PRISM Sequence Detector System according to the manufacturer's instructions (Applied Biosystems) as described previously (23). The relative levels of miR-210 expression were calculated from the relevant signals by normalization with the signal for U6B miRNA expression. The assay names for miR-210 were has-mir-210 (Applied Biosystems).

Immunohistochemical Analysis

ERα and PgR protein expression status was confirmed by immunohistochemistry (IHC) as follows. One 4-μm section of each submitted paraffin block was stained first with hematoxylin and eosin to verify that an adequate number of invasive carcinoma cells were present and that the fixation quality was adequate for IHC analysis. Serial sections (4 μm) were prepared from selected blocks and float mounted on adhesive-coated glass slides, for staining with monoclonal mouse anti-human ERα antibody (1D5; DAKO, Glostrup, Denmark) at 1:100 dilution and monoclonal mouse anti-human PgR antibody (636; DAKO) as described previously (21). The DAKO Envision system (DAKO EnVision-labeled polymer, peroxidase) was used for detection. Immunostaining for epidermal growth factor receptor (EGFR) was performed using the EGFRpharmDx assay detection system (prediluted; DAKO). After the entire slide was evaluated by light microscopy, expression of ERα and PgR was scored by proportion and intensity, according to Allred's procedure (24). In brief, the proportion scores that represented the estimated proportion of tumor cells staining positive were as follows: 0 (none), 1 ($<1/100$), 2 ($\geq 1/100$, $<1/10$), 3 ($\geq 1/10$, $<1/3$), 4 ($\geq 1/3$, $<2/3$) and 5 ($\geq 2/3$). Any brown nuclear staining in invasive breast epithelium counted toward the proportion score. The intensity scores, representing the average intensity of the positive cells, were as follows: 0 (none), 1 (weak), 2 (intermediate) and 3 (strong). The proportion and intensity scores were then added to obtain a total score, which could range from 0 to 8. Tumors with a score of 0 or 2 were considered to be negative and those with a score of 3 or greater were considered to be positive for ERα expression. HER2 immunostaining was evaluated using the same method as is employed by the HercepTest (DAKO). To determine the score for HER2 expression the membrane staining pattern was assessed and scored on a scale of 0 to 3+. Tumors with scores of 0 and 1 were considered to be negative for HER2 overexpression. To determine the score for EGFR expression, the membrane staining pattern was assessed and scored on a scale of 0 to 3+ using the same method as for the HER2 scoring. Tumors with scores of 0 and 1 were considered to be negative and tumors with scores of 2 and 3 were considered to be positive for EGFR overexpression.

Statistical Analyses

All molecular and immunohistochemical analyses were performed blinded to clinical data. Statistical calculations were performed with StatView-J 5.0 software (SAS Institute, Inc., Cary, NC, USA). The Mann–Whitney *U*-test was performed for the analyses of ERα protein and miR-210 expression. The relationships between ERα protein expression or miR-210 expression, and clinicopathological factors were assessed by χ^2 and Fisher's exact probability tests. DFS and OS curves were generated by the Kaplan–Meier method and verified by the log-rank test. A Cox proportional hazards regression analysis was used for univariate and multivariate analyses of prognostic values. Differences were considered significant when a P value < 0.05 was obtained.

RESULTS

miR-210 Expression and ERα Status

We examined the correlation between miR-210 expression and ERα protein expression in 161 samples of Japanese breast cancer tissue (58 triple-negative TNBC, and 103 ER positive and HER2 negative), because miR-210 has been linked to the metastatic potential of TNBCs (10). In order to simplify the analysis, we excluded HER2-positive breast cancer from this analysis. In order to examine the relationship between miR-210 expression and ERα expression levels, we divided the ERα-positive, HER2-negative breast cancers ($n = 103$) into two subgroups: one group showed low ERα protein expression (Allred score: 3–6; $n = 42$) and another group showed high ERα protein expression (Allred score: 7 or 8; $n = 61$; Table 1). Except for tumor grade, the characteristics of the analyzed breast cancers were similar with regard to patient age, tumor size and nodal status among these two groups of ERα-positive, HER2-negative breast cancers and TNBCs (Table 1). TNBCs showed higher tumor grades than did the ERα-positive and HER2-negative breast cancers. As shown in Fig. 1, the miR-210 expression in TNBCs (median relative miR-210 expression: 6.2; average relative miR-210 expression: 11.1 ± 2.60) was significantly higher than that in both the high ERα expression tumors (median 1.39, average 2.48 ± 0.43; Mann–Whitney *U*-test, $P < 0.001$) and the low ERα expression tumors (median 1.51, average 3.15 ± 0.61; Mann–Whitney *U*-test, $P < 0.001$).

