

図3 EBCTCGによるメタアナリシス

About 5 years of tamoxifen versus not in ER-positive (or ER-unknown) disease, by tamoxifen dose, use of chemotherapy, age, nodal status, or period of follow-up: event rate ratios 12). Recurrence.

と高齢者総合的機能に及ぼす影響が明らかになることが期待されている.

# 2. 内分泌療法

ホルモン受容体陽性乳がんに対する術後の内分泌療法については、タモキシフェンが年齢を問わず有効であることが示されている(図 3)<sup>12)</sup>. またアロマターゼ阻害薬(AI)とタモキシフェン(TAM)の術後治療のランダム比較試験の結果から、65歳以上の高齢者でもAIがTAMより有効であることが示されている<sup>26(27)</sup>. 一方、それぞれの副作用は異なることが知られ、薬剤の選択にあたりTAMでは血栓症、AIでは骨粗鬆症、関節痛、心血管疾患等に注意を払う必要がある<sup>28)</sup>. 低リスク乳がんの場合は経過観察という選択肢もあり、リスクベネフィットを十分に勘案した上で、個々の併存症に留意しながら内分泌療法を始めることが肝要であろう.

# 3. 手 術

明確な基準はないものの,5年以上の余命が期待できる場合には,若年者と同等の手術治療を考慮すべきとされる<sup>20)</sup>.ホルモン受容体陽性乳がんの場合,TAMに加えた手術による無増悪生存期間(PFS)における利点は示唆されているものの生存期間の延長は明らかとなっていない<sup>30)</sup>.したがって,もし併存症により余命が限られている,手術に耐えられない,等の状況があれば,手術を行わずTAMまたはAIの投与を考慮する.ホルモン受容体陰性乳がんであれば,放射線照射,

radiofrequency ablationなど短期の局所コントロールに主眼をおいた姑息的治療を考慮せざるをえないことがある.

### 4. 放射線治療

乳房部分切除後の全乳房照射は標準治療であり、高齢でも忍容性に問題がないため推奨されている.一方、高齢者の場合は局所再発率が低いことから、短期照射や部分照射も試みられている.また腫瘍径2cm以下のホルモン受容体陽性乳がんでは、内分泌療法を行うことで遠隔転移と生存には差がないため、照射を省略しうるとされるが、照射の乳房内再発に対する抑制効果自体は認められているため、省略可能かどうかの議論がなされているが、非照射は生存率のリスク因子の一つという報告もあり34、安易な省略は避けるべきである.

# 高齢者の転移・再発 乳がん治療について

転移・再発乳がんは、治癒困難な病態であり 治療の目的は、症状緩和と生存期間の延長であ る. それに加え高齢者では身体機能の低下(骨髄、 肝臓、腎臓や心臓)や併存症を有していることが 多いため、薬物療法を行う場合にはリスクベネ フィットを十分に勘案する必要がある. 頻回な 通院が困難な場合、経済的な配慮や付き添いも 含めた家人の意向も必要であろう. 高齢者では 併存症, 臓器機能障害, 社会的背景等により, がん治療が十分にできず, 治療が必ずしも生存期間の延長につながっていない可能性も指摘されている.

ホルモン受容体陽性乳がんでは、有害事象の 少ない内分泌療法から始める, 内分泌療法が奏 効した場合、いくつかの内分泌療法を試みるこ とにより長期間にわたる良好なQOL期間が期待 できる. 内分泌治療は, 通常の閉経後乳癌のガ イドラインに準じて行うことが推奨される. 第 一選択は術後内分泌療法で使用していない薬剤 である. TAM抵抗性であればAIを使用する. AI 抵抗性であればTAMあるいは作用機序の異なる AIのいずれかを使用する、レトロゾールとタモ キシフェンの再発一次治療におけるランダム化 比較試験では、特に70歳以上の高齢者において レトロゾールが有効であった35)、症状を有する内 分泌薬耐性乳がんやホルモン受容体陰性乳がん においては化学療法が推奨されるが、予想され る余命と全身状態、臓器機能と治療に耐えられ るかを十分に検討する必要がある. 抗がん剤治 療は,有効性(奏効率)に関してはおおむね若年 層と変わりないが、副作用が懸念される. 高齢 者でも使用されうる薬剤の選択肢としては、ア ントラサイクリン系薬剤、タキサン系薬剤360のほ か,カペシタビン37),ビノレルビン38)などがあげ られる. 抗がん剤を単剤で治療するか同時併用 治療とするかは、通常の年齢にも増して高齢者 においては毒性の少ない単剤による逐次投与が 選択される.

新規薬剤については、エキセメスタンとの併用治療におけるmTOR阻害薬(エベロリムス)の効果を証明したBOLERO-2試験のサブ解析が高齢者とその他で比較されている。結果、有効性は同等で、口内炎、肺炎、高血糖などの有害事象の頻度も変わりなかった39)。しかし高齢者(>70)では進行(PD)以外の中止が多く、その内訳は有害事象、治験取り下げ、死亡であり、これらは課題として残る。

骨転移に対するビスホスフォネート投与は高齢者においても有効性と長期安全性が報告されている<sup>40)</sup>が、腎機能と低カルシウム血症のモニタリングが必要である.

分子標的薬剤による治療の選択肢は、抗HER2 療法ではトラスツズマブとラパチニブがある. HER2陽性に対するトラスツズマブは標準治療薬 であり有害事象が比較的軽い有用な薬剤である が、前術のように心機能には十分な注意を払う 必要がある.ラパチニブはカペシタビンとの併 用で有効である<sup>41)</sup>が、予備能力の乏しい高齢者で は下痢などに注意を払う必要があるであろう.

# おわりに

本稿では高齢者乳がん治療の現状と課題を述べた、個々における包括的な評価が重要である。それに加え抗がん剤治療についてはベースラインリスクと余命期間、併存症、臓器機能を考慮し、リスクベネフィットを慎重に勘案する、転移・再発治療では、余命、併存症、臓器機能、QOLを十分に考慮した上で治療を選択する。そのほか、家族の負担やその協力度、コスト等も考慮する必要がある。CGAを含めた高齢者における前向き臨床試験も今後は重要であろう。

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# Characteristics of Elderly Cancer Patients' Concerns and Their Quality of Life in Japan: A Web-based Survey

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**Objective:** Cancer incidence and the number of cancer patients are increasing in today's aging society. The purpose of this study was to investigate the characteristics of elderly cancer patients' concerns and examine the association between their concerns and quality of life.

