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GERIATRIC ONCOLOGY (AR MACKENZIE, SECTION EDITOR)

Predicting Life Expectancy for Older Adults with Cancer in Clinical Practice: Implications for Shared Decision-making

Haydee Cristina Verduzco-Aguirre[1] · Carolina Gomez-Moreno[2] · Yanin Chavarri-Guerra[1] · Enrique Soto-Perez-de-Celis[2]

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Abstract

Purpose of Review The calculation of noncancer-specific life expectancy can guide shared decision-making and avoid over- and undertreatment in older adults with cancer. Several factors determine life expectancy, including socio-demographic background, comorbidities, physical performance, and geriatric assessment variables. We present an overview of existing tools to estimate life expectancy, as well as practical examples of how to take into account the patient's noncancer-specific life expectancy when discussing screening decisions, initiation of treatment, and end-of-life care.

Recent Findings Life expectancy prognostication has been recently recommended by international societies as part of the initial assessment of all older adults with cancer. Additionally, online resources have been created in order to make life expectancy calculation tools accessible for clinicians.

Summary Understanding available methods to estimate life expectancy, as well as how to utilize them, is a fundamental part of geriatric oncology that should be integrated into everyday clinical practice.

Keywords Life expectancy · Mortality · Neoplasms · Older adults · Survival analysis · Geriatric assessment · Decision-making · Benefit risk assessment · Cancer screening · Adjuvant chemotherapy · End of life care · Geriatrics

Introduction

Life expectancy is defined as the average number of years a person can be expected to live, which can be calculated at birth or at any given age [1]. Before industrialization, global life expectancy was approximately 30 years, but this increased throughout the twentieth century. According to the Global Burden of Disease Study, between 1950 and 2017, global life expectancy increased from 48.1 to 70.5 years among men, and from 52.9 to 75.6 years among women [2•]. Not only has global life expectancy at birth increased, but also at older ages: a 60-year-old male can expect to live an additional 19.3 years, whereas a 60-year-old female has a remaining life expectancy of 22.6 years [2•]. This increase in life expectancy is a consequence of improvements in sanitation, housing, and healthcare (including vaccinations, antibiotics, and effective therapies for chronic diseases) [3]. However, large disparities exist between world regions, with life expectancy at birth in countries with a low socio-demographic index (SDI) of 64.4 years for men and 67.4 years for women compared with 78.4 and 83.7 years respectively in countries with high SDI [2•]. There is also a logarithmic correlation with gross domestic product (GDP), with people living in countries with higher GDP having a longer life expectancy [3].

The increase in life expectancy has led to a rise in the age of the global population, with a doubling in the number of people

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✉ Enrique Soto-Perez-de-Celis
enrique.sotop@incmnsz.mx

Haydee Cristina Verduzco-Aguirre
haydee_verduzco@hotmail.com

Carolina Gomez-Moreno
carogmz9@gmail.com

Yanin Chavarri-Guerra
yaninchg@gmail.com

[1] Department of Geriatrics, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Vasco de Quiroga 15, Seccion XVI, Tlalpan, 14080 Mexico City, CDMX, Mexico

[2] Department of Geriatrics, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Vasco de Quiroga 15, Seccion XVI, Tlalpan, 14080 Mexico City, CDMX, Mexico

aged ≥ 65 years over the last 30 years. This growth is expected to continue over the next decades, mainly due to an increase in the number of older adults living in less-developed countries [4]. This, together with the fact that cancer is mainly a disease of aging, makes it necessary to create strategies to better evaluate and treat the increasing number of older patients with cancer globally. However, this is complicated due to a great variability in the rate of functional decline and life expectancy associated with aging. Older adults with cancer of the same age may have differing overall health status, comorbidities, and disabilities, which may not only lead to a dissimilar tolerance to treatment, but also to wide variations in competing risks and life expectancy, independent of cancer-specific survival.

