

Review Article

Practical management of older adults with cancer: geriatric oncology in Japan

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Abstract

Japan has the highest proportion of older adults globally, and the average life expectancy of the Japanese population has increased in recent decades. Given that the incidence of cancer increases with age, it is a major health concern for older adults. However, geriatric oncology is a relatively new field and collaboration between oncologists and geriatricians in Japan is limited. Hence, oncologists and other healthcare professionals engaged in cancer care have not been able to adequately understand geriatric care, and information and experience are insufficient for this specific population. Thus, they may struggle with the assessment and management of older adults with cancer. Recently, several Japanese academic societies for cancer have developed practical guidelines and research policy with regard to geriatric research in older adults with cancer, in addition to organizing symposia and workshops focusing especially on geriatric oncology. Furthermore, because the Japan Geriatrics Society established a discipline committee on cancer, close collaboration between oncologists and geriatricians has grown steadily. Geriatric oncology is currently recognized as an important field of cancer care in Japan. The integration of oncology and geriatric care is anticipated in the near future. However, understanding the aspects of geriatric care and meanings of technical jargons used in geriatric oncology is difficult. Accordingly, this article provides an overview of the current knowledge and recent advancements in geriatric oncology. In addition, it outlines the current status and problems of geriatric oncology in Japan.

Key words: geriatric oncology, older adult, frailty, geriatric assessment, evidence-based medicine

Introduction

Japan has the highest proportion of older adults worldwide (1, 2). In 2021, 28.8% of the total population in Japan was aged >65 years and 14.9% were aged >75 years (3,4). The average life expectancy of the Japanese population has increased in recent decades; it is nearly 87.7 years for women and 81.6 years for men. By 2065, every 1 in 2.6 people will be aged ≥ 65 years and every 1 in 3.9 people will be aged ≥ 75 years in Japan (5). Given that the incidence of cancer increases with age, >70% of new cancer cases are reported in patients aged ≥ 65 years in Japan (6, 7). Cancer is the leading cause of death in Japan, followed by heart disease and pneumonia (8). Thus, cancer is a major health concern for older adults in Japan.

To the best of our knowledge, no standardized assessment and management approaches have been established for older adults

with cancer. Healthcare providers frequently face several challenges because of various reasons. First, there has been little collaboration between oncologists and geriatricians in Japan; oncologists and other healthcare professionals engaged in cancer care are not sufficiently knowledgeable or experienced in geriatric care for this specific population (9). Second, reliable evidence to support therapeutic decision-making in this population is limited, because older adults with cancer are generally underrepresented in clinical trials, particularly those with comorbidities and those who use concomitant medications (10). Finally, the rapid discovery and development of new approaches in medicine have resulted in ambiguities among oncologists and other healthcare professionals engaged in cancer care. Traditional therapies such as treatment with cytotoxic drugs may be less effective and associated with a greater toxicity in older adults with cancer.

However, some novel agents such as molecularly targeted or immunomodulatory agents are more effective and better tolerated in comparison with traditional therapies, even among vulnerable older adults with cancer (11,12,13). Hence, oncologists and other healthcare professionals engaged in cancer care may struggle with the management of older adults with cancer. Hence, establishing a specialized field for older adults is warranted.

Geriatric oncology is a relatively new field that focuses on the assessment and management of older adults with cancer; this field has expanded over the past two decades (14). The American Society of Clinical Oncology (ASCO) (15) and International Society of Geriatric Oncology (SIOG) (16) have been the pioneers in the field of geriatric oncology. These organizations have formulated several guidelines on geriatric oncology to assist healthcare professionals in understanding the assessment and management of older adults with cancer. Although Japan had been behind in the field of geriatric oncology, several Japanese academic societies for cancer-related research and development, such as the Japanese Society of Medical Oncology (JSMO) (17), Japanese Society of Clinical Oncology (JSCO) (18) and Japan Clinical Oncology Group (JCOG) (19), have recently developed practical guidelines and research policy with regard to geriatric research in older adults with cancer, in addition to organizing symposia and workshops focusing especially on geriatric oncology (20). Geriatric oncology has thus been recognized as a key field of cancer care in Japan. However, understanding the aspects of geriatric care and comprehending the meaning of the jargon used in geriatric oncology remain challenging. Therefore, this article provides an overview of the current knowledge and recent advances in geriatric oncology; moreover, it outlines the current status and problems of geriatric oncology in Japan.