**Methods:** This was a cross-sectional web-based survey completed by ambulatory cancer patients aged 20 years or older. The questionnaire on cancer patients' concerns, comprehensive concerns assessment tool and the European Organization for Research and Treatment of Cancer QLQ-C30 were distributed to the subjects. Multiple regression analysis was conducted to determine which patients' concerns significantly contributed to their quality of life.

**Results:** The final study population consisted of 807 cancer patients, among whom 243 (30%) were elderly (65 years or older). Elderly cancer patients had particular difficulty with self-management, psychological symptoms and medical information, and the prevalence of their concerns was generally lower than that of younger patients, with the exception of physical symptoms. Multiple types of elderly patients' concerns were independently associated with quality of life.

**Conclusions:** We found that elderly cancer patients suffered from various concerns, thus multidisciplinary intervention is important for providing them with optimal care. The results of this study suggest that elderly cancer patients' quality of life will improve if their concerns are properly handled.

*Key words: psycho-oncology – supportive care – public health – quality of life* 

# INTRODUCTION

Since aging is a major risk for the development of cancer (1,2), elderly people are more likely to develop cancer than younger people (3,4). As the average life expectancy increases, the elderly population is growing, with the result that the number of older cancer patients is increasing. In 2013

in Japan, the elderly population aged 65 years or older was estimated to be 32 270 000 and the rate of aging 25.3% (as of 1 February 2014, provisional estimates) (5,6). In 2008 in Japan, the number of cancer incidence cases in patients over 65 years old was 538 061, among which 331 150 were males and 206 911 females (7,8). More and more elderly individuals will need cancer treatment in the near future.

However, there are a number of problems with the treatment of elderly cancer patients. Older patients tend to develop complications due to organ dysfunction and vulnerability (1,3,9-11), and their poor physical condition influences their tolerance to cancer therapy and increases the mortality risk (12–14). In general, cognitive impairment and depression are common disorders in elderly persons (15,16), and especially patients with cognitive dysfunction tend to develop delirium (11,17), which may hinder their ability to make proper decisions on their treatment (15). Moreover, according to a previous study, older people usually do not talk directly about their concerns (18), and another study indicates that cancer patients are reluctant to disclose their psychosocial concerns, so healthcare professionals hesitate to express their concerns (19,20). It seems to be difficult for medical staff to identify elderly cancer patients' problems and provide them with the necessary information and optimal support (20). On the other hand, elderly cancer patients need various forms of support such as understanding medical information, ameliorating physical symptoms, dealing with financial problems and coping with anxiety about the future (21,22). The Japanese government requires designated cancer care hospitals nationwide to establish a cancer care support and information service center in their hospitals based on the 'Basic Plan to Promote Cancer Control Act' of 2007 (23). The cancer care support and information service centers are intended to meet the needs of cancer patients without having to visit other institutions (24) and any cancer patient can use them freely, but their needs have not been handled appropriately (21,22). It is also reported that elderly cancer patients have economic limitations and have difficulty taking part in social activities, are physically and emotionally unstable, and are liable to feel lonely (11).

Previous Western studies found that older adults experienced significantly lower occurrence rates compared with younger adults in almost 50% of various physical and psychological symptoms associated with cancer and its treatment (25), an elderly cancer patient group showed a lower physical functioning score compared with the younger cancer patient group in the quality of life (QOL) domains (26), and that there was a moderate-to-strong association between patients' needs and psychological distress and/or QOL (27). To the best of our knowledge, few studies in Japan have comprehensively investigated and assessed elderly cancer patients' concerns including physical and psychological symptoms, medical treatment and daily life, even though these findings are essential for providing optimal care for elderly Japanese cancer patients.

The purposes of this study were: (i) to investigate what kind of concerns elderly cancer patients have, (ii) to compare elderly with younger cancer patients' concerns to clarify the characteristics of the elderly and (iii) to examine the association between elderly cancer patients' concerns and their QOL. We hypothesized that elderly cancer patients' concerns are multidimensional, that they had fewer concerns than younger cancer patients, and that there is a significant association between elderly cancer patients' concerns and their QOL.

# **METHODS**

### Subjects

This survey was conducted via the Internet using Lyche-web of INTAGE Inc., Tokyo, Japan. The company recruited and registered monitors who could use the Internet through advertisement. We extracted potential participants who met the eligibility criteria and performed a questionnaire investigation from 22–24 October 2012.

The eligibility criteria for inclusion in this study were as follows: (i) subjects of 20 years or older, (ii) subjects who were diagnosed with cancer (any primary site and clinical stage, at any time point after diagnosis) and under treatment and (iii) subjects who have been to the hospital for cancer treatment for at least 1 year. The exclusion criteria were: (i) workers of mass media, advertisement agencies, market research companies and (ii) healthcare providers such as doctors, nurses, social workers and so on. Monitors were paid with points in return for participating in this investigation, that is, they could earn points if they answered all questions, and then they could exchange points for cash, net points or donation to some organization.

This study was approved by the Institutional Review Board and Ethics Committee of the National Cancer Center Hospital, Japan. The return of completed forms was considered consent.

# PROCEDURE

This was a cross-sectional survey by internet to examine the characteristics of elderly cancer patients' concerns and the association between their concerns and QOL. We defined 65 years or older as the elderly in this investigation. The subjects were asked to fill out the online self-administered questionnaire. Inappropriate returns such as duplicate responses from the same terminal, mismatch between registered information and answer contents and inappropriate response time were deleted. As the participants were required to answer all questions, there should be no missing values in this investigation. The questionnaire consisted of the three sections described below.

# Instruments

CANCER PATIENTS' CONCERNS: COMPREHENSIVE CONCERNS ASSESSMENT TOOL (CCAT)

This self-reported questionnaire was developed to comprehensively assess cancer patients' concerns for our investigation, and its validity and reliability have been confirmed in Japanese cancer patients (28). The questionnaire includes four different types of concerns: physical symptoms (five items), psychological symptoms (five items), daily living (six items), self-management (three items), medical information (five items) and two symptoms: pain (one item) and constipation (one item). Participants were asked to respond to this questionnaire which evaluated the level or frequency of their concerns in the previous week on a four-point Likert scale

(1: no concerns, 2: slight concerns [once or twice a week], 3: moderate concerns [more than half of a week], 4: serious concerns [Every day]). We defined a rating of 3 or 4 as the presence of concerns.