Estimating life expectancy is therefore an essential step in order to provide high-quality care for older adults with cancer, and it is currently recommended in geriatric oncology guidelines. However, physician estimates are usually inaccurate for predicting life expectancy among older adults [5], and personalized prediction tools remain underutilized. Furthermore, physicians tend to overestimate survival in patients with advanced cancer, which may result in overtreatment or inadequate end-of-life planning [5]. Therefore, older adults with limited life expectancy are at risk of receiving inadequate cancer screening or aggressive treatments without a positive impact on their quality of life (QoL) [6]. Conversely, foregoing potentially beneficial cancer screening or treatment in healthy older adults by failing to take into account life expectancy calculations can also derive in undertreatment, worse survival, and deterioration in QoL.

In this review, we discuss various methods which can be utilized to calculate the life expectancy and competing risks of mortality among older adults with cancer, focusing on their practical implications for cancer screening, diagnosis, and treatment.

Life-expectancy Calculation Methods

Actuarial Methods

The actuarial method, also known as life tables, consists in the estimation, for a pre-determined period of time, of the probability that the event of interest (mortality) does not occur until a certain amount of time has passed by. Life tables are used to measure mortality, survivorship, and life expectancy among a population at varying ages [7, 8]. However, since life tables are designed for entire populations, it is important not to confuse the calculation of life expectancy for a specific person with a prediction of their actuarial survival time [9, 10].

Among patients with cancer, the net survival of a cohort is sometimes estimated as the probability of survival derived solely from the cancer-specific risk of death. In other words, it is the proportion of patients who survive up to a given time after diagnosis, after eliminating the impact of other causes of death. However, among older adults, it is essential to separate cancer-specific mortality from competing mortality risks, also known as the "background mortality." Separating the "background mortality" from cancer-specific mortality is a potentially useful application of life tables, which should ideally be organized by calendar year, age, sex, race, and overall health status [10]. However, such high-quality life tables are generally not available, and most countries often have national or, at most, regional life tables.

In order to fill in this gap, international organizations such as the Cancer Survival Group (CSG) have constructed life tables to accurately reflect the background mortality for various populations [11•]. The CSG has developed up to 6000 life tables covering over 300 different populations, which are available online at http://csg.lshtm.ac.uk/life-tables. However, despite this and other efforts, this method is limited due to the difficulty of creating a life table for every demographic group worldwide [12–14]. Additionally, since life tables fail to take into account patient-specific data, there is a need for personalized tools aimed at providing a more detailed snapshot of an individual's life expectancy.

Personalized Life-expectancy Calculators

Since personal characteristics, function, and comorbidity have a profound effect on life expectancy, several tools designed to assess these on an individual basis have been developed and validated. Many of these tools can be found online on the ePrognosis website (www.eprognosis.org), which is recommended as a resource by the recently issued American Society of Clinical Oncology (ASCO) Geriatric Oncology Guidelines [15••], as well as by the International Society of Geriatric Oncology (SIOG) [16] and the National Comprehensive Cancer Network (NCCN) [17] (Table 1). ePrognosis is a repository of published prognostic indices intended as a rough guide to inform clinicians regarding possible mortality outcomes. Importantly, ePrognosis is not a definitive means of prognostication, and the tools should not be the only basis of medical decision-making. Most of the included indices are designed for older adults who do not have a dominant terminal illness, such as advanced dementia, cancer, or heart failure [18••]. The most common variables included in these indices are age, gender, comorbidities, body mass index (BMI), lifestyle factors, activities of daily living (ADL: bathing, dressing, toileting, transferring, self-feeding and continence), instrumental activities of daily living (IADL: housekeeping, finances, transportation, cooking, doing laundry, taking medications, using the telephone, and shopping), physical function, and self-reported health, many of which are obtained through a geriatric assessment (Fig. 1) [15••, 16]. Several of these indices include a diagnosis of cancer as an important

Table 1 Guideline recommendations for life expectancy calculation in older adults with cancer

American Society of Clinical Oncology (ASCO) [15••]	International Society for Geriatric Oncology (SIOG) [16]	National Comprehensive Cancer Network (NCCN) [17]
• Use validated tools to estimate noncancer life expectancy to determine if patients have adequate life expectancy beyond 4 years to expect benefits from specific cancer interventions such as chemotherapy • Use either the Schonberg or Lee index • Answer "no" when prompted to enter "presence of cancer" as a variable, in order to allow for estimation of noncancer life expectancy to consider competing risks of mortality	• Multidisciplinary guidelines recommend considering life expectancy for management decisions • Geriatric assessment is the recommended method of assessing life expectancy	• Consider overall life expectancy for all cancer-related decision-making • Use of life tables or ePrognosis calculators is recommended

variable and, in accordance with ASCO recommendations, answering "no" to that question is required to allow for the estimation of background mortality and noncancer-specific life expectancy [15••].

