Geriatrics Gerontology International

DOI: 10.1111/ggi.14292

ORIGINAL ARTICLE

EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Treatment and prognosis of patients with both cancer and impaired decision-patient with both cancer and dementia making as a symptom of dementia

Tomomi Fujii,[1,2] Michiko Wada,[2] Shinji Hasebe,[2,3] Kazuto Takeuchi,[4] Toshihiro Yorozuya[5] and Yoshihiro Yakushijin[2,3]

[1]Palliative Care Center, Ehime University Hospital, Toon, Japan
[2]Department of Clinical Oncology, Ehime University Graduate School of Medicine, Toon, Japan
[3]Cancer Center, Ehime University Hospital, Toon, Japan
[4]Department of Medical Technology, Faculty of Health Sciences, Ehime Prefectural University of Health Sciences, Tobe-cho, Japan
[5]Departments of Anesthesia and Perioperative Medicine, Ehime University Graduate School of Medicine, Toon, Japan

Correspondence
Yoshihiro Yakushijin MD, PhD, Department of Clinical Oncology, Ehime University Graduate School of Medicine, Shitsukawa, Toon 791-0295, Japan.
Email: yoshiyak@m.ehime-u.ac.jp

Received: 24 March 2021
Revised: 2 September 2021
Accepted: 18 September 2021

Aim: In our aging society, the number of patients with both cancer and dementia has recently been increasing. One of the major clinical questions is whether patients with dementia could receive appropriate cancer treatment. The purpose of this study is to know the prognosis of patients with both cancer and impaired decision-making as a symptom of dementia, and to discuss the proper cancer treatment of the patients with dementia.

Methods: Patients newly diagnosed with both cancer and impaired decision-making as a symptom of dementia at Ehime University Hospital between January 2010 and December 2016 were reviewed. The data of patients with cancer were retrospectively analyzed using an electronic medical record system.

Results: In total, 9354 cases were diagnosed with cancer in the Ehime University Hospital over 7 years, and only 105 (1.1%) cases with impaired decision-making as a symptom of dementia were recorded by medical professionals, probably due to poor attention to the cognitive functions of patients with cancer. Analysis of the cancer prognosis of these patients showed that a better prognosis was seen in patients with any therapeutic interventions than in those with no treatment for the cancer itself. However, the prognosis of patients was not significantly different between standard and non-standard treatments.

Conclusions: This study suggests that the poor interest of medical professionals in the cognitive function of patients with cancer at the time of diagnosis of cancer and the lack of any guidelines for patients with both cancer and dementia are major problems in our aging society. **Geriatr Gerontol Int 2021; 21: 1105–1110**.

Keywords: cancer treatment, prognosis, patient with both cancer and dementia.

Introduction

According to the World Health Organization (WHO), 50 million people had dementia in 2019, and nearly 10 million new dementia cases were reported each year.[1] Cancer, which is another important disease in advanced countries, is also increasing annually, and one-third of the population dies of cancers. Therefore, the number of patients with cancer who have impaired cognitive function with respect to making decisions regarding their own cancer treatment has been increasing. However, there are no clear guidelines for patients with both cancer and impaired decision-making as a symptom of dementia, despite the cognitive decline affecting treatment decisions, and the majority of patients with both cancer and dementia are treated based on the decisions of their doctors and their families. Therefore, whether patients with dementia can receive appropriate cancer treatment should be one of the major clinical questions in geriatric oncology today. This retrospective study focused on the cancer treatments and the prognosis of patients with impaired decision-making and discussed the treatment of patients with both cancer and dementia.

Methods

Patients with both cancer and impaired decision-making

Patients who were newly diagnosed with both cancer and impaired decision-making as a symptom of dementia at Ehime University Hospital between January 2010 and December 2016 were reviewed using an electronic medical record system. Patients who had metastasis in the central nervous system (CNS tumor involvement) or primary CNS tumor were excluded because they were

unsuitable for the current analysis. Patients whose dementia was derived from Alzheimer's disease, cognitive dysfunction, or dementia with Lewy bodies were included. Clinical examinations were performed to ascertain patient survival and the physical condition of all surviving patients.