QOL: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) is a 30-item cancer-specific questionnaire for assessing the general health-related QOL of cancer survivors (29). The questionnaire includes five functional scales (physical, role, emotional, cognitive and social) and nine symptom scales (fatigue, pain, nausea and vomiting and others) and a global health status/QOL scale. The reliability and validity of the Japanese version of the EORTC QLQ-C30 has been confirmed in a previous study (30). The present study uses a global health status score of 0–100, with a higher score indicating a higher QOL.

# SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS

An *ad hoc* self-administered questionnaire was used to obtain information on the patients' sociodemographic status, including age, sex, marital status, educational level, cancer site (all cancer types), clinical stage (the presence of recurrence or metastasis), anti-cancer treatment (surgery, chemotherapy, hormonal therapy and radiation therapy), duration since diagnosis (<6 months, 6 months to 5 years and  $\geq 5$  years), employment status (full-time/part-time or unemployed). As to the performance status (PS) defined by the Eastern Cooperative Oncology Group (ECOG), we described physical symptoms clearly in the questionnaire and asked participants to assess themselves using a rating from 0 (no symptoms) to 4 (bedridden).

# STATISTICAL ANALYSES

First, we conducted an unpaired t-test to show the demographic differences between elderly (≥65 years old) and younger (<65 years old) cancer patients. Second, we calculated the prevalence of concerns in each subscale and item of CCAT among elderly and younger cancer patients, respectively. We regarded a rating of 3 or 4 on the four-point Likert scale as the presence of concern for each item, and we defined the presence of concern as having one or more items of concern in each subscale. We subsequently conducted an unpaired t-test to investigate the differences between elderly and younger cancer patients' concerns. Lastly, we conducted a multiple regression analysis to examine the association between elderly cancer patients' concerns and their QOL. In this analysis, the global health status score of EORTC QLQ-C30 was entered as a dependent variable, and the concerns present in the seven subscales were entered as independent variables. Age, sex, marital status (two groups: married or others), clinical stage (two groups: presence or non-presence of recurrence/ metastasis), duration since diagnosis (three groups: <6 months, 6 months to 5 years,  $\geq$ 5 years), employment status (two groups: full-time/part-time or unemployed), educational level (two groups: more than high school graduate or others) were also entered as independent variables for adjustment.

All P values were two-sided, and a P value of < 0.05 was regarded as being statistically significant. All statistical procedures were conducted using SPSS software for Windows (Version 21.0 J, SPSS Inc., 2012).

# RESULTS

# PATIENT CHARACTERISTICS

A total of 1009 cancer patients were recruited in this study and data were available for 807 cancer patients. The response rate was 80.0%. The patients' sociodemographic and clinical characteristics are shown in Table 1. Based on the data collected, 243 subjects (30%) were over 65 years old; mean ( $\pm$ SD) and median age were 71.3 ( $\pm$ 4.7) and 71 years, respectively. More than 90% were married, male, and did not have any impairment of physical functioning (PS 0 or 1). About 40% were prostate cancer and  $\sim$ 30% were diagnosed with recurrent/metastatic cancer. The background characteristics of the two age-specific subject groups were significantly different in sex, marital status, employment status, cancer site, history of anti-cancer treatment and global health status score, as shown in Table 1.

Prevalence of Concerns and Differences Between Elderly  $(\geq 65 \text{ Years})$  and Younger (< 65 Years) Subjects

The most commonly perceived concerns among the elderly cancer patients were self-management, containing 'Want to know what I can do in poor health' (46.1%), 'Want to know what I can do for curing disease by myself' (45.3%), 'Want to know what I can do to take care of myself' (35.0%), followed by psychological symptoms 'Insomnia' (34.6%) and medical information 'Want to know about other treatments' (34.2%). We also found differences between older and younger cancer patients' concerns using univariate analysis, as shown in Table 2. The elderly subject group suffered significantly more from 'Loss of weight' (P = 0.04) in Physical symptoms but suffered less from 'Not being insightful' (P = 0.01), 'Feeling down and/or depressed' (P < 0.01) in psychological symptoms compared with the younger subject group. The elderly group also had significantly less difficulty with selfmanagement (P = 0.03), daily living (P < 0.01) and constipation (P = 0.02) compared with the younger group.

Association Between Elderly Cancer patients' Concerns and  $\operatorname{QOL}$ 

The results of the multiple regression analysis are shown in Table 3. Five subscales other than medical information and self-management were significantly associated with the elderly cancer patients' QOL, among which the most significantly associated was pain (P < 0.01), followed by physical

Table 1. Demographics and clinical characteristics of all participants

Characteristics	All		≥65 years	≥65 years		<65 years	
	N	%	N	%	N	%	
No.	807	100.0	243	30.1	564	69.9	
Age	Mean: 57.6	5 (SD = 11.6)	Mean: 71.3	8  (SD = 4.7)	Mean: 51.7	7 (SD = 8.3)	
	Median: 57	(range, 23-86)	Median: 71 (	range, 65-86)	Median: 52 (	range, 23-64)	
Sex							
Male	433	53.7	219	90.1	214	37.9	0.00
Female	374	46.3	24	9.9	350	62.1	
Marital status							
Married	640	79.3	221	90.9	419	74.3	0.00
Education							
>12 years	513	63.5	139	57.2	374	66.3	0.93
Employment status							
Full-time/part-time	365	45.2	49	20.2	316	56.0	0.00
Cancer site							
Breast	237	29.4	8	3.3	229	40.6	0.00
Prostate	126	15.6	102	42.0	24	4.3	
Colon	58	7.2	20	8.2	38	6.7	
Stomach	48	5.9	22	9.1	26	4.6	
Lung	34	4.2	13	5.3	21	3.7	
Bladder	31	3.8	12	4.9	19	3.4	
Uterus	31	3.8	0	0.0	31	5.5	
Hematopoietic system	29	3.6	5	2.1	24	4.3	
Liver	23	2.9	10	4.1	13	2.3	
Rectum	22	2.7	10	4.1	12	2.1	
Esophagus	15	1.9	7	2.9	8	1.4	
Head and neck	12	1.5	1	0.4	11	2.0	
Kidney	10	1.2	5	2.1	5	0.9	
Ovary	10	1.2	0	0.0	10	1.8	
Pancreas	9	1.1	6	2.5	3	0.5	
Biliary system	5	0.6	2	0.8	3	0.5	
Undiagnosed	9	1.1	3	1.2	6	1.1	
Others	98	12.1	17	7.0	81	14.4	
Clinical stage							
Recurrence/metastasis	213	26.4	66	27.2	147	26.1	0.75
History of anti-cancer treatmen	t <sup>a</sup>						
Surgery	678	84.0	175	72.0	503	89.2	0.00
Chemotherapy	384	47.6	94	38.7	290	51.4	0.00
Hormonal therapy	318	39.4	83	34.2	235	41.7	0.05
Radiation therapy	293	36.3	64	26.3	229	40.6	0.00

