authors.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijnurstu.2018.12.013>.

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