Palliative Prognostic Index

The Palliative Prognostic Index (PPI), which predicts survival among terminally ill patients with cancer, was developed and validated among 245 patients with incurable tumors who were unlikely to live for 6 months or more (mean age 66 years). The PPI includes performance status, oral intake, and the presence of three disease-related symptoms: edema, dyspnea at rest, and delirium. With two cut-off points (4 and 6 points), it predicts survival at > 6 and < 3 weeks with a sensitivity of 80%, a specificity of 77–85%, and an accuracy of 80% [19].

Gagne Index

The Gagne Index, which predicts all-cause 1-year mortality, was developed in a cohort of 120,679 community-dwelling Medicare patients from Pennsylvania aged ≥ 65 years with drug coverage through a pharmacy assistance program. The main objective was to develop and validate a single numerical comorbidity score for predicting short- and long-term mortality, combining conditions from the Charlson and Elixhauser

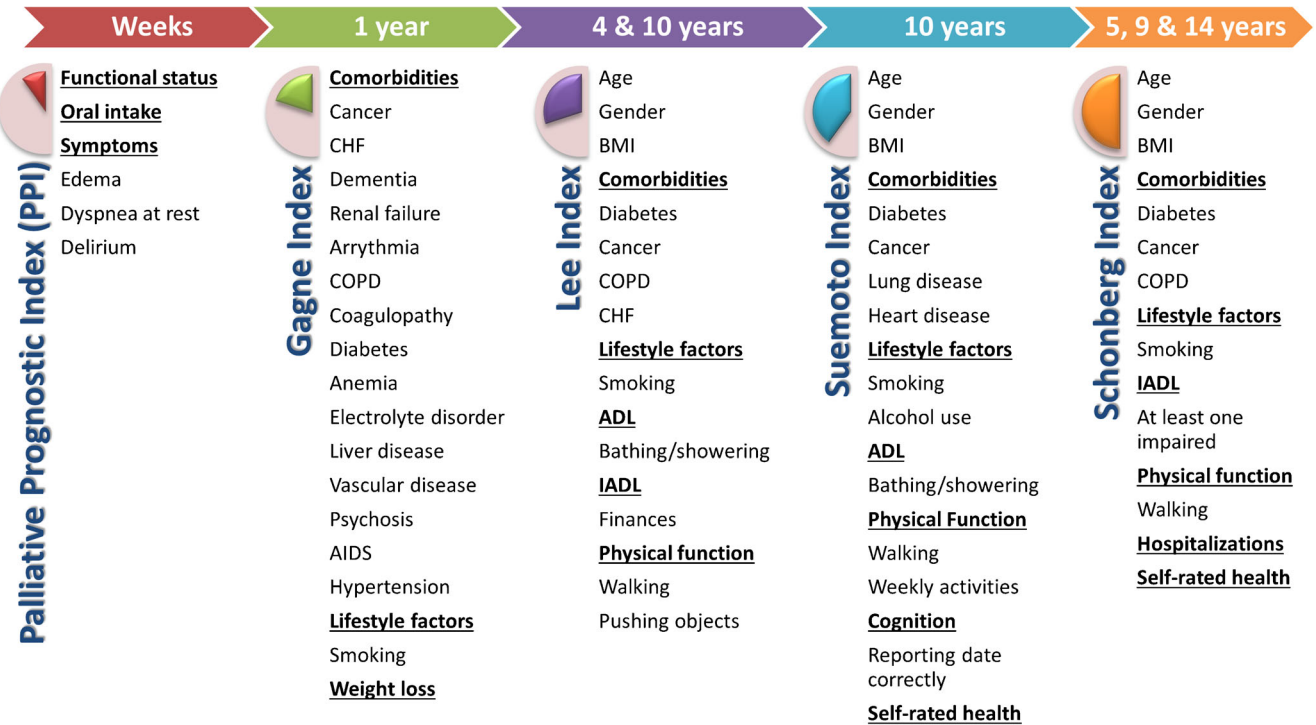

Fig. 1 Selected life expectancy estimation tools sorted by prognostication timeframe. Demographic, clinical, lifestyle, and functional factors included in each tool are mentioned. CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; AIDS, acquired immunodeficiency syndrome; BMI, body mass index; ADL, activities of daily living; IADL, instrumental activities of daily living [19–23, 24•, 25•]