Eligibility and grading of patients with both cancer and impaired decision-making in dementia

Several evaluation systems for dementia have recently been reported. Major detection tools for possible dementia include the Mini-Mental State Examination (MMSE; Folstein test)[2,3] worldwide and the Hasegawa Dementia Rating Scale-Revised (HDS-R) in Asian countries.[4–9] However, these evaluations are based on intellectual abilities such as calculation, memory, cognition, and its speed and orientation. Of these evaluation systems and criteria, the focus of the present study was primarily on the decision-making of patients with cancer for their treatment. To investigate grades (levels) of decision-making in people with dementia, the Social Scale for Care Givers with Dementia in Japan (Table 1) was used, and the patients were classified according to it.[10] The Social Scale for Care Givers with Dementia, which is available throughout Japan, can be easily checked and calculated from nursing records, which is why this scale was selected. This scale can judge the state and the severity of dementia of the elderly population based on reports by Niet *et al.*[11] and Yoon *et al.*,[12] which indicates the tight relationship between cognitive function and body mobility based on independence in the activities in daily life. In addition, the severity of dementia depends on how independent the caregivers can be in daily life, which is similar to the Scale for Care Givers with Dementia.[13]

Table 1 Social scale for caregivers with dementia in Japan

Mildly disturbed ability of decision making	Level I	Have some kind of dementia, but the ability of decision-making in everyday life is almost socially independent
	Level II	Even if there are some symptoms of dementia and difficulties in communication that interfere with daily life; however, they can make decisions independently, if someone provides care
	Level III	Symptoms and behaviors that interfere with daily life and difficulty in decision-making are sometimes seen; care is often required
Moderately disturbed ability of decision-making	Level IV	Symptoms and behaviors of dementia that interfere with daily life and difficulty in communication and decision-making are frequently seen; care is required at all times
Highly disturbed ability of decision-making	Level M	Remarkable mental symptoms, problematic behavior, or serious physical illness are seen as symptoms of dementia, requiring specialized medical care

Analysis of overall survival of patients with both cancer and dementia

Survival time was from the date of starting any treatment to the date of the last follow-up (at the end of 2018) or death. Overall survival (OS) curves were calculated for each prognostic group according to the Kaplan–Meier method and analyzed using the univariate Wilcoxon test. Fisher's exact test and the chi-squared test were used to detect significant differences among the groups. $P < 0.05$ was considered significant. All statistical analyses were performed using the SAS software package version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethics of the study

This study was approved by the Ethics Committee for Clinical Studies at Ehime University Graduate School of Medicine (study

Table 2 Characteristics of the patients with cancer with impaired decision-making[†]

	n (%)
Age, years (average ± SD)	
Male	76.8 ± 7.8
Female	79.2 ± 6.7
Sex	
Male	56 (53.3)
Female	49 (46.7)
Disease	
Gastric	21 (20.0)
Urological	16 (15.2)
Head and neck	13 (12.4)
Hematological	13 (12.4)
Liver, gallbladder and pancreatic	11 (10.5)
Gynecologic	11 (10.5)
Pulmonary	9 (8.6)
Breast	6 (5.7)
Dermatologic	4 (3.8)
Unknown organ	1 (1.0)
Treatment	
Operative therapy	36 (34.3)
Chemotherapy	21 (20.0)
Radiotherapy	10 (9.5)
Others	20 (19.0)
Never treated	18 (17.1)
Social scale for care givers with dementia in Japan	
Level I	26 (24.7)
Level II	43 (41.0)
Level III	27 (25.7)
Level IV	9 (8.6)
Level M	0 (0)

[†]Data are *n* (%) unless otherwise indicated.