Continued

Table 1. Continued

Characteristics	All		≥65 years		<65 years		. P
	N	%	$N_{\perp}$	%	N	%	
ECOG performance status		,					
0	453	56.1	144	59.3	309	54.8	0.44
1	323	40.0	88	36.2	235	41.7	
2	25	3.1	9	3.7	16	2.8	
3	5	0.6	2	0.8	3	0.5	
4	1	0.1	0	0.0	1	0.2	
Duration since diagnosis							
<6 months	45	5.6	19	7.8	26	4.6	0.61
$\geq$ 6 months to <1 year	112	13.9	32	13.2	80	14.2	
$\geq$ 1 year to $\leq$ 2 years	190	23.5	50	20.6	140	24.8	
$\geq$ 2 years to $<$ 5 years	288	35.7	92	37.9	196	34.8	
≥5 years	172	21.3	50	20.6	122	21.6	
EORTC QLQ-C30	Mean: $62.2 (SD = 22.7)$		Mean: $64.7 (SD = 22.3)$		Mean: $61.2 \text{ (SD} = 22.8)$		0.04
Global health status score		66.7 (range, 100)		66.7 (range, 100)		66.7 (range, 100)	

ECOG, Eastern Cooperative Oncology Group; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Ouestionnaire-Core 30.

symptoms (P < 0.01), constipation (P < 0.01), psychological symptoms (P = 0.01) and daily living (P = 0.01), after adjusting for age, sex, marital status, clinical stage, duration since diagnosis, employment status and educational level. As the coefficient of determination ( $R^2$ ) in this survey was 0.31, we could not sufficiently estimate QOL from the concerns of elderly cancer patients.

# DISCUSSION

As to the elderly cancer patients' concerns, about half of them had difficulty with self-management, psychological symptoms and medical information. In terms of self-management, it appears that they would like to decide their own treatment and they are likely to do something on their own without relying on others. As for psychological symptoms and medical information, a previous study reported that the prevalence of unmet needs among cancer patients aged over 70 years was high in the Psychological and Health system and Information domains and slightly >50% of them appeared to be unsatisfied (26), which is consistent with our findings. This indicates that they have not obtained sufficient information for living with medical treatment, even though cancer care support and information service centers play an important role in providing cancer patients and their families with useful information such as how to deal with side effects at home, available treatment or treatment options and interpersonal communication. The reasons for this are that many cancer patients are still not familiar with the centers (31), or older patients with cognitive dysfunction might not be able to approach the centers because of their inadequate health literacy (32), so it may be necessary to simply remind them about the centers. With regard to psychological symptoms of older cancer patients such as insomnia, medical staff must handle this properly, for example, by regularly making assessments in clinical practices and objectively asking the families or visiting nurses about the patient's home life (33). Moreover, it would be necessary for oncologists to receive training on the primary approach for dealing with psychological symptoms of older cancer patients (34).

With respect to the comparison between elderly and younger cancer patients' concerns, a previous study reported that the elderly had less trouble with psychological symptoms and social functioning than younger cancer patients (25), and another study suggested that the elderly showed lower physical functioning scores in the QOL domains compared with the younger cancer patients (26), and these results are in agreement with our study. The reason for this seems to be that older cancer patients in Japan receive their pension or financial support from their children, which alleviates concerns about money. In addition, since they have finished raising their children and are retired from work, they have fewer demands on their time and resources compared with younger cancer patients (35,36). Since younger individuals still have work and family responsibilities, they seem to have more difficulty with psychosocial problems, financial problems, social functioning and so on (35,36). Regarding QOL, it is generally considered

<sup>&</sup>lt;sup>a</sup>Multiple choice.

Table 2. Prevalence of concerns<sup>a</sup> and differences between elderly (≥65 years) and younger (<65 years) cancer patients—univariate analysis

Concerns	All		≥65 years		<65 years		P
	n = 807	%	n = 243	%	n = 564	%	
Physical symptoms (having one or more concerns in the following five items)	123	15.2	39	16.0	84	14.9	0.68
Loss of weight	51	6.3	22	9.1	29	5.1	0.04
Loss of appetite	49	6.1	16	6.6	33	5.9	0.69
Dyspnea	43	5.3	9	3.7	34	6.0	0.18
Diarrhea	35	4.3	12	4.9	23	4.1	0.58
Nausea and/or vomiting	21	2.6	6	2.5	15	2.7	0.88
Psychological symptoms (having one or more concerns in the following five items)	391	48.5	114	46.9	277	49.1	0.53
Insomnia	257	31.8	84	34.6	173	30.7	0.28
Being tired and/or feeling sluggish	226	28.0	51	21.0	175	31.0	0.00
Not being insightful	146	18.1	31	12.8	115	20.4	0.01
Feeling down and/or depressed	123	15.2	21	8.6	102	18.1	0.00
Feeling agitated and/or nervous	71	8.8	16	6.6	55	9.8	0.15
Daily living (having one or more concerns in the following six items)	241	29.9	51	21.0	190	33.7	0.00
Concerns about medical fees	179	22.2	35	14.4	144	25.5	0.00
Inability to do job	133	16.5	18	7.4	115	20.4	0.00
Inability to do housework and/or to take care of family	69	8.6	12	4.9	57	10.1	0.02
Concerns about nursing care insurance	66	8.2	24	9.9	42	7.4	0.25
Inability to take care of oneself	58	7.2	11	4.5	47	8.3	0.06
Having no means of going to hospital	37	4.6	7	2.9	30	5.3	0.13
Self-management (having one or more concerns in the following three items)	494	61.2	135	55.6	359	63.7	0.03
Want to know what I can do for curing of disease by myself	423	52.4	110	45.3	313	55.5	0.01
Want to know what I can do in poor health	414	51.3	112	46.1	302	53.5	0.05
Want to know what I can do to take care of myself	334	41.4	85	35.0	249	44.1	0.02
Medical information (having one or more concerns in the following five items)	373	46.2	103	42.4	270	47.9	0.15
Want to know about other treatments	289	35.8	83	34.2	206	36.5	0.52
Want to know about other hospitals	235	29.1	73	30.0	162	28.7	0.71
Unable to understand explanation about disease and/or treatment	149	18.5	54	22.2	95	16.8	0.07
Unable to communicate well with doctor	140	17.3	42	17.3	98	17.4	0.98
Want to know about fertility	66	8.2	15	6.2	51	9.0	0.17
Pain							
Painful	142	17.6	41	16.9	101	17.9	0.72
Constipation							
Constipated	126	15.6	27	11.1	99	17.6	0.02