Definition of older adults

There are no concrete definitions of ‘older adults.’ A chronological definition is commonly used, but to the best of our knowledge, there is no universally accepted cutoff age for identifying patients as ‘older adults.’ However, in many countries including Japan, individuals aged >65 years are typically referred to as ‘older adults’ (2,21). The use of chronological age is a simple way to describe senior citizens, particularly at regulatory institutions. However, the existing medical or biological evidence to support this definition remains unclear. Chronological age alone fails to address the heterogeneity in the physiological and functional statuses of older adults (22,23). Thus, factors other than chronological age are needed to clarify this heterogeneity in older adults with cancer.

Frailty is a state of increased vulnerability that increases the risk of adverse health-related outcomes following a stressor event (24,25,26). Although there is no particular definition for frailty (27,28,29,30), previous studies have stated that it is an extreme consequence of the normal aging process; it is a multidimensional state with both physical and psychosocial factors, as well as a dynamic state; i.e. it may be reversed or attenuated by interventions focusing on its underlying causes (31,25). The concept of frailty is being increasingly recognized as a crucial healthcare issue (32,33,34) given its association with increased risks of mortality, hospitalization, falls and admission to long-term care. Frailty may be reversed, i.e. individuals can dynamically transition between severity states through interventions focusing on the underlying causes and identifying their presence of such underlying causes of frailty, such as nutritional deficiency, poor mobility, incontinence and delirium; this may help

oncologists and other healthcare professionals engaged in cancer care personalize treatment plans for older adults with cancer (35).

Although frailty is a popular concept that can appropriately describe the heterogeneity in older adults, the comprehension of this concept differs between oncologists and geriatricians (Table 1) (36,37). Geriatricians typically use the term ‘frailty’ to describe a dynamic state of increased vulnerability that increases the risk of adverse health-related outcomes after a stressor and is associated with a higher likelihood of functional decline, disability, hospitalization and mortality. Conversely, geriatric oncologists typically use the term to describe an older adult who is generally unfit to receive cancer treatment and is best suited for supportive care or palliative treatment (38). This inconsistency has led to ambiguities among geriatricians and oncologists as well as other healthcare professionals engaged in cancer care. To the best of our knowledge, there is no robust definition of ‘older adults’ or ‘frailty’ in geriatric oncology, and the meaning of these terms can change depending on the context; thus, the terms must not be used interchangeably and only as per the context.

Assessment of older adults with cancer

Assessing the health status of older adults with cancer is important to support therapeutic decision-making for this population. Chronological age and performance status (PS) such as the Eastern Cooperative Oncology Group or Karnofsky performance status, cannot address the heterogeneity in older adults with cancer; thus, they are not good indicators of their physiological and functional statuses (39,40).

Comprehensive geriatric assessment and geriatric assessment

The term ‘comprehensive geriatric assessment (CGA)’ is commonly used in the field of geriatrics and has been defined as a multidimensional and interdisciplinary, diagnostic process to identify the care needs of older adults with vulnerability, plan their care and improve treatment outcomes (41,42,43). The key domains of CGA include physical health (i.e. comorbidities, medication use and nutritional status), functional status (i.e. basic and instrumental activities of daily living), psychological status (i.e. cognitive and emotional status) and socioeconomic factors (i.e. living situation and financial resources) (37). Fundamentally, CGA has six components: (1) data gathering, (2) discussion among the team, (3) development of a treatment plan, (4) implementation of the treatment plan, (5) monitoring treatment response and (6) revising the treatment plan, if needed. All these components indicate that CGA is not only a diagnostic process, but also aids the development and implementation of a treatment plan (44). For instance, after evaluating the key domains, the patients’ preferences and treatment goals should be discussed, for the care plan to reflect these crucial aspects of care (45). In addition, tailored interventions that address the patient’s vulnerability should be subsequently recommended, such as nutritional supplements or home nursing to help with medications (46,47,42). Monitoring and replanning are also essential (48).

