Trajectories of Activities of Daily Living in the Last 8 Weeks of Life Among Patients With Terminal Cancer in a Palliative Care Unit: A Retrospective Study

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Abstract

Purpose: To clarify the multiple trajectories of activities of daily living (ADL) in patients with terminal cancer using a comprehensive assessment measure.

Methods: This retrospective study analyzed hospitalized patients with cancer who died or were discharged from a palliative care unit. Multiple trajectories were estimated using group-based trajectory modeling (GBTM) by collecting Functional Independence Measure (FIM) total scores for 8 weeks retrospectively.

Results: In total, 306 patients were analyzed. GBTM analysis estimated four groups as the best model for the FIM trajectory over 8 weeks using the following trajectories: (1) the No Decline group, in which ADL did not decline until just before death; (2) the Rapid Decline group, in which ADL declined rapidly 2 weeks before death from a trajectory similar to the No Decline group; (3) the Moderate Disability and Slow Decline group, in which the patient slowly declined from requiring mild to severe assistance; and (4) the Severe Disability group, in which the patient continuously required severe assistance.

Conclusions: Multiple ADL trajectories were identified in the last 8 weeks of life of patients with terminal cancer. These findings suggest that palliative care needs to be tailored to the characteristics of each patient.

Introduction

Understanding the disabling process at the end of life is essential for informed decision-making among cancer patients, their families, and medical professionals. Activities of daily living (ADL) represent one of the main factors comprising a good death, and maintain the ability to carry out ADL is important for a better end of life [1, 2]. Previous studies have reported that, unlike patients with organ failure or frailty, patients with cancer experience a decline in ADL just before death [3]. The ADL of patients with terminal cancer has been reported to decline rapidly 1 month before death [3, 4] and to require complete assistance 1 week to several days before death [3–6]. However, those previous studies have several limitations. First, the ADL assessments in those studies evaluated only whether the patient was independent and did not have sufficient scale to detect gradual changes in the level of assistance [3, 5, 6]. Second, only one trajectory was revealed because the mean and median were used [3–5].

Group-based trajectory modeling (GBTM) is a semiparametric method used to identify different subgroups of individuals who have shown similar patterns of change over time for a given variable [7, 8]. An analysis of the trajectories of ADL disability in the last year of life among community-dwelling older adults using GBTM revealed multiple trajectories [9]. Yasui et al. [6] analyzed the ADL of patients with terminal cancer using GBTM, but the sample size in their study was too small for GBTM analysis, so only a simple assessment of ADL was performed.

Given this background, the present study aimed to identify the ADL trajectories of patients with terminal cancer before death as assessed using GBTM combined with the Functional Independence Measure (FIM), a widely used method for assessing ADL characterized by its ability to evaluate ADL comprehensively and to identify gradual changes in detail.

Methods

Design and study participants

This study was designed as a retrospective cohort study. The data were collected from electronic medical records from the medical database of the Rehabilitation Department of Tsurumaki-Onsen Hospital in Kanagawa, Japan.

The study participants were patients with cancer who had been discharged from the palliative care unit of Tsurumaki-Onsen Hospital between April 1, 2015 and August 31, 2019. The eligibility criteria were as follows: 1) patients who died and were discharged from the hospital, 2) patients aged 18 years or older, and 3) more than one FIM assessment. The exclusion criteria were: 1) a hospital stay of more than 13 weeks, 2) not discharged due to death (e.g., to home, another hospital or institution). Patients with a hospital stay of more than 13 weeks were not considered to have the same characteristics as other patients because of having a social background such as living alone.

Primary outcome

FIM data on total FIM scores assessed at, and every 2 weeks after, admission were collected retrospectively from the patients' medical records. The data for 8 weeks before death was included in the analysis, with the assessment immediately before death set as week 0.

The FIM [10] is an ADL rating scale composed of 18 items: 13 motor and 5 cognitive items. Each item is scored on a seven-point scale, from 7 (complete independence) to 1 (total assistance), with total scores ranging from 18 to 126. Although each item on the FIM is an ordinal scale, the total score is treated as an interval scale, since a Rasch analysis has confirmed that the scale is unidimensional [11].