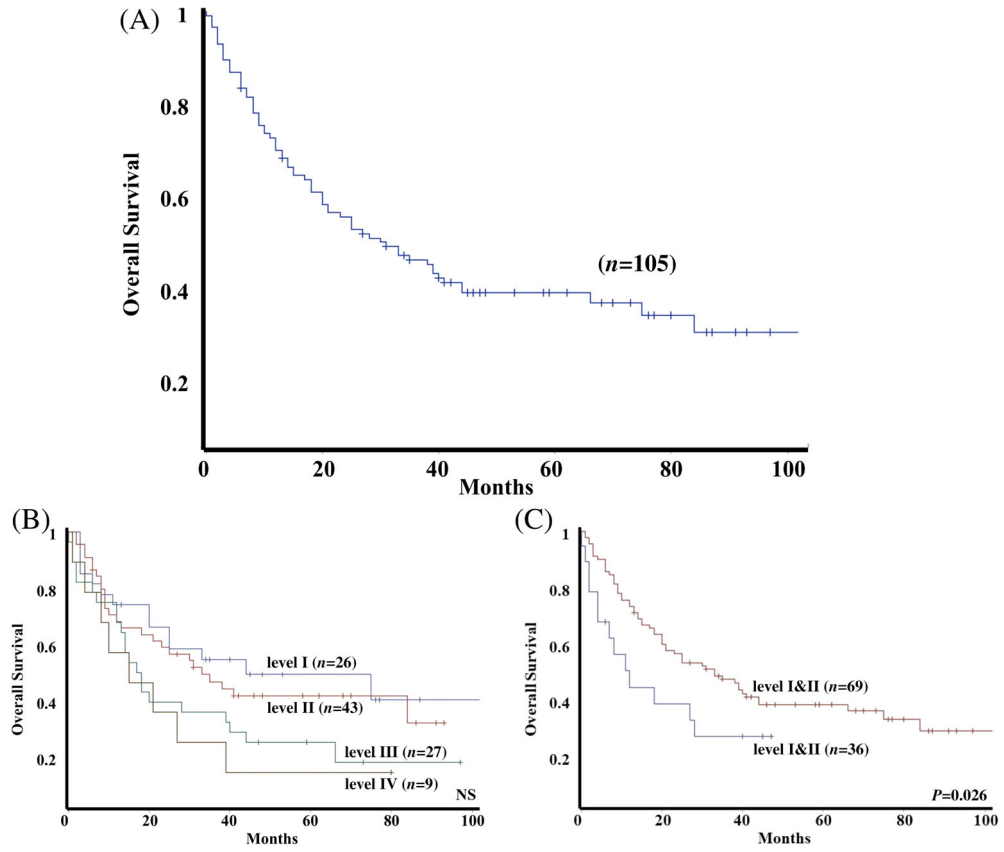

Figure 1 Overall survival: (a) of patients with both cancer and impaired decision-making as a symptom of dementia ($n = 105$); (b) according to the level of impaired decision-making of patients with dementia; (c) according to level of impaired decision-making of patients with dementia (Level I + II vs. Level III + IV). There are no patients in Level M in this study.

IRB no. 1508011) and carried out in accordance with the ethical standards of the 1995 Declaration of Helsinki (as revised in Brazil 2013). Informed consent was by the opt-out principle; information about the study was disclosed on the associated website (https://www.m.ehime-u.ac.jp/school/clinical.oncology/?page_id=25), and an opportunity to decline to participate in this study was provided.

Results

Clinical characteristics

In total, 105 patients with cancer and impaired decision-making as a symptom of dementia were screened in the current study from 9354 patients with cancer between January 2010 and December 2016. These cases did not include the patients who met the exclusion criteria. Of the analyzed patients, 49 (47%) were women. The median and average ages were 76.7 and 79.2 (range, 56–91) years, respectively. The clinical characteristics and the type of cancer of each patient are shown in Table 2. Table 2 also shows the patients' levels of impairment of decision-making as a symptom of dementia.

Patient prognosis according to the level of impaired decision-making and cancer treatment

Kaplan–Meier analysis was performed to estimate the OS of patients with cancer with various levels of impaired decision-making as a symptom of dementia. Figure 1a shows the Kaplan–Meier curves of OS of the currently analyzed patients ($n = 105$), with OS at 24 months of 50%. Figure 1b shows OS according to the levels of impaired decision-making of the patients with cancer. The patients with greater impairment of decision-making seemed to show a worse prognosis, with a significant difference between Level I + II and Level III + IV (Fig. 1c).