 $<sup>^{\</sup>mathrm{a}}\mathrm{Rated}$  3 or 4 on the four-point Likert scale on each item of the comprehensive concerns assessment tool.

to be lower in elderly compared with younger cancer patients, because the physical functions of elderly patients are weakened and they tend to have more comorbidities than younger patients (37), and the severity of comorbidities adversely affects QOL (38). In a previous study, however, the QOL of elderly cancer patients was the same degree as in younger cancer patients after adjustment for PS (39), and another study reported that QOL was not significantly different between

elderly and younger cancer patients (26). In our study, QOL was higher in the elderly than in the younger cancer patients. One of the reasons for this seems to be that older cancer patients are better able to adapt to severe situations compared with younger patients, although the elderly are more strongly affected by cancer itself or the treatment (40,41).

Regarding the association between concerns and QOL of elderly cancer patients, we found that there is a significant

Table 3. Association between elderly cancer patients' concerns and quality of life<sup>a</sup>—multiple regression analysis<sup>b</sup>

Concerns	Coefficient (B)	Standardizing coefficient ( $\beta$ )	T	Р	Partial R <sup>2</sup>
Physical symptoms	-11.77	-0.19	-3.23	0.00	0.14
Psychological symptoms	-6.70	-0.15	-2.53	0.01	0.11
Daily living	-8.34	-0.15	-2.53	0.01	0.11
Self-management	-4.67	-0.10	-1.61	0.11	0.08
Medical information	-3.44	-0.08	-1.20	0.23	0.06
Pain	-12.23	-0.21	-3.64	0.00	0.11
Constipation	-11.96	-0.17	-3.07	0.00	0.05
					Total $R^2 = 0$

<sup>&</sup>lt;sup>a</sup>Global health status score of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30.

association, but self-management and medical information, which are highly prevalent concerns among the elderly subjects, do not significantly contribute to QOL. Nevertheless, elderly subjects have great difficulty with these two subscales. On the other hand, the other five subscales that are significantly associated with QOL do not pose much difficulty for the elderly cancer patients. Therefore, we consider it important to comprehensively intervene in their multiple concerns. Several previous studies have suggested that the more adequate information cancer patients obtain, the more satisfied they are (20), and the more able they are to adapt to their psychological and emotional states (42); therefore the QOL of elderly cancer patients is expected to improve with multifaceted intervention and the provision of sufficient information about their concerns.

The present study has several limitations. First, there was the potential for selection bias in that the subjects were outpatients, over 90% of them were diagnosed >6 months earlier,  $\sim$ 90% of them were male and 40% were prostate cancer, and moreover, they were all able to participate in this internet survey. Based on these factors, it was estimated that most of the subjects were physically and mentally stable, and they had little cognitive dysfunction and high health literacy because they were capable enough to use the internet. As more men than women use the internet in general, it is believed that most subjects in this study were men. That is to say, subjects in this study were not representative elderly cancer patients in Japan. Further investigations need to be conducted other than through the internet, such as by interviews with not only outpatients but inpatients in clinical sites, in the future. In addition, we should point out that there was a possibility that most of the study subjects had normal cognitive function. In fact, the number of cognitive deficit patients in Japan was estimated to be 4 620 000 in 2013 (43), and many elderly cancer patients have cognitive impairment. Therefore, we should evaluate the cognitive function of elderly cancer patients first, positively detect their concerns including concerns of patients with cognitive dysfunction by using assessment tool like comprehensive geriatric assessment (CGA) after that, and examine whether we can clarify their concerns.

Second, the CCAT questionnaire for cancer patients' concerns proved to be valid and reliable in a previous study, but it is not specific to elderly cancer patients (28). Finally, since our investigation was cross-sectional in design, we cannot conclude the causal relationship between patients' concerns and their QOL. This problem needs further investigation in a longitudinal study; for example, we should reinvestigate after an interval of several months. In addition, further research needs to focus on various patients and clinical characteristics such as age, sex, cancer type, PS and so forth.

Despite these limitations, this study has several strengths. To our knowledge, it is the first study to comprehensively assess elderly cancer patients' concerns in Japan; in doing so, we could understand the characteristics of elderly cancer patients' concerns in detail. The response rate of this study was 80%, which was considered to be relatively high.

In today's aging society, multidisciplinary intervention and training for healthcare professionals will be required to deal with different and complex concerns of elderly patients with cancer. We should also make an active effort to investigate concerns of elderly cancer patients who do not complain, predict their possible problems such as upset, and intervene in them. This will make it possible to provide them with optimal oncological care to improve their QOL.

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<sup>&</sup>lt;sup>b</sup>Adjusted for age, sex, marital status (two groups), clinical stage (two groups), duration since diagnosis (three groups), employment status (two groups) and educational level (two groups).

# Conflict of interest statement

None declared

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# 特集

# CGAを考慮した高齢者に対するがん治療の特性と適応

# 高齢がん患者の サイコオンコロジー\*

小川朝华\*\*

Key Words: cancer, psycho-oncology, dementia, delirium, comprehensive geriatric assessment

# はじめに

わが国は、2013年には65歳以上の老年人口は3,079万人となり、全人口の24.1%を占めるにいたった<sup>1)</sup>. がんは45歳から89歳までの男性、40歳から84歳までの女性の最大の死因であるように広い年齢に分布する. その中で特に高齢者の罹患に注目すると、全悪性新生物死亡数のうち、65歳以上が78%を占めている. がんはまさに高齢者の疾患である.

平均寿命が延びることは、高齢者のがん発症率・有病率が増大することを意味する。同時に高齢者の人口が増加することは、がん治療において高齢がん患者が増加することを示唆する。 超高齢化社会を迎えたわが国は、高齢がん患者特有の問題を考慮に入れたがん治療のあり方を検討する必要に迫られている。

高齢がん患者に対して、適切で包括的ながん 治療を提供するために、高齢者総合的機能評価 (comprehensive geriatric assessment; CGA)の 実施が強く奨められている。

CGAの実施が推奨される理由に、加齢はがん 医療の不均衡に強く関連することがあげられる. 一般に患者の年齢が高くなるほど、治療をひか える傾向がある.担当医は、高齢がん患者では 治療の有益性を低く見積もり、高齢者には若年 者と異なる選択肢を提示する傾向がある<sup>30</sup>.しか し、高齢がん患者でも適切な手術、薬物療法に より生存期間を改善することは可能である<sup>30</sup>.単 に高齢というだけで、quality of life (QOL)の改 善や生命予後の改善を期待できる治療を受ける 機会を失うことがあってはならないが<sup>40</sup>、一方、 明らかに有益性のない治療は避けなければなら ない.