miR-210 Expression as a Prognostic Marker in Breast Cancer

Next, we examined the relationship between the expression of miR-210 in tumor specimens and patient outcome in 58 TNBCs with long-term follow-up. miR-210 expression showed a significant inverse correlation with DFS when divided at the median miR-210 expression level (log-rank test; $P = 0.046$). Then, TNBCs were divided into three groups according to miR-210 expression levels: low expression (relative miR-210 expression <4; $n = 19$), intermediate expression ($4 \leq$ relative miR-210 expression <9; $n = 19$)

Table 1. Patient and tumor characteristics in ERα-positive and HER2-negative breast cancers, and TNBCs

	Total (161)	ERα(+) HER2(−)			Triple negative ($n = 58$)	P value[a]
		Subtotal ($n = 103$)	Allred score: 3–6 ($n = 42$)	Allred score: 7, 8 ($n = 61$)		
Age (years)						
≤50	51	30	18	12	21	0.38
>50	110	73	24	49	37	
Tumor size (cm)						
≤2	42	27	10	17	15	>0.99
>2	117	74	30	44	43	
Unknown	2	2	2	0	0	
Nodal status						
Negative	95	55	25	30	40	0.12
Positive	58	41	15	26	17	
Unknown	8	7	2	5	1	
Grade						
1	21	18	9	9	3	<0.0001
2	65	49	20	29	16	
3	53	14	7	7	39	
Unknown	22	22	6	16	0	

ER, estrogen receptor.
[a]ERα (+) HER2(−) vs. triple negative.

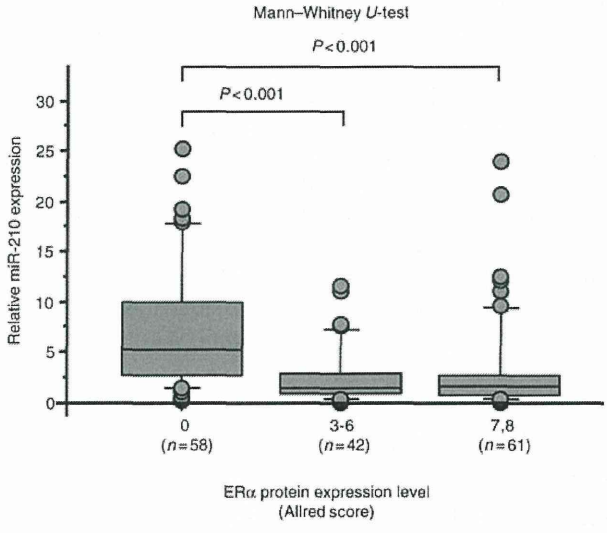

Figure 1. miR-210 expression and estrogen receptor (ERα) protein expression levels according to the Allred score (Allred score 0: $n = 58$; Allred score: 3–6: $n = 42$; Allred score: 7 or 8: $n = 61$). The horizontal line indicates the median concentration, the box covers the 25th–75th percentiles and the maximum length of each whisker shows the 10th or 90th percentiles, respectively. There was no tumor showing ERα protein expression at the level of Allred score 2 in this study.

and high expression (relative miR-210 expression ≥9; $n = 20$; Table 2). The characteristics of patients and their tumors in each group were similar with regard to age, tumor size, nodal status, grade, EGFR protein expression and adjuvant chemotherapy (Table 2). As shown in Fig. 2a and b, patients with TNBCs showing low miR-210 expression had significantly better DFS compared with TNBC patients showing intermediate or high miR-210 expression (log-rank test; $P = 0.03$ and 0.02, respectively), and TNBC patients showing low miR-210 expression also had marginally better OS than did those with high miR-210 expression (log-rank test; $P = 0.05$). The Cox univariate and multivariate analyses demonstrated that miR-210 was an independent prognostic indicator of a poor outcome in TNBCs (Table 3). Next, we studied the relationship between the expression of miR-210 and patient outcome in 40 node-negative TNBCs. Interestingly, the 5-year DFS was ~60% in patients with high miR-210 expression tumors ($n = 11$), while no patient with low-miR-210 expression tumors ($n = 14$) revealed recurrent disease (Fig. 3a and b). DFS and OS curves in intermediate miR-210 expression tumors ($n = 15$) fall between the curves representing low- and high miR-210 expression tumors (Fig. 3a and b).