Prognosis of patients with impaired decision-making as a symptom of dementia by cancer treatment

The prognosis was analyzed among the types of treatments for patients with both cancer and impaired decision-making. Treatment requires a purpose and a goal, in particular cancer treatment for patients with dementia. The goal of therapy should differ depending on whether the purpose of the cancer treatment is cure, life extension, or palliation. In the current study, two groups of patients were considered, those who had been treated with a goal of cure or life extension ($n = 87$), and those whose cancers were never treated and received only palliative care ($n = 18$), and their prognoses were compared. Not surprisingly, the prognosis for patients who had received any therapeutic intervention was better than that of those with no treatment for the cancer itself (Fig. 2a). In another analysis, patient prognosis was compared between cases treated with standard treatments regardless of the patients' cognitive function ($n = 64$) and cases treated with reduced dose intensity (relative dose intensity less than 50%), reduced radiotherapy, or limited surgery as non-standard treatments because the patient had impaired decision-making ($n = 23$). Of course, the disease (cancer) status of the patients treated with non-standard therapies should be in the advanced stage of the disease, but no significant difference in prognosis was seen (Fig. 2b). Both groups (treated with cancer vs. never treated with cancer, standard therapy vs. non-standard therapy) did not show any significant

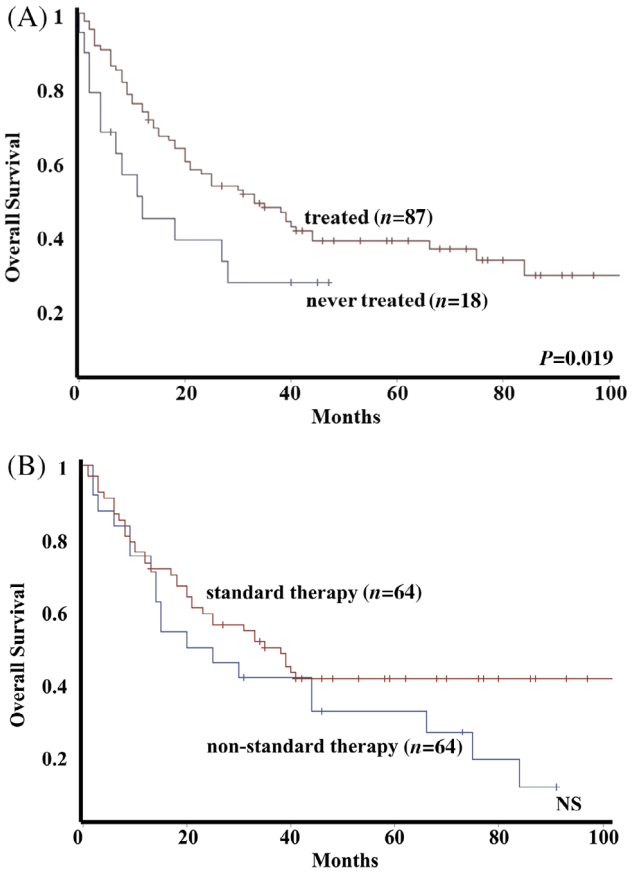

Figure 2 Prognosis of patients with impaired decision-making as a symptom of dementia according to the cancer treatments: (a) treatment versus never treatment, and (b) standard treatment versus non-standard treatment.

differences in the severity of dementia (data not shown). These results (Fig. 2a,b) show that some treatment, regardless of the intensity of the treatment, even in patients with dementia, may improve their prognosis.