Secondary outcome

Information on the primary tumor was collected retrospectively from the patients' medical records. We also used the revised Tokuhashi score to predict life expectancy in patients with metastatic cancer of the spine [12], and calculated the score according to the type of primary cancer as follows: 0, lung, osteosarcoma, stomach, bladder, esophagus, and pancreas; 1, liver, gallbladder, and unidentified; 2, others; 3, kidney and uterus; 4, rectum; and 5, thyroid, breast, prostate, and carcinoid tumor.

Background factors and medical information

Information on the patients' age, gender, diagnosis, presence of metastasis (e.g., brain, bone, liver, lung), and duration of stay in the palliative care unit were also collected from the patients' medical records.

Statistical analysis

We estimated the trajectory groups and analyzed associated factors using the estimated trajectory groups as variables. We used GBTM to estimate the FIM trajectory groups in patients with terminal cancer. GBTM uses the maximum likelihood method and PROC TRAJ in SAS (SAS Institute, Inc., Cary, NC, USA) to fit a semi-parametric mixture model to the longitudinal data [7, 13]. We based GBTM on previous studies [7, 8, 13, 14]. The study participants were hospitalized for different durations of stay, so the number of FIM assessments also differed. Including only patients with all assessment periods would produce results with participants having biased characteristics only. However, GBTM can supplement the missing data. Therefore, we could adapt the data of patients with different durations of hospitalization in this study.

First, a censored normal distribution method was applied, and estimation models were generated for groups 1 to 6. In each model, we determined whether each trajectory was the best fit by linear, quadratic, or cubic terms, referring to the output estimates and p-values.

Second, we compared the Bayesian information criterion (BIC) to determine the optimal number of trajectory groups; a higher BIC value indicates a better fit, so the model that showed the largest BIC from the output results was considered the best-fitting model.

We further evaluated the validity of the final model using the average posterior probability (AvePP). Estimating the model outputs the probability of membership in each group. The AvePP is the average of the probabilities that an individual is most likely to belong to a specific group. Previous studies recommend that it should be greater than 0.7 [7, 14]; therefore, we adopted the same criterion in the present study.

We used multinomial logistic regression analysis to analyze the factors associated with each of the estimated trajectory groups and the backgrounds of the patients. The estimated trajectory group was the dependent variable. Gender, age over 65 years, presence of metastasis to the brain, bone, liver, and lung, and the revised Tokuhashi score [12] (type of primary tumor) were used as the independent variables.

The statistical significance threshold was set at 5%. SAS 9.3 (SAS Institute, Inc.) was used for the GBTM and multinomial logistic regression analysis and SPSS version 25.0 software for MAC OS (SPSS Inc., Chicago, IL) was used for the descriptive statistics.

Results

Demographics of the study participants

The study participants were 306 patients (162 males [52.9%], 144 females [47.1%]; median age, 77 years) who met the eligibility criteria from among a total of 418 who had been discharged from the palliative care unit of Tsurumaki-Onsen Hospital and evaluated in terms of the FIM over time. Of these, 54 patients were discharged home, 1 was transferred to another hospital, and 38 were hospitalized for more than 13 weeks; 17 patients who did not have an FIM evaluation were excluded. Among all patients, 134 (43.8%) were hospitalized from home, 18 (5.9%) from institutions, 15 (4.9%) from convalescent hospitals, and 139 (45.4%) from hospitals where they had been hospitalized for cancer treatment. The median duration of hospitalization was 23 days. Table 1 shows the patients' primary site of cancer and classification of distant metastasis. In total, 120 (39.2%) patients were without metastasis; the remaining patients had one or more metastases. Single metastasis was the most prevalent (n=109 patients [35.6%]), and metastasis to three sites was the least prevalent (n=18 [5.9%]). The revised Tokuhashi score was 0 for 139 patients (45.4%), 1 for 30 (9.8%), 2 for 57 (18.6%), 3 for 25 (8.2%), 4 for 34 (11.1%), and 5 for 21 (6.9%).

The number of patients evaluated at each time point was 41 (13.4%) at 8 weeks before death, 75 (24.5%) at 6 weeks, 126 (41.2%) at 4 weeks, 207 (67.6%) at 2 weeks, and 306 (100%) at just before death.