Table 2. Correlations between miR-210 expression and clinicopathological parameters in TNBCs

	Total ($n = 58$)	miR-210 expression			*P* value
		Low ($n = 19$)	Intermediate ($n = 19$)	High ($n = 20$)	
Age (years)					
≤50	21	6	7	8	0.77
>50	37	13	12	12	
Tumor size (cm)					
≤2	15	5	4	6	>0.99
>2	43	14	15	14	
Nodal status					
Negative	40	14	15	11	0.22
Positive	17	4	4	9	
Unknown	1	1	0	0	
Grade					
1	3	1	1	1	0.44
2	16	7	5	4	
3	39	11	13	15	
EGFR					
0, 1+	37	14	12	11	0.18
2+, 3+	13	2	5	6	
Unknown	8	3	2	3	
Chemotherapy					
+	42	14	13	15	0.76
−	15	5	6	4	
Unknown	1	0	0	1	

EGFR, epidermal growth factor receptor.

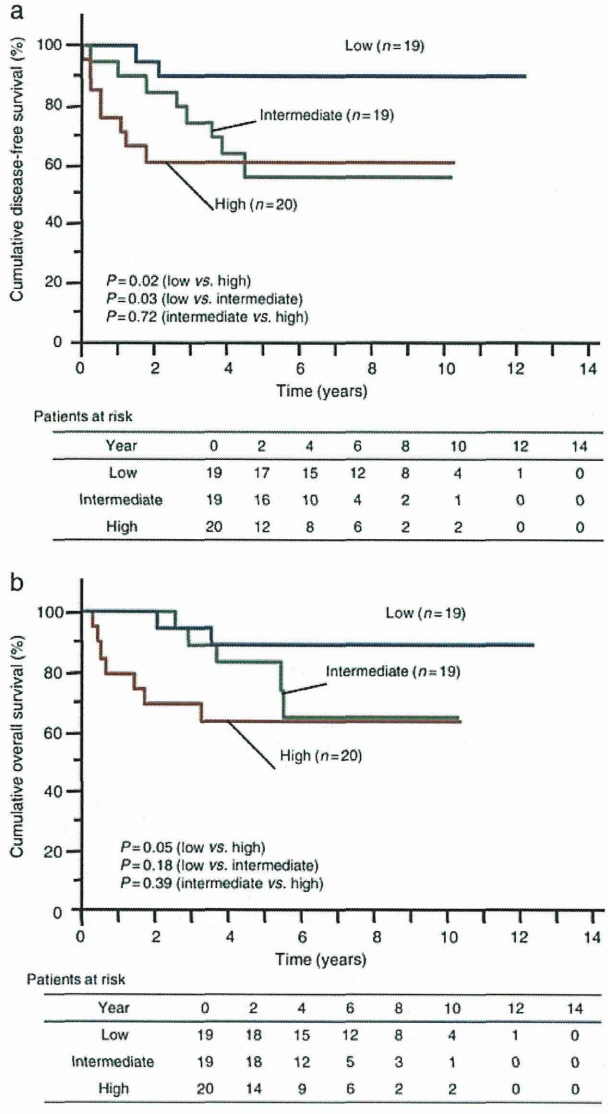

Figure 2. Kaplan–Meier survival curves are shown for disease-free survival (DFS) (a) and overall survival (OS) (b) for all patients with triple negative breast cancer (TNBC; $n = 58$) stratified according to miR-210 expression. The expression levels were stratified by the median value. The DFS (c) and OS (d) are shown for patients with different miR-210 levels. According to miR-210 expression level, TNBCs were divided into three groups.

DISCUSSION

TNBCs are of higher histological grades and have more aggressive clinical behavior than do hormone receptor-positive breast cancers. TNBCs include tumors with the BRCA1 mutation. BRCA1 is a tumor suppressor gene which, when mutated, is associated with the development of hereditary breast cancer. Recently, it has been reported that polyadenosine diphosphate ribose polymerase (PARP) inhibitor, which is believed to induce synthetic lethality in BRCA-deficient cells, might have therapeutic effect in patients with BRCA1 or BRCA2 mutations (25). However, the efficacy of PARP inhibitor in patients without BRCA1 or BRCA2 mutations is unclear. Although effective tailored therapies have been developed for patients with hormone receptor-positive or HER2-positive disease, patients with TNBCs are unlikely to benefit from currently available targeted systemic therapy. Therefore, it is an urgent matter in the treatment of TNBCs that some useful tools are developed and made available, such as new prognostic factors and/or new predictive factors for antitumor agents.