高齢がん患者に対する適切ながん治療を考える上で、身体症状のみならず、患者をとりまく精神医学的問題、心理・社会的問題に対する適切な評価が望まれる。がんと精神心理的問題との関連を扱う分野である精神腫瘍学(サイコオンコロジー; psycho-oncology)においても、高齢者特有の問題に配慮をした支持療法を考慮する必要がある。本稿では、高齢者の精神症状として重要な課題である認知機能障害・認知症を中心に紹介を進めたい。

# 高齢者総合的機能評価(comprehensive geriatric assessment; CGA)

CGAとは、comprehensive geriatric assessment の略で、疾患のある高齢者に対して、機能的、社会的、精神心理的観点からその高齢者の生活機能障害を総合的に評価する手法である50. CGA

<sup>\*</sup> Supportive care for the elder patients with cancer.

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が必要とされるようになった背景には、生活機能障害を持つ高齢患者数が著しく増加したことにより、疾患や生活機能障害相互の関連を把握し、適切なケアを幅広く提供する必要が高まったことによる。特にがん医療においては、CGAを実施することにより、合併症(たとえば神経障害性疼痛による転倒)や社会的支援不足(日中独居の患者への支援)、栄養不良[認知症によるアパシー(意欲低下)]などがん治療の阻害因子となりうる問題をあらかじめ同定することができる。

精神心理的問題としては、認知機能障害(認知症, せん妄)とうつ病、意欲低下(アパシー)への対応が重要である. 認知機能障害を持つがん患者は、セルフケア能力が低下するため、体調が悪化した場合の対応が遅れたり、困難になりやすい. また認知機能障害自体が、社会適応を困難にするため、抑うつ状態や意欲低下を招きやすく、治療のアドヒアランスを低下させたり、死亡リスクの上昇を招く<sup>6</sup>. そのためNCCN (National Comprehensive Cancer Network)の推奨するCGAにおいても、認知機能障害と抑うつ、意欲低下のスクリーニングが盛り込まれている<sup>7</sup>.

# 認知機能障害

# 1. せん妄

せん妄は、急性に生じる注意力障害を主体とした精神神経症状の総称である。せん妄はがん 患者において最も高頻度に認められる精神神経症状であり、治療の初期段階から終末期まであらゆる時期に出現する。せん妄では、注意力の障害に加えて、不眠や昼夜逆転などの睡眠覚醒リズムの障害、感情の変動、精神運動興奮、幻視や錯視などの知覚障害、妄想など多彩な症状が夜間を中心に出現し、数時間から数日のレベルで変動する。

せん妄は、精神症状による苦痛に加えて、家族や医療者とのコミュニケーションを阻害する 因子となり、身体症状のコントロールを不良に する<sup>80</sup>. また、せん妄自体が全身状態の不良を示 す兆候であり、早期に発見し対応することは、 身体症状管理上も重要である。

# (1)疫学

急性期一般病院においては, 入院中のがん患

者の有症率は15%(95%CI9~18%)である<sup>900</sup>. より進行して、緩和ケアへ移行する段階では一 般病棟よりも高くなり、緩和ケア病棟入院時点 で28%であった<sup>10</sup>.

緩和ケア病棟入院後は20~45%で、最終的に 全身状態が悪くなるにつれて上昇し、死亡前に は83%に達する<sup>12)13)</sup>.

### (2)アセスメント

せん妄の診断は診断基準[アメリカ精神医学会精神疾患の分類と診断の手引き(Diagnostic and Statistical Manual of Mental Disorders. 5th Edition; DSM-5)あるいはICD-10〕がgold standardである<sup>14)</sup>.

日常臨床では、Confusion Assessment Method (CAM)が用いられる。CAMはDSM-IVの操作基準のうち4つ(①急性発症と症状の変動、②注意力障害、③まとまりのない思考、④意識レベルの変化)を用いて演繹的に判定する方法で、使用方法のトレーニングを受けた医療者が使用することで、感度(94~100%)、特異度(90~95%)と高い判定率を持つ<sup>15)</sup>.

(3)マネジメント(薬物療法,非薬物療法,日 常生活の支援)

せん妄は診断をつけると同時に, せん妄の原因を検索し, 回復・修正可能な原因を同定する必要がある,

がん患者の場合,単独要因のみでせん妄を発症することはなく,潜在的な関連要因が絡むことがほとんどである. 見落としてはならないのは,アルコールと薬剤(特にオピオイド,ベンゾジアゼピン系薬剤,抗コリン薬)である. 次にせん妄のリスク因子である身体合併症や脆弱性の評価,認知症の有無,多剤併用,感染,脱水,腎機能障害,電解質異常(NaやCa),肝機能障害,低栄養などを評価する. 症候性てんかんを疑う場合には脳波を,頭蓋内病変を疑う場合には画像検査を併用する.

がん患者においては、オピオイドが関連する せん妄が20~50%と多い、オピオイドのタイト レーションとあわせてせん妄への対応を進める 必要があり、せん妄の評価と同時に疼痛のアセ スメントも実施する、

# (4)薬物療法

せん妄の治療は、ほとんどの場合は抗精神病薬を用いた薬物療法を実施する. 抗精神病薬は、もともとは統合失調症や双極性障害の治療薬として開発された薬剤であるが、せん妄の治療においても標準治療薬に位置づけられる. 抗精神病薬の治療効果は症例報告やオープントライアルを中心に検討されてきたが、2000年以降、術後せん妄を対象に無作為化比較試験も行われるようになった16. 抗精神病薬の有効性を示した報告が多いが、概して小規模な試験が多く背景因子が整えられていないこと、有害事象評価が十分になされていないことなどの問題がある.

### (5)非薬物療法

非薬物療法では、せん妄の増悪因子となる環境要因を減らすために多職種による複数の介入をまとめたプログラムが検討されている。高齢者病棟においてCAM (Confusion Assessment Method) やNu-DESC (The Nursing Delirium Screening Scale) など評価の定まったスクリーニングを実施し、その上で老年医学の専門家によるコンサルテーションの介入が行われたが、在院期間や死亡リスクには影響しなかった<sup>17)</sup>.