Patient prognosis by level of impaired decision-making and type of treatment

Finally, the better option for the treatment of patients with both cancer and dementia was examined in the current cases. Figure 3 shows survival benefits among operative therapy (Figure 3a), chemotherapy (Figure 3b) and radiotherapy (Figure 3c), compared with the prognosis of patients who were never treated for the cancer itself and were treated with palliative care only. In this analysis, patients treated with combination therapies ($n = 23$) were removed to clarify the efficacy of each treatment. Figure 3 shows that the prognosis of the patients treated with operative therapy was better than the prognosis of those who were never treated for their cancers. On the other hand, no significant difference was observed in the prognosis of the patients treated with chemotherapy or radiotherapy compared with the prognosis of those who were never treated. These results show that short-term treatments in an environment where physical restraint can be obtained, such as operative cases with the use of anesthesia, may provide survival benefits for patients with impaired decision-making if the cancer is localized and/or operable. These

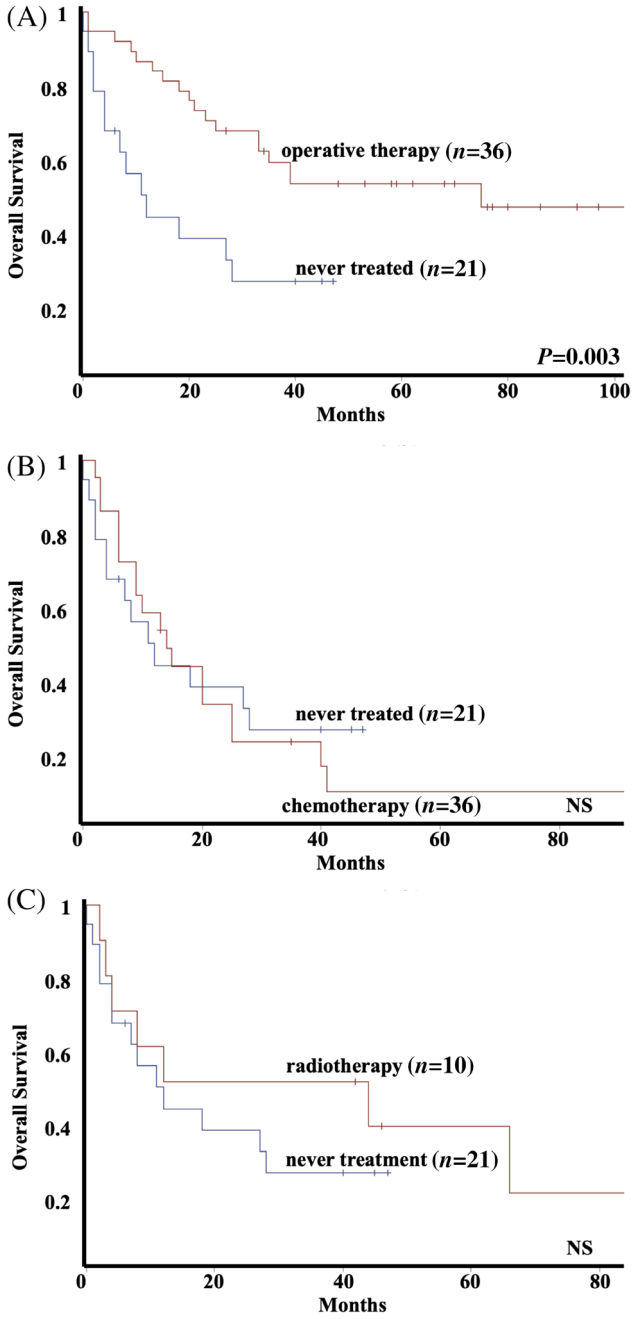

Figure 3 Therapy-related survival benefits among (a) operative therapy, (b) radiotherapy and (c) chemotherapy. Prognosis of each treatment for patients with impaired decision-making compared with those who were never treated.

clinical analyses suggest that any treatment, even in patients with dementia, has a possibility to improve their prognosis, if the therapeutic interventions are done appropriately for the patient's situation.

Discussion

Evaluation of impaired decision-making in the elderly population with cancers is extraordinarily important in our aging society, and

it may affect treatment outcomes. However, to the best of our knowledge, studies of this important area in cancer treatment are quite few. In addition, few medical records that include quantitative cognitive evaluations of patients with cancer are seen in daily clinical practice, which indicates lower attention to the cognitive ability of patients with cancer. We would like to emphasize these significant aspects of our study, and bring them to the attention of medical staff.