The role of miRNAs in cancer and their potential utility as prognostic factors have become apparent (26). miR-210 has been reported to be highly up-regulated miRNAs in hypoxic cells, and its transcription is regulated by both HIF-1α (7,9,27) and HIF-2α (8). HIF-1α directly binds to an HRE on the proximal miR-210 promoter (7). When the miR-210 core promoter is compared across species, this HRE is highly conserved, indicating the importance of hypoxia in regulating miR-210 expression across species (28). Recently, two groups have reported that a high

Table 3. miR-210 expression in TNBCs. Cox proportional hazards regression analysis

	Univariate	Multivariate	
	P value	*P* value	HR of recurrence (95% CI)
miR-210 expression			
Low			1.0 (reference)
High or intermediate	0.036	0.049	4.39 (1.00 to 19.28)
Nodal status			
Negative			1.0 (reference)
Positive	0.011	0.018	3.06 (1.20 to 7.80)
Tumor size (cm)			
≤2			1.0 (reference)
>2	0.653	0.710	1.23 (0.40 to 3.76)
Grade			
1 or 2			1.0 (reference)
3	0.557	0.280	0.59 (0.22 to 1.53)

HR, hazard ratio; CI, confidence interval.

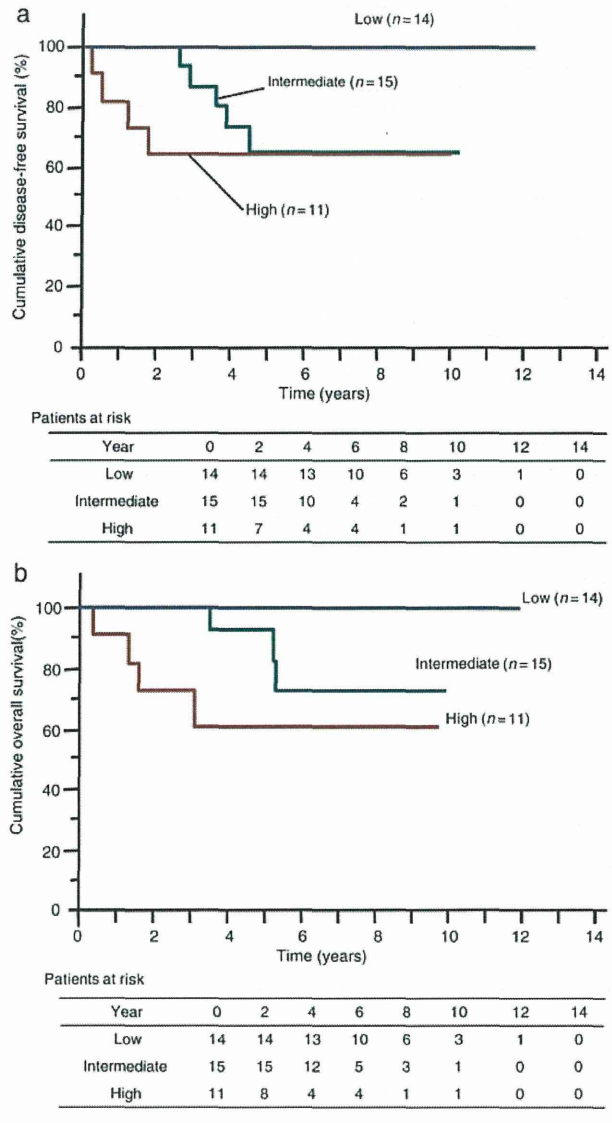

Figure 3. Kaplan–Meier survival curves are shown for DFS (a) and OS (b) for node-negative patients with TNBC ($n = 40$) stratified according to miR-210 expression. According to miR-210 expression level, TNBCs were divided into three groups.

expression of miR-210 in breast cancer patients was associated with a poor prognosis (9,10). As breast cancers are classified into several subtypes and the biology and the clinical outcome are different among its subtypes (17,18,21), we hypothesized that miR-210 expression would vary among them. In this study, we showed that miR-210 expression in TNBCs was significantly higher than that in ER-positive and HER2-negative tumors. Because TNBCs are heterogeneous, we classified the tumors according to their miR-210 expression levels. We found that TNBC patients with low expression of miR-210 had a better prognosis than did those with intermediate- and high miR-210 expression tumors despite the clinicopathological characteristics of the patients, such as tumor grade and the rate of adjuvant chemotherapy, being similar among the three groups. Our data thus supported the report presented by another group (10). Notably, among 40 node-negative TNBCs, the 5-year DFS was ~60% in patients whose tumors had high or intermediate miR-210 expression, while no patient with low miR-210 expression experienced recurrent disease. As we did not perform microdissection to obtain cancer cells, the proportion of the normal cell fraction, e.g. lymphoid cells and stromal cells, in TNBC samples might have influenced our results.