# 2. 認知症

認知症とは、正常に発達した認知機能が、後天的な器質性障害(神経変性など)により持続的に低下し、日常生活や社会生活に支障をきたすようになった状態である。認知症の定義はいくつか提唱されているが、代表的なものにDSM-5がある。認知症の罹患率は65歳で1.5%、70歳で約4%、75歳で約7%、80歳で約15%であり、およそ65歳以上の10人に1人が診断基準を満たすい。わが国では高齢化に伴い認知症患者も増加していると見積もられ、2009~2012年度の調査では、認知症の全国有病率推定値は15%(約439万人)、mild cognitive impairment(正常と認知症の中間状態)の全国有病率推定値は13%(MCI有症者数は約380万人)と推定されている181。

認知症には大きく4種の病型があり、最も有 病率の高いアルツハイマー病をはじめとして血 管性認知症、レビー小体病、前頭側頭葉型認知 症とある(表 1). それぞれの病型ごとに、臨床 症状が異なり、日常生活への支障の現れ方が異 なる.

認知症はがん患者の診断・治療にさまざまな 障害をもたらす, 認知機能障害とがん治療との 関係では、以下のような問題がある.

- ①認知機能障害が治療の意思決定能力自体に 影響を与える.
- ②認知機能障害があると,経口抗がん剤のスケジュール通りの内服が難しくなり,過量 投与のリスクとなる.
- ③有害事象を理解し、受診や支援が必要なとき に、自ら判断することができない。

たとえば外来の場においては、以下のような 問題が生じる危険性がある.

- ①経口抗がん剤の服薬を間違える,
- ②化学療法に伴うセルフケアができない.
- ③治療方針が理解できない、決定できない.
- ④オピオイドの内服を間違える.

特に経口内服薬のアドヒアランス(医療者の勧めに同意をして,患者が自ら行動を起こすこと)を確保することは治療成績を向上させる上でも重要であるが,臨床試験においても決して高くはない

治療と関連して、認知症を合併したがん患者 は、進行がんの比率が高く、stagingが不明の患 者が多いい。また、認知症の既往は予後にも影響 する、乳がんや前立腺がん、大腸がんを対象と した米国のMedicareのデータベースを用いた後 方視的研究では200, 非認知症のがん患者の6か 月以内の死亡率が8.5%であったのに対して、認 知症を合併した場合には33%に上った、死因別 に検討すると、認知症を合併した患者では、が んに関連する死亡もがんに関連しない死亡もと もに上昇していた、認知症を合併したがん患者 では、stageが不明の症例が多く、死亡率上昇の 13.6%(結腸・直腸がん)から16.4%(乳がん)は、 がんが進行期であることで説明ができた.一方, 前立腺がんにおいては、病期を調整すると、認 知症はがん関連死にはほとんど影響しないと見 積もられており、がん種による差は今後の検討 課題である.

認知症に関しては,前向き研究による詳細な 検討が必要であるが,認知症を合併した場合に 病期の影響が小さいことは,早期発見のための

表 1 認知症の病態,病状の比較

	発症のメカニズム	障害部位	中核症状	周辺症状	ケアのポイント
アルツハイマー病	アミロイド β タン パクの脳内沈音が原 因となって、神経原 線維変化が生じ、神 経細胞死に至る	側頭葉・・・ ・・・・ ・・・・・・・・・・・・・・・・・・・・・・・・・・・・	記憶障害:最近の出来事が思い出せない,思い出せない・忘れたこと自体に気づくことが難しい 見当識障害:時間や場所,人物の認識が難しくなる.最初は昼と夜を間違え,夜中に雨戸を開けたりすることで気づかれる.しだいに道に迷うようになる. 実行機能障害:物事の段取りを組むことが難しくなる.仕事を効率よくこなせなくなる.女性では,切る・焼く・炒めるなどのそれぞれの動作はできるものの,一つの料理を完成させることができなくなる。	の低下に伴って、作業の負荷が 大きくなるなどの環境要因と神 経細胞の脱落という器質的な要 素がからむ 妄想:物盗られ妄想が多い(物を どこかにしまい、しまった場所 がわからなくなる、そうなると、 身近な介護者が盗んだと確信し	認知症の進行を遅らせる塩酸ドネペジルの使用 周辺症状(意欲の低下、妄想、徘徊、失禁)などの行動障害が出現するメカニズムを発見し、その対処をする
血管性認知症	脳血管障害に関連して出現した認知症を 総称する	便塞・出血を 生じた部位に 関連して機能 障害が生じる	情動の変動:気分の変化(怒りっぽくなる,ちょっとしたことで泣く)が生じやすい 党醒レベルの変動:1日や数日の中で意識レベルの変動があり、せん妄を生じやすい 記憶障害:最近の出来事が思い出せない、思い出せない・忘れたこと自体に気づくことが難しい 実行機能障害:物事の段取りを組むことが難しい くなる。仕事を効率よくこなせなくなる、女性 では、切る・焼く・炒めるなどのそれぞれの動 作はできるものの、一つの料理を完成させることができなくなる	意欲の低下、抑うつ:梗塞・出 血に関連した脳機能の低下 人格の先鋭化:人格の特徴がよ り強く出てくる、慎重な性格が	便塞・出血に関連した神経症 状への対応(嚥下困難, 片麻 痺など) 安定した環境の提供 せん妄の予防と対処
レビー小体病	αシヌクレインが蓄 積し、レビー小体と なり、神経細胞死を 誘導する	とした症状(幻	党醒レベルの変動:1日の中で意識レベルの変動があり、注意力の障害が出る。せん妄を生じやすい 幻視:鮮明でありありとした幻視が出やすい パーキンソン症状:前傾姿勢やすり足歩行、姿勢反射障害、固縮などが出やすい 抗精神病薬への過敏性:少量でもパーキンソン 症状や過額静が生じやすい	<b>抑うつ・不安</b> :病初期には記憶 障害や幻視に先行して、意欲の 低下や抑うつ気分,不安焦燥感 で受診する場合がある パーキンソン症状:突進歩行, 転倒	抑うつ・不安への対応:環境 調整や薬物療法を行う 幻視に対しては、塩酸ドネペ ジルを使用 せん妄に対しては、パーキン ソン症状の出現しにくい非定 型抗精神病薬を少量使用する
前頭側頭葉型認知症	3 リピートタウの蓄 積が関係	前頭葉から側 頭葉にかけて の機能障害		被影響性の亢進:外界からの刺激に影響されて、相手の動作をまねたり、同じ言葉を発する(オウム返し)がでる 自発性の低下、感情の平板化: 進行すると無関心が目立ちはじめ、最終的には意欲も低下する	常同行為による時刻表的な生活をうまく利用する. 外界からの刺激をすくなくなるように割整して, 同じ時間に同じ職員が同じ対応を取れるようにする

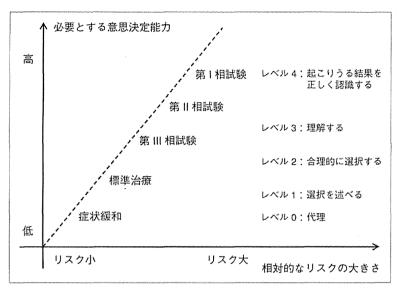


図 1 治療に伴うリスクと必要となる意思決定能力のレベルとの関係

スクリーニングの有効性も認知症の有無で異なることが考えられる.