The term ‘geriatric assessment (GA)’ is specifically used in the field of geriatric oncology. Most clinical studies on CGA in the field of oncology have focused on gathering data but not on providing tailored care based on CGA findings. Because of this, the SIOG recommends using the term ‘GA’ rather than ‘CGA’ (49). Thus, GA is generally recognized as a diagnostic process for evaluating the physical health, functional status, psychological status and socioeconomic

Table 1. Definitions of various terms used by geriatric oncologists and geriatricians

Term	Geriatric oncology	Geriatrics
Frailty	Commonly used: an older individual who is generally unfit for cancer treatment and should receive best-suited supportive care or palliative treatment	Commonly used: A state of increased vulnerability, including an extreme consequence of the normal aging process; it is a multidimensional state with physical and psychosocial factors as well as a dynamic state; i.e. it may be reversed
CGA	Commonly used: often confused with GA or several domains of GA	Commonly used: A multidimensional diagnostic process to identify the care needs older adults with vulnerability, plan their care, and improve their outcomes
GA	Commonly used: diagnostic process that is sometimes not a systematic evaluation	Not used
GA and intervention (GA and management)	Commonly used: evaluation and development of a treatment plan based on GA	Not used
Geriatric screening (abbreviated as CGA, mini-CGA)	Commonly used: any short measure or series of measures designed to identify patients who would benefit from a CGA or several domains of GA	Rarely used: any short measure or series of measures designed to identify patients who would benefit from a CGA

CGA, comprehensive geriatric assessment; GA, geriatric assessment

factors for older adults with cancer (49,37) (Table 1). However, lack of clarity among geriatricians and oncologists may be attributable to the fact that GA is performed regardless of whether all or some of the aforementioned domains are evaluated. Identifying the domains evaluated is essential. Nevertheless, GA is considered to be valuable in oncology practice owing to its abilities to detect an impairment not identified in the routine history or physical examination, predict severe treatment-induced toxicity, and predict overall survival in various tumours and treatment settings (50). In addition, GA can guide decision-making via discussion among oncologists and other healthcare professionals engaged in cancer care (51). Thus, several academic societies such as the ASCO, SIOG, European Society for Medical Oncology (ESMO) (52), Cancer and Aging Research Group (CARG) (53) and National Comprehensive Cancer Network (54) have recommended GA for use in clinical practice and research.

As mentioned previously, CGA is performed for both the evaluation and implantation of interventions to improve the outcomes of older adults; conversely, GA is performed only for diagnostic purposes among older adults with cancer. Recently, several studies have reported that GA and interventions focused on the vulnerability of older adults may improve treatment outcomes, resulting in low chemotherapy-induced toxicity, low rate of postoperative complications, and improved functional status and quality of life (QOL) (38,51,55–57,58, 59). GA outcomes and required interventions can enable the development of integrated and individualized plans for the management of patients with cancer and identification of nononcologic concerns that are amenable to intervention (Table 1).