Several targets of miR-210 have been reported recently (7,8,29–31). According to these reports, one of the most important roles of miR-210 appears to be associated with 'mitochondrial dysfunction'. Chan et al. (29) have recently reported that miR-210 targeted the iron–sulfur cluster assembly protein (ISCU), and two other groups also supported this conclusion (30,31). By repressing ISCU1/2 during hypoxia, miR-210 decreases the activity of prototypical iron–sulfur proteins controlling mitochondrial metabolism (29). Consequently, miR-210 represses mitochondrial respiration. Puisségur et al. (11) have also reported that subunit D of succinate dehydrogenase complex (SDHD) is a direct target of miR-210. SDHD is an enzyme of the tricarboxylic acid cycle and a functional member of the mitochondrial respiratory chain (complex II) (32).

The regulation of these mitochondrial components by the miR-210 pathway has contrasting consequences for the regulation of cell death and survival under normoxic or hypoxic conditions (11,31). miR-210 overexpression in normoxia would create a mitochondrial dysfunction including a mismatch in electron transport that could lead to an increase in toxic reactive oxygen species (31) and increased apoptosis

(11,31). miR-210 thus appears to exert a maladaptive role in normoxia (11,31). In contrast, during hypoxia, the miR-210-dependent repression of the electron transport chain via ISCU1/2 and SDHD would be protective by participating in the homeostatic down-regulation of mitochondrial respiration (6,11,29,31).

The reduced mitochondrial respiration could be responsible for the tumor cell growth advantage in a hypoxic microenvironment. One hypothesis suggests that a reduced mitochondrial function could conserve O_2 for alternative use (33). When the distance travelled by O_2 to reach the outermost cell was defined as the diffusion limit, the limit is a function of the O_2 content within the blood vessels and the rate of consumption within the tumor cells as O_2 diffuses out from the vessels. Decreasing consumption is theoretically the most efficient way to extend this diffusion limit *in vivo* (33,34). The second hypothesis suggests that a reduced mitochondrial function could yield an increase in anabolic substrates (33). Rapidly dividing tumor cells require large amounts of precursors for proteins, nucleic acids and lipids (35). An increased glucose uptake by tumor cells and a decreased consumption of metabolites for energy in the mitochondria provide more substrates for lipid and nucleic acid synthesis (33).

Tumors with high miR-210 expression might have a growth advantage via reduced mitochondrial respiration in a hypoxic microenvironment. Because TNBCs usually have aggressive clinical behavior, they could have some areas of hypoxic microenvironment inside their tumors, where miR-210 could be highly expressed. On the other hand, HR-positive tumors are usually of lower histological grade and less aggressive than TNBCs. We demonstrated that miR-210 expression in TNBCs was higher than in HR-positive tumors. We consider that our data support the hypothesis described above. However, Camps et al. (9) have reported no interaction between ER and miR-210 expression levels. They evaluated ER status by ELISA while ER expression was confirmed by IHC analysis in the present study. Therefore, the methodology for evaluation of ER status might be responsible for these different results.

In this study, patients with TNBCs that expressed low levels of miR-210 had a more favorable prognosis, although the prognosis of TNBCs is relatively poor. Thus, the degree of miR-210 expression might be a clinically useful prognostic factor for decision-making regarding treatment in the adjuvant setting, especially in node-negative TNBC patients. Although we used frozen samples for this study, miRNA assays could also have been performed using formalin-fixed paraffin-embedded samples because technology has been rapidly advancing in this field. Although the multifaceted roles of miR-210 have been gradually clarified under hypoxia and normoxia status, the biological functions of miR-210 that are involved in providing a growth advantage for TNBCs are not fully understood. Further research might help to reveal that miR-210 could be not only a prognostic factor, but also a therapeutic target in TNBCs.

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Conflict of interest statement

None declared.

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Perceived Needs, Psychological Distress and Quality of Life of Elderly Cancer Patients

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Objective: Very few findings regarding the perceived needs of elderly cancer patients have been reported. This study investigated needs and psychological distress perceived by and/or quality of life of elderly cancer patients.
Methods: Randomly selected ambulatory patients with cancer participated in this study. The patients were asked to complete the Short-form Supportive Care Needs Survey questionnaire, which covers five domains of need (health system and information, psychological, physical, care and support, and sexual); the Hospital Anxiety and Depression Scale and the European Organization for Research and Treatment of Cancer QLQ-C 30.
Results: Complete data were available for 619 cancer patients, including 113 subjects who were over 70 years old. The needs and the psychological distress perceived by the elderly patients were comparable with those perceived by relatively younger patients, although elderly patients perceived fewer sexual needs. Regarding the quality of life global health status, most symptom-related quality of life parameters were not significantly different between the two groups, while significant differences were observed with regard to several functional domains, including physical, emotional and social domains in addition to financial difficulties.
Conclusions: Only a few differences in the needs and the psychological distress perceived by patients existed between the elderly and the younger subjects, although some differences in the quality of life domains were noted, probably as a result of the influence of aging itself. Medical staff should provide elderly cancer patients with good clinical care similar to that provided to younger patients while considering the different impacts of aging on each quality of life dimension.