FIM trajectory and related factors in the eight weeks before death

Based on the output results for selecting the best model for groups 1 to 6, four groups were selected as the best model. The GBTM analysis estimated the following four trajectories (Fig. 1): 1) the No Decline group, with a total FIM of 111 points at 8 weeks before death and a total FIM of 94 points at just before death, which is still nearly independent; 2) the Rapid Decline group, with a total FIM of approximately 100 points with the same trajectory as the No Decline group from 8 weeks to 4 weeks before death, a decrease to 82 points at 2 weeks before death, and a further decrease to 26 points at just before death, indicating the need for severe assistance; 3) the Moderate Disability and Slow Decline group, in which the patient already required moderate assistance at 8 weeks before death (total FIM of 72 points), and then slowly decreased to 39 points at just before death, indicating the need for severe assistance; and 4) the Severe Disability group, with a total FIM of 30 points at 8 weeks before death and 22 points at just before death, indicating the need for persistent severe assistance. The percentage of patients belonging to each trajectory was 20.9% (n=63), 18.8% (n=43), 34.3% (n=115), and 26.1% (n=85) in the No Decline, Rapid Decline, Moderate Disability and Slow Decline, and Severe Disability groups, respectively.

Multinomial logistic regression analysis was performed with the No Decline group as the reference, the trajectory group as the dependent variable, and patient background as the independent variable (Table 2). In the Severe Disability group, brain metastasis (odds ratio [OR]: 10.3, 95% confidence interval [CI]: 2.6–40.5, $p<0.001$), lung metastasis (OR: 0.36, 95% CI: 0.17–0.80, $p=0.03$), age 65 years and older (OR: 2.93, 95% CI: 1.11–7.72, $p=0.03$), and bone metastasis (OR: 2.93, 95% CI: 1.28–6.74 $p=0.01$) were extracted from the Moderate Disability and Slow Decline group. No significant differences were found for the other independent variables.

Discussion

In this study, we used GBTM to analyze the trajectory of ADL among patients with terminal cancer as assessed by FIM for 8 weeks before death. As a result, we identified four trajectories (Fig. 1). We also identified brain metastasis, bone metastasis, age over 65 years, and lung metastasis as related factors. To our knowledge, this is the first to show accurately the ADL trajectories of groups of patients with terminal cancer using a sample size sufficient for GBTM analysis and a standardized ADL measure.

ADL trajectory of patients with terminal cancer

Previous studies have reported that ADL among patients with terminal cancer begin to decline slowly at about 6 months before death [4] and sharply at between 3 months and 1 month before death [3, 4], resulting in most patients requiring full assistance from 1 week before death [4, 5]. Seow et al. [4] reported that palliative performance status (PPS) decreased to an average of 54.7% (often assisted level) at 1 month before death and to an average of 41.3% (mostly assisted level) at one week before death. PPS is based on a rating scale from 100% to 10% of the most applicable level for each of the following items: standing, activities and symptoms, ADL, oral intake, and level of consciousness. The lower the PPS score, the worse the condition. Lunney et al. [3] evaluated changes in the ADL of patients with cancer in the year before death based on whether they were able to perform seven ADL items independently. They reported that the average number of ADL items requiring assistance at 1 year before death was 0.77, but increased to 4.09 at 1 month before death. McCarthy et al. [5] evaluated the ADL of patients with rectal and non-small-cell lung cancer in the six months before death using a modified version of the Katz Index of independence in ADL, which assesses seven items: bathing, dressing, urinary control, transfers, toileting, eating, and walking. They reported that patients had five ADL disabilities from 1 month to 3 days before death, and seven disabilities at 3 days before death. However, these previous studies have shown changes in ADL according to the median or mean, and thus reported only one trajectory. In addition, PPS cannot evaluate each ADL item in detail. It is difficult to detect changes in the level of assistance required for ADL by using methods such as the Katz index, which evaluates only whether a person is independent.

To overcome these issues, in the present study, we evaluated ADL using the FIM and estimated multiple trajectories using GBTM. The FIM can capture sensitive changes in the level of assistance and indicate patients who require assistance with some ADL. We identified three different trajectories in addition to that of the “Rapid Decline” group, as in previous studies.