Geriatric screening

The term ‘geriatric screening’ is also used in the field of oncology. It refers to the use of one or more short screening tools to identify older adults with cancer who may benefit from CGA (60,61) (Table 1). Despite accumulating evidence suggesting the importance of GA in geriatric oncology, the lack of time and resources prevents the routine implementation of GA in oncological practice (62). Geriatric screening may be less burdening in terms of time and resources than CGA or several domains of GA in older adults with cancer; however, GA cannot replace CGA. Geriatric screening helps identify patients at the highest risk of poor outcomes following cancer treatment and

devise better treatment strategies for them (63). Among the available geriatric screening tools, G8—the Triage Risk Screening Tool—and Vulnerable Elders Survey-13 are supported with the highest amount of evidence with regard to their use in clinical practice (64,65). To the best of our knowledge, no single tool or approach has been recommended for this specific population. However, any tool is encouraged as the initial step to aid clinicians in identifying the at-risk older adults with cancer before treatment initiation. The ASCO guidelines encourage clinicians to routinely incorporate geriatric measures to assess baseline function and other geriatric domains in older adults with cancer who are undergoing or considering chemotherapy (43).

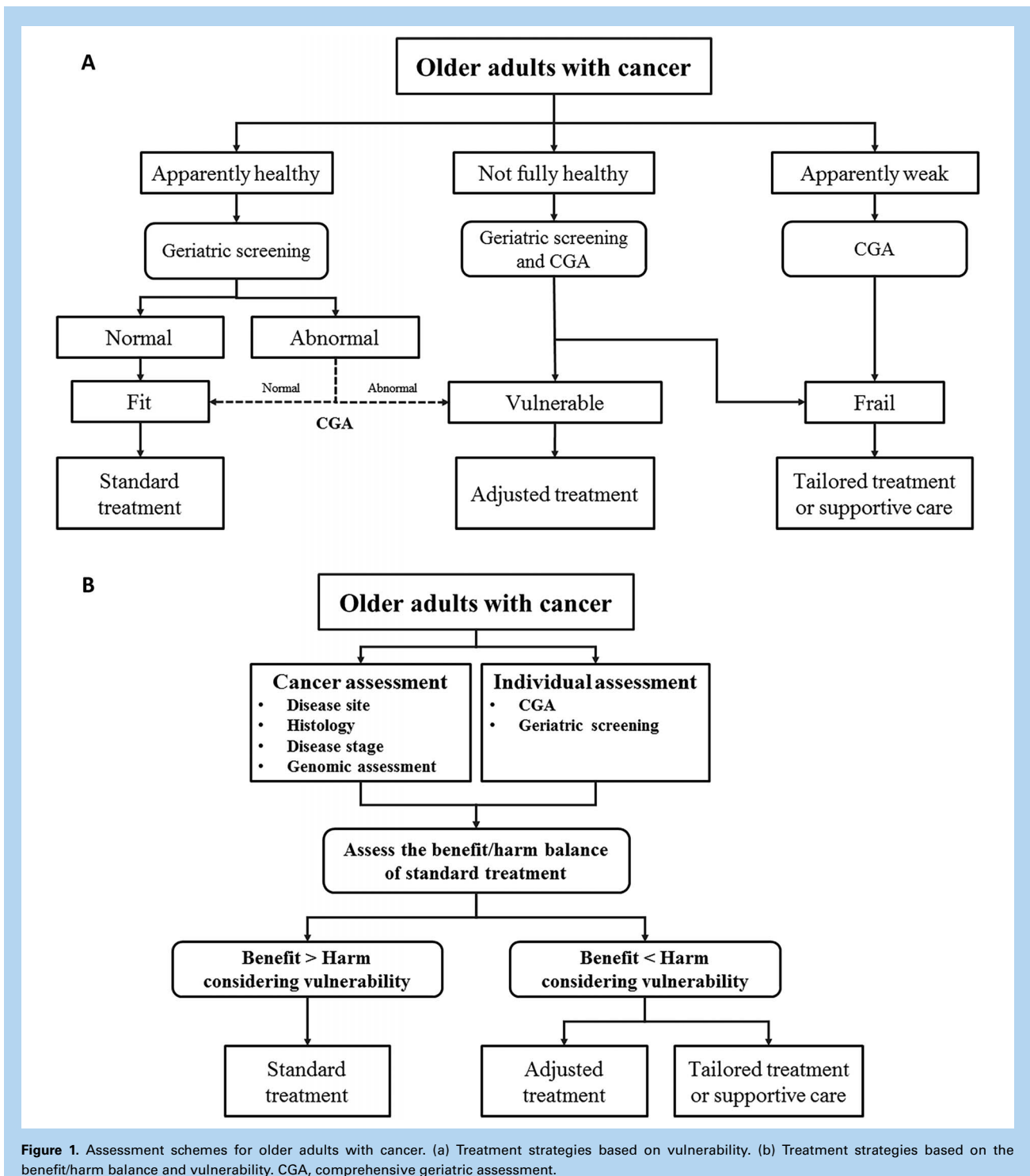
Risk prediction models for chemotherapy

Models predicting the risk of severe chemotherapy-induced toxicity may aid treatment decisions for older adults with cancer and can be made after considering the balance between the benefits and drawbacks of cancer treatment. The CARG toxicity score and Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score are widely used for predicting severe chemotherapy-induced toxicity in older adults with cancer (66–68,69). Both scores are recommended for assessing the risk of chemotherapy-induced toxicity.

Management of older adults with cancer

General approach for older adults with cancer