measures. In an independent external validation study, the Gagne Index outperformed both the Charlson and Elixhauser indices in predicting both short- and long-term mortality [20].

Lee Index

The Lee index, which predicts for 4- and 10-year all-cause mortality, and is recommended by ASCO guidelines, was developed among 11,701 community-dwelling adults aged ≥ 50 years included in the Health Retirement Survey. Information regarding demographic characteristics, comorbidities, and various functional measures was collected, and patients were followed prospectively. At the end of the study, 12 independent predictors of mortality were identified and included in the index. The Lee index was subsequently validated among 8009 community-dwelling individuals and showed excellent discrimination, with a c-statistic of 0.82, meaning that the index is able to sort patients who died from patients who lived correctly 82% of the time [21].

Schonberg Index

The Schonberg index, which predicts for 5- and 9-year all-cause mortality and is also recommended by ASCO guidelines, was developed among 16,077 community-dwelling older adults included in the 1997–2000 National Health Interview [22]. After its development, the Schonberg index was internally and externally validated in a sample of 8038 older adults, showing a c-statistic of 0.75 [23]. The Schonberg index can also be utilized to predict 14-year all-cause mortality, with a c-statistic of 0.72 [24•].

Suemoto Index

Although the Lee and Schonberg indices are useful for predicting long-term life expectancy, both were developed and validated in the USA, and thus, there are doubts regarding their applicability in other countries. The Suemoto index is a 10-year all-cause mortality prediction model that was developed and validated using data from five global longitudinal studies of community-dwelling adults: the Survey on Health, Ageing and Retirement in Europe (SHARE); the Brazilian Sao Paulo Survey on Health, Well-being, and Aging (SABE); the Mexican Health and Aging Study (MHAS), the US Health and Retirement Study (HRS); and the English Longitudinal Study of Aging (ELSA). The total population included 35,367 participants (two thirds for the training dataset and one third for the testing dataset) with a mean age of 70 years. With a median of 8.6 years of follow-up, the model showed good discrimination in the testing dataset, with a c-statistic of 0.76 [25•].

Brief Geriatric Screening Tools

Several screening tools have been developed in order to identify which patients might benefit from a comprehensive geriatric assessment (CGA) [26]. One such tool, the G8, was developed in a multicenter prospective cohort of 1435 patients with cancer treated with first-line chemotherapy in France. The results of the tool were compared with those of a CGA, and the sensitivity and specificity of the tool for detecting deficits upon the performance of CGA were determined [26]. As a secondary analysis, the predictive value of an abnormal G8 (with a cut-off value of ≤ 14/17 points) for all-cause mortality at 1 year was also assessed. G8 was found to accurately predict a worse overall survival, with a hazard ratio (HR) of 2.72 among patients aged ≥ 70 years with a diagnosis of cancer (including colon, lung, neck, breast, prostate, and nonHodgkin's lymphoma) [26]. Importantly, the G8 items were strongly associated with common elements of the CGA such as functional status, nutritional status, depression, and cognition. Furthermore, the time to perform it is under 10 min and it can be easily administered by various healthcare team members, including nurses and physician assistants [16].

Physical Performance Measures

Evaluating the physical performance of an older adult is an essential part of the geriatric assessment, and various objective measures to assess it have been developed. Interestingly, some of those measures have been correlated with all-cause survival both in community-dwelling older adults and in patients with cancer. An advantage of using physical performance tools to calculate life expectancy is that these are easy to perform, and provide an objective result.