Concerning previous studies using GBTM, Gill et al. [9] reported five trajectories of ADL in 383 community-dwelling older adults with cancer, advanced dementia, organ failure, sudden death, frailty, and other conditions in the year before death. However, the participants in their study were older adults living in the community with various diseases, which made comparisons with our study difficult. On the other hand, Yasui et al. [6] analyzed ADL trajectories assessed by seven items in 22 patients with cancer using GBTM. Their results showed three trajectories in the month before death. They reported that the youngest group showed a rapid decline in ADL at 1 week before death, whereas the ADL in the other two groups, which consisted of older patients, had already declined.

In contrast to the report by Yasui et al. [6], four trajectories were revealed in the present study (Fig. 1). The reason for the different trajectories could be due to the evaluation measures and the number of participants. Yasui et al. [6] assessed whether patients could perform ADL independently, whereas in the present study, the FIM [10] was used to evaluate gradual declines, such as in the Moderate Disability and Slow Decline group. We were able to show this group because the FIM evaluates 18 items on a seven-point scale, which allowed us to detect gradual declines. This group could not be identified by independent or dependent assessment only. Also, according to Nagin [7], 300 to 500 cases are required for analysis using GBTM. The study by Yasui et al. [6] only included 22 patients, which is not a sufficient number of cases to identify the number of trajectory groups and their respective trajectories.

Factors associated with the trajectories

With reference to the No Decline group, multinomial logistic regression analysis revealed brain metastasis as a factor with an OR of 10.3, age over 65 as a factor with an OR of 2.93, and lung metastasis as a factor with an OR of 0.36 in the Severe Disability group (Table 2).

Patients with cancer with brain metastases or brain cancer have been reported to have neurological disorders and reduced ADL [15, 16]. When these patients reach the end of life, they tend to have symptoms of consciousness disorder, drowsiness, and cognitive impairment [17, 18]. Such patients have also been reported to have more nursing problems in regard to ADL than other patients with cancer [19]. Patients with cancer with brain metastases are thought to require severe assistance in ADL because of not only impaired physical and mental functions, but also a decreased level of consciousness.

Another factor was that the patients in this study were aged 65 years or older (i.e., older), with a median age of 77 years. It is known that ADL before death are more likely to be lower in older than in younger patients with cancer. Yasui et al. [6] reported that among patients with terminal cancer, older patients adults (mean age, 78.5 years) had a lower ADL trajectory in the month before death than did their younger counterparts (mean age, 57.1 years). In addition, Costantini et al. [20] investigated ADL in patients with cancer at 52 weeks before death and reported that ADL tended to be lower in the 65–84 and 85+ age groups than in the 18–64 age group. In the present study, we considered that the ADL of older patients with cancer were low and extracted as a factor associated with the Severe Disability group.

By contrast, lung metastasis had a weak association with the Severe Disability group. Although a few reports have investigated the effect of lung metastasis on ADL, Yoshioka [21] reported finding no significant difference in the Barthel Mobility Index between patients with and without lung metastases. Patients with lung cancer often experience dyspnea [22], which may affect their mobility. However, unlike brain or bone metastases, lung lesions do not directly cause central nervous system or motor system disorders. Therefore, cognitive dysfunction such as attention and memory impairment and physical dysfunction such as motor paralysis and sensory impairment are less likely to occur; thereby, such associations would be lower.

On the other hand, bone metastasis was extracted as a factor in the Moderate Disability and Slow Decline group. It has been reported that patients with bone metastases have lower ADL than do those without [21]. Pain, pathological fractures, spinal cord compression symptoms, and hypercalcemia, which can occur with bone metastases, are referred to as skeletal-related events (SREs) [23]. When SREs occur and cause pain at rest and during movement, as well as motor and sensory paralysis of the limbs, the ability to sit, stand, and walk is impaired, and ADL are reduced [24, 25]. However, bone metastases tend to spread to the spine, pelvis, and femur [26], and when patients are able to use their upper extremities in bed or in a wheelchair, they may not need assistance with some activities such as eating and dressing. Therefore, bone metastasis may have been a factor in the trajectory group with mild to moderate ADL disability.

Limitations

This study had several limitations. First, it was conducted at a palliative care unit. Of the four trajectories, the proportions of patients in the Moderate Disability and Slow Decline and Severe Disability groups were higher. The hospital environment, such as the room size and corridor distance, differs from that at home. In addition, in hospitals, patients may be assisted more than necessary to prioritize safety and help prevent falls. Therefore, the patients in this study may have had less independence in carrying out ADL.