After assessment of the patient, a treatment strategy is selected. The most frequently used approach for developing treatment strategies in the field of geriatric oncology is categorizing older adults with cancer into three groups based on their vulnerability: fit, vulnerable, and frail (14,70) (Fig. 1a). Fit patients may benefit from standard cancer treatment similarly as younger patients, vulnerable patients may benefit from adjusted therapy, and frail patients may benefit from best-suited supportive care or palliative treatment. Given the simplicity of this approach and that it is easy to understand, it has gained popularity. However, it has resulted in ambiguity among geriatricians and oncologists for various reasons. First, the term ‘frail’ has distinctly different meanings in the fields of geriatrics and oncology (Table 1). Second, to the best of our knowledge there is



no standard method for categorizing older adults with cancer using the aforementioned classification (52). Although some classification strategies have been postulated based on GA or geriatric screening, these classifications were inconsistent and based only on clinical expertise and consensus (35). Third, this approach was developed >20 years ago; it does not reflect the advancements in medicine, such as the development of molecularly targeted or immunomodulatory agents with greater efficacy and less toxicity than cytotoxic drugs.

Another approach for developing treatment strategies is based on the consideration of both patients' vulnerability and the benefit/harm balance of cancer treatments (71) (Fig. 1b). This approach reflects the advancements in medicine, which means that treatment-induced toxicity can be changed based on the characteristics of each type of cancer treatment. In addition, this approach is flexible according to the condition of older adults with cancer. The fit, vulnerable, and frail classification is generally based on patients' vulnerability before

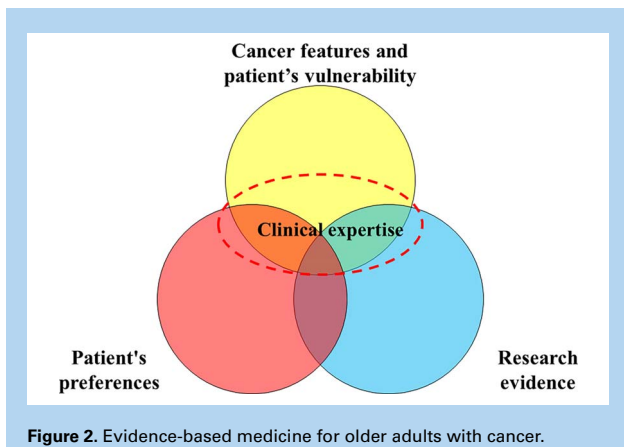


Figure 2. Evidence-based medicine for older adults with cancer.

receiving treatment, but the vulnerability of older adults is based on their condition throughout the treatment period. The approach of benefit/harm balance allows treatment intensity to be adjusted according to the patients' vulnerability at any point during the treatment course.