# 意思決定能力の評価

がん医療において、インフォームドコンセントの重要性は指摘するまでもないが、適切なインフォームドコンセントが成立するためには、患者が医療者から受けた説明内容を適切に判断する能力を有することが前提となる。この前提となる能力を「意思決定能力(competency)」という。

意思決定能力の有無は、本来は法的に決定されるものである。しかし、わが国の代理人制度である成年後見制度の後見人には、生命を左右する医療行為については同意権が与えられていない。現時点で、意思決定能力がないと判断された治療拒否のケースにどのように対応したらよいのか、法的な回答はない。そのため、生命に関連する事態において、医師は自らが行う説明を患者が判断できるかどうかを個々の事態にあわせて判断していかなればならない。意思決定能力の判断には一定の原則はあっても、確立した法的判断基準があるわけではなく、患者の利益を第一に、慎重に個別に対応する。

臨床場面において、意思決定能力が適切に判 断されていないとの指摘が以前よりなされてき た<sup>21)</sup>. 大きくは,認知症と診断された患者に対しては,能力低下が過度に評価され,適切な医療が提供されていない問題がある一方<sup>22)</sup>,軽度認知障害のある患者では,見落とされている.

意思決定能力の評価について、Appelbaumらの 提唱する 4 つの機能に分けて検討することを勧 めている<sup>23)</sup>.

- ①理解力(understanding):提供された情報を 理解・保持し、自分の言葉で説明できる. 診断や治療を理解できる.
- ②認識する能力(appreciation):自分自身の診断や治療、治療の選択により将来起こりうる結果を自分のこととして認識し考える能力。
- ③論理的な思考能力(reasoning):診断や治療 に関する情報を参考に,論理的に比較考察 する能力.
- ④選択を表明する能力(states a choice):意思 決定の内容を明瞭に表明する能力.

選択に必要な意思決定能力は、その状況に応じて必要となるレベルも異なる(図 1). 治療方針の決定や治験の同意を得る際に、インフォームドコンセントに支障があると疑った場合には、保護者に情報を伝え対応を相談し、多職種を交えた検討が望まれる.

# 高齢者とのコミュニケーション

意思決定能力の評価に加えて、高齢がん患者 のインフォームドコンセントを得る場合にはコ ミュニケーションへの配慮も必要である.

高齢がん患者では、若年がん患者と異なるコミュニケーションに関するニーズを持ち、その関心、情報源も異なっていることが知られている。高齢がん患者ほど、診断や治療に関する情報を担当医のみから得る傾向が強い。またインターネットなどの情報源を用いることはあっても、友人や知人を通して得る情報を好む傾向がある<sup>240</sup>。

担当医は高齢がん患者の場合には、治療の有害事象と引き替えに得られる有益性の少なさから、高齢者には若年者と異なる選択肢を提示しがちである2.この問題の背景には、補助療法を実施することの利益と治療のリスクを踏まえた評価・情報提供が必要になるが、そのためには追加する治療が再発までの期間をどれだけ延長しているのか、あるいはその高齢者ががん以外の原因で死亡する可能性を踏まえて、再発のリスクをどれだけ落としているのか(天寿をまっとうする可能性が高まるのか)という情報が必要になり、問題は複雑である。不正確な情報しかないために、担当医は強く治療を推しづらい面も事実である。

# おわりに

高齢者の抗がん治療と関連して、精神症状で合併率の高い認知機能障害を中心に精神腫瘍学の課題を取り上げた. 高齢者の抗がん治療の目標は、平均余命が相対的に短く、ストレス耐性の低下した集団に対して、治療による利益がリスクを上回るかどうかを判断することになる.

これは,以下の問題を検討しなければならない.

- ①患者はがん死するかどうか.
- ②生存中にがんに伴う合併症を併発するリスク はあるのか.
- ③患者はがん治療に耐えられるのか.

治療効果を最大限に高め、患者のQOLの向上 を図るためには、CGAをベースとした実臨床を 反映した大規模な症例登録をもとに、治療成績と身体機能、社会支援の影響を検討する必要がある。高齢化社会をすでに迎えたわが国が、世界に貢献できる領域であり、多領域が連携した取り組みが期待される。

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# Original Article

# Randomized controlled trial comparing docetaxel-cisplatin combination with weekly docetaxel alone in elderly patients with advanced non-small-cell lung cancer: Japan Clinical Oncology Group (JCOG) 0207<sup>†</sup>

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# Abstract

**Objective:** Prospective trials specifically designed for elderly patients with advanced non-small-cell lung cancer demonstrating the benefit of platinum-based therapies are still lacking. This trial was designed to clarify whether the addition of cisplatin to monotherapy could improve survival for elderly patients.

**Methods:** Elderly patients (age  $\geq$ 70 years, ECOG performance Status 0–1) with advanced non-small-cell lung cancer were randomized to receive docetaxel 20 mg/m² plus cisplatin 25 mg/m² on Day 1, 8 and 15 (docetaxel plus cisplatin) or docetaxel 25 mg/m² on the same schedule (docetaxel). Both regimens were repeated every 4 weeks until disease progression.

Results: One hundred and twenty-six patients were enrolled. Sixty-three were randomly assigned docetaxel plus cisplatin and 63 docetaxel monotherapy. Median age was 76 years (range 70–88). The second planned interim analysis was performed on 112 assessable patients (docetaxel/docetaxel plus cisplatin: 56/56). Although the formal criterion for stopping the trial was not met, the Data and Safety Monitoring Committee recommended study termination on ethical grounds based on the interaction (two-sided P=0.077, hazard ratios for  $\leq 74/\geq 75$ : 0.23/0.72) between age and subgroup and treatment arm, which suggested that docetaxel may not represent an adequate control arm regimen for the age subgroup of 70–74 years.

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