Second, since the FIM is assessed every 2 weeks after admission, the assessment at just before death (0 weeks) can range from 1 to 13 days. Therefore, ADL are expected to decline further during this period. In particular, the No Decline group may have experienced a rapid decline in ADL during this period. We cannot deny the possibility that there may be a decline in ADL that was not revealed because of the range of assessment periods.

Third, the size of the metastases and presence of symptoms were not assessed. It is possible that small metastases with minimal influence and large metastases with severe impairment of physical and mental functions were equally assessed. In the future, the quality and impact of metastases should be evaluated.

Finally, each patient had a different number of FIM assessments. Therefore, we cannot exclude the possibility that this may have affected the model. However, if only patients with terminal cancer surviving for more than 8 weeks were included, biases in terms of the patients' characteristics would likely occur. In this study, we were able to develop a more realistic ADL trajectory model by including patients with various hospitalization durations and using GBTM, which can withstand deficits.

Conclusion

The ADL trajectory group involving patients with terminal cancer who died and were discharged from the palliative care unit for 8 weeks before death was analyzed using GBTM. The results revealed the existence of four different trajectory groups and associated factors. Patients aged over 65 years or brain metastases were more likely to require severe assistance at 8 weeks before death, whereas patients with bone metastases were more likely to require mild to moderate assistance. When providing ADL support

for patients with terminal cancer, support plans and interventions that consider the trajectory group and its associated factors are therefore necessary. These results could help clarify the multiple ADL trajectories of patients with cancer before death and the associated factors, thereby providing essential knowledge for examining the medical and nursing care services required for patients with terminal cancer

Declarations

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Conflicts of interest/competing interests:

The authors declare that they have no conflict of interest.

Availability of data and material:

The data sets analyzed during the present study are available from the corresponding author on reasonable request.

Code availability:

Not applicable.

Authors' contributions:

RS and TT contributed to the study concept and design, data acquisition and analysis, data interpretation, and drafting of the manuscript. MM, AY, YI, and TO contributed to the data interpretation and data acquisition. AI contributed to the data interpretation and editing of the manuscript.

Ethics approval:

Ethical approval was obtained from the Ethical Review Subcommittee of Tsurumaki-Onsen Hospital in accordance with the Declaration of Helsinki. Informed consent was obtained on an opt-out basis. A summary of the study was published in the institution, and participants were guaranteed the right to refuse participation.

Consent to participate:

Written consent was unnecessary, and patients were provided the opportunity to opt-out.

Consent for publication:

Not applicable

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Tables

Table 1. Primary cancer site and number of metastasis

Primary cancer site	n (%)
Brain	6 (2)
Head and neck	26 (8.5)
Lung	66 (21.6)
Breast	11 (3.6)
Gastrointestinal tract	71 (23.2)
Liver/gallbladder/pancreas	55 (18)
Urological	20 (6.5)
Prostate	8 (2.6)
Gynecological	27 (8.8)
Skin	3 (1)
Blood/lymph	5 (1.6)
Bone/soft tissue	5 (1.6)
Unknown	3 (1)
Total	306 (100)
Metastasis site	n (%)
Brain	38 (12.4)
Bone	71 (23.2)
Lung	92 (30.1)
Liver	80 (26.1)