Practical approaches for older adults with cancer

In daily medical practice, making treatment decisions for older adults with cancer is complex because oncologists and other healthcare professionals engaged in cancer care must consider substantial information about not only cancer but also their patients, such as the patients' vulnerability, preferences and circumstances. This practical approach is an actual evidence-based medicine (EBM) approach (72,73). In the EBM approach, treatment decisions must consider the following: (1) patients' clinical and physical circumstances, (2) research evidence, (3) patients' preferences and (4) critical appraisal with clinical expertise. This approach is useful for routine medical practice of oncologists and other healthcare professionals engaged in cancer care (Fig. 2).

Patient's clinical and physical circumstances. The first step is to understand the clinical status of both the cancer and patients. Treatment decisions in older adults with cancer should be made considering the abovementioned clinical and physical circumstances, to determine available treatment options. The clinical status of cancers includes disease site, histology, disease stage, genomic assessment, disease prognosis and treatment-related benefits and drawbacks; conversely, patient status includes their vulnerabilities, such as physical health, functional status, psychological status and socioeconomic factors other than PS. CGA or GA may help clarify the heterogeneity in older adults with cancer. Moreover, the field of genomics is developing rapidly; understanding the molecular biology of cancer is becoming increasingly important, even in geriatric oncology. In the era of precision medicine for older adults with cancer, the concept of precision medicine should extend beyond the use of tumour-specific markers to incorporate the evaluation of the health status of older adults with cancer; the latter is assessed as part of routine GA and has been demonstrated to significantly affect patient outcomes (74).

Research evidence. The second step is to identify and critically appraise the best evidence. However, there are very few reliable

studies that support therapeutic decision-making for older adults with cancer, a population that is generally underrepresented in clinical trials, particularly those with severe comorbidities or functional dependencies (75,76,77). In addition, if the enrolled patients are healthier than the general population of older adults with cancer, the results of the trials may not be generalizable to real-world situations. Thus, it is important to carefully interpret the results of clinical trials for older adults with cancer (78,79).

Patient preferences. The third step is to consider the patients' preferences. Recently, patient preferences were incorporated into the first model of EBM; the importance of these preferences was emphasized in a revised version (73). It is important to determine the preferences of older adults with cancer, because intensive treatment may result in greater all-cause mortality in this population, although the practice of oncology often focuses on survival-related outcomes (80,81,82). Oncologists and other cancer healthcare professionals engaged in cancer care should ensure that the patient's own priorities are congruent with the provider's treatment goals in the case of advanced disease (83,84,85,86). A Japanese study demonstrated a discrepancy in the prioritization of healthcare outcomes between healthcare professionals and older patients and their families (87). Healthcare professionals considered 'improvement of QOL' to be the most important goal, but older patients and their families considered this less important than the 'effective treatment of illness' and 'improvement of physical function.' Thus, it is important to discuss treatment goals with patients and their families, making efforts to involve patients in treatment decisions and consider their preferences whenever possible.

Critical appraisal with clinical expertise. The last step is to integrate these considerations into clinical expertise. Critical appraisal with clinical expertise is needed to integrate patients' clinical and physical circumstances, research evidence and patients' preferences. Shared decision-making is important, particularly for older adults with cancer, to recommend the most appropriate treatment that is neither overtreatment nor undertreatment (88).

Practical approach for older adults with cancer and dementia

Cognitive impairment is highly prevalent among older adults, which hampers their decision-making capacity. In addition, brain metastases occur in approximately 25% of adults with cancer, with nearly 50% of such events impairing patients' understanding of medical decisions (89). Although discussions with patients regarding the treatment goals are important, this is sometimes difficult (90). However, this does not mean that treatment goals should be decided without any input from the patients (91). Patients with cognitive impairment do not always possess decision-making capacity, the Japanese government published a guideline for healthcare professionals to support decision-making when treating patients with cognitive impairment.

Advance care planning (ACP) enables individuals to define goals and preferences for future medical treatment and care, discuss these goals and preferences with their families and healthcare providers, and record and review them, if appropriate (92,93,94,95, 96). Furthermore, the Japanese government has published guidelines to select the most suitable and best decision support model and encouraged the promotion of ACP.