The current retrospective data were extracted from the medical records of patients with cancer from January 2010 to December 2016 in Ehime University Hospital. In total, 9354 cases with cancer were diagnosed during this period, but only 105 cases (1.1% of the total patients with cancer) with impaired decision-making as a symptom of dementia were extracted from the medical records. This is an extremely low rate for a university hospital in a developed country compared with the estimated prevalence of people with dementia in Japan (from 10% to 15%).[1] Two reasons might explain the low rate of patients with both cancer and impaired decision-making in our institute.

First, evaluation of cognitive functions as described in the medical records was not properly performed in the process of cancer treatment. This suggests that medical professionals may not pay much attention to the cognitive functions of patients with cancer in the process of cancer diagnosis compared with their observation of the physical condition of patients with cancer. Appropriate judgments of patients' cognitive function are also essential for the proper treatment of cancer. Medical professionals and practitioners involved in cancer treatments and care should take proper training and have knowledge about dementia and decision-making, and they should obtain much information in close contact with patients with cancer and their families. Furthermore, the most sought after recent medical treatments should be the clear guideline for the cancer treatment of patients with dementia. Careful observation and proper diagnosis of the level of impaired decision-making of patients with cancer under the treatment guidelines for patients with both cancer and dementia may result in less intense cancer treatment that, nevertheless, may improve the patients' prognosis.[14]

As a second explanation of the low incidence of patients with both cancer and impaired decision-making, patients might not be referred to treatment institutes for therapy due to the symptoms of dementia, even with the diagnosis of cancer. In other words, patients could be excluded from cancer treatment just because of their cognitive problems. Several reports of the association between cognitive function and body mobility have been published. Niet *et al.*[11] reported a tight association between cognitive function and lower limb function, and Yoon *et al.*[12] reported the relationship between cognitive function and body mobility (e.g., muscular strength in the lower limbs, walking ability). Moreover, the severity of dementia depends on how independent the caregivers can be in daily life, which is similar to the Scale for Care Givers with Dementia.[13]

Interestingly, some kinds of treatment prolonged the patients' prognosis, even if they had a symptom of dementia in the current analysis of cancer treatment for patients with impaired decision-making as a symptom of dementia (Figs 2 and 3). These results show that cancer treatment for patients with dementia may be deliberately decreased. However, cancer therapies involve several risks. A treatment that seemed to be appropriate before could often lead to unforeseen risks and vice versa. These treatment-based survival analyses should be compared between patients with normal cognition and those with cognitive impairment. However, it was not possible in the current retrospective study, because patients with normal cognition would usually come to the hospital to receive their cancer treatment, so that the number of patients with normal cognition and no cancer treatment is extremely small. Taken together, more studies based on cognition and cancer, are needed.

Not only the treatment guidelines, but also the decisions of medical professionals do not determine all treatments and the prognosis, as medical professionals should respect the will of the patient at the time when the patient can make his or her own decisions, as well as respect the will of family members.[15] The recent introduction of Advance Care Planning (ACP) in cancer treatment, which is the process that supports patients with a serious illness in understanding and sharing their personal values, the goals of their lives and their preferences regarding their medical care in the future,[16,17] may provide one of the directions for cancer treatment.[18] More discussion may be necessary to provide the proper treatment for patients with cancer with or without impaired decision-making as a symptom of dementia.

There are several limitations of the present analysis. It was confined to a single institution and a study with a small number of patients. Whether the results obtained from a small number of cases can be applied to all patients with both cancer and dementia depends on further research. The problems of patients with both cancer and dementia are important in the aged society. Further studies and discussion are needed to provide proper treatment and guidelines for patients with both cancer and impaired decision-making as a symptom of dementia to improve their prognosis.