Key words: oncology – elderly need – psychological distress – quality of life – supportive care

INTRODUCTION

One of the most important risk factors for the development of cancer is aging because of which more than half of all new cancers occur in elderly people (1). In Japan, which currently has the greatest life expectancy at birth in the world (averaging 83 years for men and women), cancer has continuously been the leading cause of death since 1981, and more than one-third of Japanese people die of cancer (2). Thus, Japan has attracted the attention of many countries as one of the most rapidly aging societies in the world, and Japan will become a super-aging society with people aged 65 years and over accounting for 25% of the population in the near future.

Needless to say, providing appropriate patient-centered care as well as optimal active anti-cancer treatment to elderly cancer patients is part of good clinical oncology practice. Nevertheless, very few studies have specifically focused on the treatment and care for elderly cancer patients, as many studies exclude elderly patients (3). Furthermore, since elderly cancer patients are physically, psychologically and socially heterogeneous in addition to differing from younger patients with regard to their physical functioning, psychological well-being, life circumstances, role demands, values and preferences, the treatment and care for elderly cancer patients is complex, especially considering individualized optimal care (1,4,5).

Several previous studies have investigated differences in quality of life (QOL) between young and old cancer patients, and many of these studies have revealed that older subjects' emotional, social and economical functioning are generally better and their physical functioning is worse than that of their younger counterparts, despite the absence of significant differences in their total and/or global QOL (6–9). Concerning other relevant outcomes, including patients' psychological distress and supportive care needs, older cancer patients experience similar or somewhat less psychological distress and generally have less information and sexual needs (10–12,13), although very few studies have investigated age differences among other domains of patients' supportive care needs.

Findings regarding older cancer patients' supportive care needs are essential because the assessment of needs offers a number of advantages. First, needs perceived by patients and patient-important outcomes can be directly assessed, enabling a more direct determination of necessary resources. Actually, the patients' problems and symptoms do not necessarily reflect the actual needs (14). Second, such assessments enable the magnitude of a particular need to be identified, thereby allowing some prioritization of service needs so that the available resources can be allocated where the need is most urgent. Third, an assessment of needs enables identification of individuals and/or patient subgroups with higher need levels, thereby enabling prevention or minimization of problems through appropriate early interventions (15). Thus, understanding the needs perceived by elderly patients will enable medical staff to develop services or procedures specially designed to meet them, providing valuable guidance for forthcoming super-aging societies.

To the best our knowledge, no large study has investigated age-specific differences regarding QOL and psychological distress in addition to supportive care needs among elderly cancer patients in an Asian country.

The purposes of this study were: (i) to investigate age-specific differences in supportive care needs in addition to psychological distress and QOL of elderly cancer patients and (ii) to determine the frequency of unmet supportive care needs in such individuals. Our hypotheses were that elderly cancer patients generally perceive fewer supportive care needs and less psychological distress, compared with younger patients, because our previous studies demonstrated that older cancer patients are less likely to be referred to the psycho-oncology service and that the incidence of psychiatric morbidity is lower (16,17).

PATIENTS AND METHODS

Participants and Procedures

This study was conducted with data obtained from our two previous studies that were published in 2010 and 2011. The first study subjects were randomly sampled ambulatory cancer patients of the outpatient oncology unit at Nagoya City University Hospital (Study 1) (18). The other study subjects were randomly sampled ambulatory female patients with breast cancer attending the outpatient clinic for Oncology, Immunology and Surgery at Nagoya City University Hospital (Study 2) (19).

The eligibility criteria for inclusion in both the studies were as follows: (i) a diagnosis of cancer (all stages and any time point after diagnosis), (ii) an age of 20 years or older, (iii) an awareness of the diagnosis of cancer and (iv) a general condition sufficient to enable the completion of the survey questionnaire [0-3 on the Eastern Cooperative Oncology Group (ECOG) performance status]. The exclusion criteria were patients with (i) severe mental or cognitive disorders (e.g. uncontrolled schizophrenia, dementia and delirium) or (ii) an inability to understand the Japanese language.