Table 2. Multinominal logistic regression analysis

	Group (No Decline group as the reference)	OR	95%CI	p
Male	Severe Disability	0.81	0.40–1.62	0.54
	Moderate Disability and Slow Decline	0.80	0.42–1.53	0.50
	Rapid Decline	0.46	0.20–1.03	0.06
Brain metastasis	Severe Disability	10.30	2.60–40.5	<0.001
	Moderate Disability and Slow Decline	3.31	0.83–13.2	0.09
	Rapid Decline	2.42	0.43–13.8	0.32
Bone metastasis	Severe Disability	2.32	0.94–5.73	0.07
	Moderate Disability and Slow Decline	2.93	1.28–6.74	0.01
	Rapid Decline	0.47	0.12–1.87	0.28
Lung metastasis	Severe Disability	0.36	0.17–0.80	0.03
	Moderate Disability and Slow Decline	0.64	0.32–1.27	0.20
	Rapid Decline	0.61	0.25–1.46	0.26
Liver metastasis	Severe Disability	0.82	0.35–1.91	0.65
	Moderate Disability and Slow Decline	1.47	0.71–3.07	0.30
	Rapid Decline	1.91	0.79–4.63	0.15
Over 65 years old	Severe Disability	2.93	1.11–7.72	0.03
	Moderate Disability and Slow Decline	2.34	0.98–5.60	0.06
	Rapid Decline	1.54	0.54–4.45	0.42
Tokuhashi score	Severe Disability	1.03	0.83–1.27	0.80
	Moderate Disability and Slow Decline	0.99	0.82–1.21	0.97
	Rapid Decline	1.03	0.80–1.32	0.82

The factors of each group were analyzed with reference to the No Decline group. Metastasis was analyzed with reference to the no metastasis group.

OR: odds ratio, CI: confidence interval.

Figures

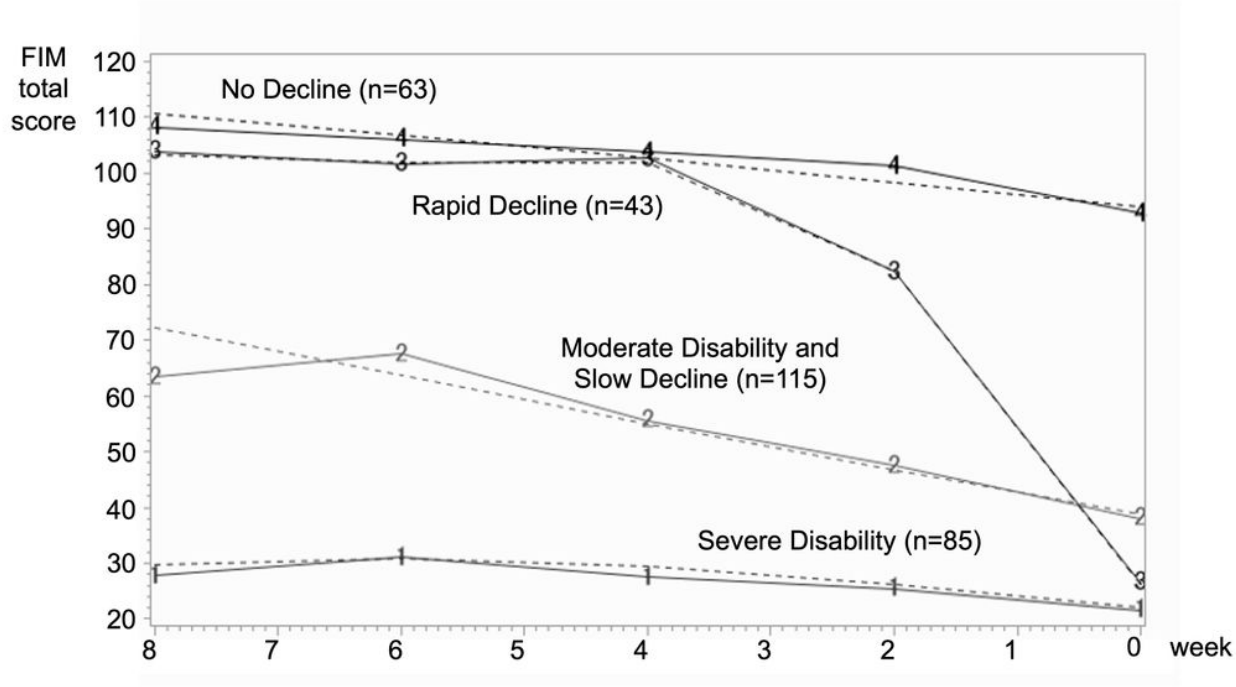

Figure 1

Functional Independence Measure trajectory groups in the 8 weeks before death as estimated by group-based trajectory modeling. The solid line shows the mean value, and the dotted line shows the estimated value. From the top of the figure, the No Decline group (No. 4 on the solid line), the Rapid decline group (No. 3 on the solid line), the Moderate Disability group (No. 2 on the solid line), and the Severe Disability group (No. 1 on the solid line).