Current situation and future prospects of geriatric oncology in Japan

Geriatric oncology is an emerging field that is undergoing continuous development worldwide. In 2021, the SIOG updated their list of priorities for improving the care of older adults with cancer worldwide with the goal of incorporating various data into clinical practice (97). The present list includes four priority domains: (1) education, (2) clinical practice, (3) research and (4) strengthening collaborations and partnerships. It is important to evaluate geriatric oncology in Japan according to this list. With regard to education, several academic societies for cancer have provided educational materials and held conferences focused on geriatric oncology (17,18). Although the SIOG policy review recommends integrating geriatric oncology into educational programs in medical, nursing and allied health profession schools, in addition to educating the general public about the relevance of providing age-appropriate care for older adults with cancer, efforts have been insufficient in Japan. The next step is to develop an educational system to address these issues.

With regard to clinical practice, the JSMO and JSCO published a clinical practical guideline for older adults with cancer that presents recommended treatment options for older adults with several types of cancer (17). Given few clinical practice guidelines for older adults with cancer worldwide, these guidelines may be useful for Japanese clinicians. The SIOG policy review recommended establishing centres of excellence in geriatric oncology for providing clinical care. ESMO has launched multiple programs for cancer centres that provide highly advanced and integrated oncology and palliative care services. The next step is to integrate geriatrics with oncology and palliative care. The SIOG policy review further recommends developing and implementing models to provide optimal care for older adults with cancer. The Japanese government has attempted to establish 'a community-based integrated care system'; this system includes healthcare professionals who fully understand the physical and mental characteristics of older adults (98). This system is intended for older adults without cancer, but it may also help older adults with cancer and their families.

With regard to research, the JCOG has developed a geriatric research policy, establishing the standard endpoints and methodological schemes for geriatric research (10). Japanese researchers have published several important studies on older adults with cancer (99,100,101,102, 103,104,105). However, methodological schemes for geriatric research are rarely designed for older adults. Instead, the methodological schemes developed for younger patients are usually applied to older adults. For instance, the primary endpoints of clinical trials conducted in adults are usually survival-related outcomes such as overall survival, which may not reflect the true benefit for older adults with cancer (106,107,108). A more optimal method for older adults with cancer is warranted, for instance, to allow the evaluation of treatment outcomes among other aspects.

The SIOG policy review recommended strengthening collaborations and partnerships with other fields. Traditionally, geriatricians have treated older adults 'without' cancer and oncologists have treated older adults 'with' cancer, which resulted in poor collaboration between these professionals. Recently, as the Japan Geriatrics Society has established a discipline committee on cancer (109), close collaboration between oncologists and geriatricians may be possible in the near future.

Japan's demographics have substantially changed in recent years, with substantial reductions in fertility rates and considerable increase in life expectancy (5, 4). These factors have increased the cost of

maintaining the healthcare system and the burden on families (110). Japan's Healthcare Insurance System ensures that anyone can receive necessary medical treatment (111,112), and it has a system called 'high-cost medical expense benefit,' wherein patients are required to pay a fixed ceiling amount despite extremely high medical costs. Because the government allows all patients with universal health insurance to use expensive drugs, most clinicians prescribe such drugs to all patients, even the centenarians with vulnerabilities. The medical costs for treating individuals aged ≥ 75 years in the fiscal year 2019 comprised approximately 37% of the national medical care expenditure, reflecting a slight upward trend. The Japanese government must devise a new plan which maintains the current standard of healthcare facilities, while prolonging the life expectancy and quality of older adults with cancer.

Conclusions

The field of geriatric oncology is undoubtedly developing in Japan; however, several challenges remain with regard to the care of older adults with cancer. However, because the collaboration between oncologists and geriatricians has grown steadily, the integration of oncology and geriatric care is anticipated in the near future.

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Conflict of interest statement

None declared.

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