Both the studies were approved by the Institutional Review Board and Ethics Committee of Nagoya City University Graduate School of Medical Sciences, Japan, and were conducted in accordance with the principles outlined in the Helsinki Declaration. Written consent was obtained from each patient after a thorough explanation of the purpose and the methods involved in the study had been provided.

Procedure

After informed consent had been obtained, the patients were asked to complete the following self-administered questionnaires (described in the following section) at home and to

return them the following day. If any of the questions were answered inadequately, clarifications were sought over the telephone.

Patients' Perceived Needs: The Short-form Supportive Care Needs Survey Questionnaire

The Short-form Supportive Care Needs Survey (SCNS-SF34) is a self-administered instrument for assessing the needs perceived by patients with cancer (20,21). The SCNS-SF34 consisted of 34 items covering five domains of need: psychological (10 items), health system and information (11 items), physical and daily living (5 items), patient care and support (5 items) and sexual (3 items). The respondents were asked to indicate the level of their need for help over the previous month in relation to their cancer, using the following five response options: [1, No Need (Not applicable); 2, No Need (Satisfied); 3, Low Need; 4, Moderate Need and 5, High Need]. Subscale scores were obtained by summing the individual items. In addition, the total score was obtained by summing all the subscales (range, 34–170). A higher score indicated a higher perceived need. Besides, the scale could be used to obtain information on the presence/absence and the number of unmet perceived needs (a rating of three or higher was regarded as an unmet need), depending on the researcher's question on a clinical aspect. The validity and the reliability of the Japanese version of the SCNS-SF34 have been established (22).

Psychological Distress: Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) has been developed for use in medically ill patients and does not contain any questions regarding physical symptoms (23). The HADS is a self-reported questionnaire consisting of 14 items. The subjects are asked to rate on a 4-point Likert scale how they felt during the previous week. The HADS consists of an anxiety and a depression subscale (0–21 points each), and the total score can range from 0 to 42. A higher score indicates more severe depression and anxiety. The Japanese version of the HADS has been validated for cancer populations (24). The optimal cut-off point for screening for adjustment disorders and/or major depressive disorders (indicating psychological distress) was 10/11, while the cut-off for major depression (indicating serious psychological distress) was 19/20.

Quality of Life

The QOL of the patients was assessed using the European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C30 (25). The QLQ-C30 is a 30 item, self-reported questionnaire covering functional (Global Health Status, Physical Functioning, Role Functioning, Emotional Functioning, Cognitive Functioning and Social Functioning) and symptom-related aspects (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties) of QOL in cancer patients. The validity and the reliability of the Japanese version of the EORTC QLQ-C30 have been confirmed (26). A high functional score represents a high QOL. A high symptom score indicates a strong symptom.

Sociodemographic and Biomedical Factors

An *ad hoc* self-administered questionnaire was used to obtain information on the patients' sociodemographic statuses, including their marital status, level of education and employment status. The performance status, as defined by the ECOG, was evaluated by the attending physicians and was an objective index of a patient's physical functioning, ranging from 0 (no symptoms) to 4 (bedridden). All other medical information (duration since diagnosis, clinical stage and anti-cancer treatment) was obtained from the patients' medical records.

Statistical Analysis

To investigate the differences regarding the needs and psychological distress perceived by and/or QOL of the patients between two different age groups, an unpaired *t*-test and a Mann–Whitney test were conducted, as appropriate. We chose 70 years of age as the cut-off in this study because many age-related changes occur after this age (27). After these univariate analyses, we used an analysis of covariance (ANCOVA) to examine whether the differences were observed even after adjustments for potential confounding factors, including sex, cancer site (breast cancer vs. other cancers), clinical stage (IV or recurrence vs. other stages) and performance status (defined by ECOG).

To determine the frequencies of perceived needs of the elderly patients, data only for the subjects in their 70s were extracted. Then, each score for the 34 items of need was used (a rating of three or higher was regarded as the presence of an unmet need) to evaluate the frequencies of individual unmet perceived needs.

A P value of < 0.05 was regarded as statistically significant, and all the reported P values were two-tailed. All statistical procedures were conducted using the SPSS 18.0J version software for Windows (SPSS Inc., 2009).