Acknowledgements

The authors appreciate the cooperation of the staff members of the chemotherapy service and the palliative care team in Ehime University Hospital.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

TF and YY carried out the design of the study, collected the clinical data, and drafted the manuscript. TF, MW, KT and TY participated in the design of the study and oversaw the clinical data. SH carried out the statistical analysis of the study. YY conceived the study, participated in its design and coordination, and helped to draft the manuscript. All authors read the draft, revised it critically, and approved the final manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1 World Health Organization. Dementia. [Cited May 2019.] Available from URL: https://www.who.int/news-room/facts-in-pictures/detail/dementia
2 Folstein MF, Folstein SE, McHugh PR. "Mini-mental status". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–198.
3 Creavin ST, Wisniewski S, Noel-Storr AH *et al.* Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database Syst Rev* 2016; **13**: CD011145.

4 Kato S, Simogaki H, Onodera A *et al*. Preparation of revised Hasegawa's Dementia Scale (HDS-R) (in Japanese). *Jpn J Geriatr Psychiatry* 1991; **2**: 1339–1347.
5 Imai Y, Hasegawa K. The revised Hasegawa's Dementia Scale (HDS-R) - evaluation of its usefulness as a screening test for dementia. *J Hong Kong Coll Psychiatry* 1994; **4**: 20–24. https://www.easap.asia/index.php/find-issues/past-issue/item/503-v4n2-9402-p20-24
6 Jeong JW, Kim KW, Lee DY *et al*. A normative study of the revised Hasegawa Dementia Scale: comparison of demographic influences between the revised Hasegawa Dementia Scale and the Mini-Mental Status Examination. *Dement Geriatr Cogn Disord* 2007; **24**: 288–293.
7 Tsai N, Gao ZX. Validity of Hasegawa's Dementia Scale for screening dementia among aged Chinese. *Int Psychogeriatr* 1989; **1**: 145–152.
8 Kounnavong S, Soundavong K, Xayavong S *et al*. Lao language version of the Revised Hasegawa's Dementia Scale. *Nagoya J Med Sci* 2017; **79**: 241–249.
9 Saw YM, Than TM, Win EM *et al*. Myanmar language version of the Revised Hasegawa's Dementia Scale. *Nagoya J Med Sci* 2018; **80**: 435–450.
10 Ministry of Health, Labor and Welfare. [Cited Nov 2020.] Available from URL: https://www.mhlw.go.jp/stf/shingi/2r9852000001hi4o-att/2r9852000001hi8n.pdf (in Japanese)
11 Nieto ML, Albert SM, Morrow LA, Saxton J. Cognitive status and physical function in older African Americans. *J Am Geriatr Soc* 2008; **56**: 2014–2019.
12 Yoon J, Okura T, Tsunoda K *et al*. Relationship between cognitive function and physical performance in order adults. *Jpn J Phys Fitness Sports Med* 2010; **59**: 313–322.
13 Ankri J, Andrieu S, Beaufils B, Grand A, Henrard JC. Beyond the global score of the Zarit Burden Interview: useful dimensions for clinicians. *Int J Geriatr Psychiatry* 2005; **20**: 254–260.
14 Mohile SG, Dale W, Somerfield MR *et al*. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. *J Clin Oncol* 2018; **36**: 2326–2347.
15 Griffiths AW, Ashley L, Kelley R *et al*. Decision-making in cancer care for people living with dementia. *Psycho-oncology* 2020; **29**: 1347–1354.
16 Sudore RL, Lum HD, You JJ *et al*. Defining advance care planning for adults: a consensus definition from a multidisciplinary Delphi panel. *J Pain Symptom Manage* 2017; **53**: 821–832.el.
17 Sudore RL, Heyland DK, Lum HD *et al*. Outcomes that define successful advance care planning: a Delphi panel consensus. *J Pain Symptom Manage* 2018; **55**: 245–255.e8.
18 Myers J, Cosby R, Gzik D *et al*. Provider tools for advance care planning and goals of care discussions: a systematic review. *Am J Hosp Palliat Care* 2018; **35**: 1123–1132.

How to cite this article: Fujii T, Wada M, Hasebe S, Takeuchi K, Yorozuya T, Yakushijin Y. Treatment and prognosis of patients with both cancer and impaired decision-patient with both cancer and dementia making as a symptom of dementia. Geriatr. Gerontol. Int. 2021;21:1105–1110. https://doi.org/10.1111/ggi.14292