RESULTS

Patient Characteristics

A total of 619 patients (response rate, 93%), including 405 subjects from Study 1 (cancer patients attending the outpatient oncology unit) and 214 subjects from Study 2 (breast cancer patients attending the outpatient clinic), participated in the study. The sociodemographic and clinical characteristics of these 619 patients are shown in Table 1. Among

Table 1. Participant characteristics

Characteristics	All	%	≥70 years	%	<70 years	%
No.	619	100	113	18	506	82
Sex						
Female	536	87	86	76	450	89
Male	83	13	27	24	56	11
Marital status						
Married	467	75	68	60	399	79
Living with others						
Present	549	89	92	81	457	90
Education						
>12 years	227	37	18	16	209	41
Employment status						
Full-time/part-time	248	40	20	18	228	45
Cancer site						
Breast	480	78	65	58	415	82
Colorectal	55	9	18	16	37	7
Lung	19	3	8	7	11	2
Lymphoma	16	3	3	3	13	3
Stomach	14	2	7	6	7	1
Others	35	6	12	11	23	5
Clinical stage						
Recurrent/metastatic	193	31	53	47	140	28
Performance status[a]						
0	536	87	90	80	446	88
1	72	12	17	15	55	11
2	8	1	4	4	4	1
3	3	1	2	2	1	0.2
Current anti-cancer treatment[b]						
Chemotherapy	265	43	57	50	208	41
Radiation therapy	14	2	0	0	14	3

[a]Eastern Cooperative Oncology Group criteria.
[b]Multiple choice.

Table 2. Differences in needs, psychological distress and quality of life (QOL) between the elderly and the younger subjects

Variables	Mean (SD)		*P*	*P*[a]
	≥70 years	<70 years		
Needs				
Psychological	24.0 (10.3)	24.2 (10.5)	0.87	—
Health system and information	29.6 (11.5)	27.0 (11.8)	0.04	0.11
Physical and daily living	9.8 (4.3)	9.7 (4.4)	0.90	—
Patient care and support	11.2 (4.6)	10.6 (4.6)	0.21	—
Sexual	3.9 (2.0)	4.6 (2.4)	<0.01	<0.01
Total score	78.5 (26.7)	76.1 (28.3)	0.40	—
Psychological distress				
Anxiety	4.5 (3.2)	4.9 (3.7)	0.26	—
Depression	5.1 (3.5)	4.9 (3.7)	0.53	—
Total score	9.6 (6.0)	9.8 (6.9)	0.81	—
Quality of life				
Global Health Status	65.3 (20.8)	62.7 (23.4)	0.28	—
Physical functioning	78.5 (20.1)	85.8 (15.5)	<0.01	0.02
Role functioning	78.0 (26.4)	76.4 (26.1)	0.56	—
Emotional functioning	83.6 (16.6)	78.5 (19.8)	0.01	<0.01
Cognitive functioning	75.4 (18.4)	79.2 (19.7)	0.06	—
Social functioning	84.5 (20.1)	79.7 (23.9)	0.03	<0.01
Fatigue	34.6 (22.5)	32.9 (22.9)	0.48	—
Nausea and vomiting	5.6 (12.3)	8.6 (18.1)	0.03	<0.01
Pain	16.8 (22.0)	20.2 (21.3)	0.13	—
Dyspnea	19.2 (22.6)	15.9 (21.7)	0.16	—
Insomnia	19.8 (24.7)	22.3 (25.1)	0.34	—
Appetite loss	18.3 (26.0)	15.9 (25.3)	0.36	—
Constipation	21.5 (25.9)	20.6 (25.1)	0.73	—
Diarrhea	11.5 (21.7)	9.9 (19.5)	0.45	—
Financial difficulties	13.9 (22.1)	27.4 (31.7)	<0.01	<0.01

[a]Adjusted for sex, cancer site, cancer stage and performance status if a significant difference was observed using a univariate analysis.

them, 113 subjects (18%) were more than 70 years old, of whom approximately two-thirds and one-half were married and had recurrent/metastatic cancer, respectively. The most common cancer site was the breast in both groups. The background characteristics of the two age-specific subject groups were similar, as shown in Table 1.

Age-specific Differences in Supportive Care Needs, Psychological Distress and QOL

Findings with regard to age-specific differences in supportive care needs, psychological distress and QOL are shown in Table 2. Regarding supportive care needs, the elderly subject group showed fewer sexual needs, but no significant age-specific differences were observed among the other need domains. Concerning psychological distress, both the age groups experienced similar incidences of anxiety and depression. Although the global health status was similar in the two age groups, several significant age-specific differences in the QOL domains were observed. The elderly subjects had a lower physical functioning but they had better emotional functioning, better social functioning, less nausea/vomiting and fewer financial difficulties.

Frequency of Unmet Needs of the Elderly

The most common unmet need (rated three or more on the 5-point Likert scale) is shown in Table 3. 'Fears of spreading