A pooled analysis of over 30,000 community-dwelling older adults from nine cohort studies with a median follow-up of 13.8 years evaluated the relationship between gait speed (measured in m/s), and survival [27]. Gait speed was associated with survival in all studies, with life expectancy increasing per each 0.1 m/s increase in gait speed, particularly among individuals aged ≥ 75 years. Interestingly, a prediction model based on age, sex, and gait speed had a similar accuracy to more complex models [27]. As an example, among women aged 75–84 years, 10-year survival was 73% for those with a gait speed of ≥ 1.0 to < 1.2 m/s, compared to 35% for those with a gait speed of < 0.4 m/s. Gait speed has also been shown to be predictive of survival in specific populations such as patients with brain metastases [28].

The Short Physical Performance Battery (SPPB) is a tool developed among 5000 older adults aged ≥ 71 years in order to assess lower extremity function, balance, gait, strength, and endurance [29]. A systematic review and meta-analysis of 17 studies and over 15,000 individuals found that an SPPB score

< 10 points was predictive of all-cause mortality, suggesting its usefulness as a surrogate endpoint for life expectancy [30•].

Life-expectancy Calculation in Clinical Practice

The calculation of life expectancy and competing causes of mortality is essential when providing care for older patients with chronic diseases such as cancer [15••]. It is important to consider that two older patients of the same age, and with the same diagnosis, may have completely different life expectancy outcomes when we factor in their comorbidities, lifestyle factors, and geriatric assessment domains (Table 2). In the following sections, we provide practical examples of the use of life expectancy calculation for decisions regarding cancer screening, administration of adjuvant therapy, and end-of-life care.

Cancer Screening

The most common malignant tumors in older adults (breast, prostate, lung, colorectal) are all susceptible to screening [31].

Table 2 Combined Lee-Schonberg index* calculation for two patients of the same chronological age with a diagnosis of breast cancer. In accordance with recommendations, the option "does your patient have cancer" is marked as "no" in order to calculate noncancer-related mortality risks [15••, 24•]

Item	Patient 1	Patient 2
Age	78	78
Gender	Female	Female
BMI	26	24
Self-rated health	Very good	Good
COPD	No	No
CHF	No	No
Diabetes	No	Yes
Smoking	Never smoked	Former smoker
Difficulty walking ¼ mile	No	No
Hospitalizations in past year	None	One
Help with any IADL†	No	Yes
Difficulty managing personal finances	No	No
Difficulty bathing/showering	No	No
Difficulty pushing/pulling large objects	No	Yes
5-year mortality risk	3–6%	37–41%
10-year mortality risk	9–12%	60–68%
14-year mortality risk	19–24%	81–83%

*Available online at https://eprognosis.ucsf.edu/leeschonberg.php

†Such as everyday household chores, doing necessary business, shopping, or getting around for other purposes

BMI, body mass index; *CHF*, chronic heart failure; *COPD*, chronic obstructive pulmonary disease; *IADL*, instrumental activities of daily living

However, most randomized controlled trials (RCT) of screening have included mainly younger individuals, and the benefit of these interventions in older adults is not completely known. Currently, various international guidelines suggest incorporating life expectancy into the decision to perform cancer screening [32, 33]. Obtaining a prediction of 5- to 10-year life expectancy is appropriate for screening decisions, since it has been estimated that screening has a time lag to benefit. For example, in order to prevent one cancer death per 1000 patients screened, it takes 10.7 years for screening mammography and 10.3 years for fecal occult blood testing to reach that magnitude of benefit [34]. Prostate cancer guidelines, for instance, recommend against screening in patients with a life expectancy < 10 years, since the study that showed a benefit of prostate-specific antigen (PSA) screening showed a cancer-specific mortality reduction only after 13 years of follow-up [35].

Screening: Clinical Vignette

Ms. P is a 75-year-old woman who lives in an apartment with her husband. She is overweight, has diabetes, and is a former smoker. However, her health issues do not cause any limitation on her activities of daily living, and she can walk several blocks and push large objects without help. She reports herself in excellent health and has not been hospitalized in the previous year. Her gait speed is of 1.1 m/s. During her appointment, she asks if she should have another mammography, since her last one was 3 years ago.

This patient has a Lee index of 5 points, which translates to a 5-year mortality risk of 6–8%, a 10-year mortality risk of 15–23%, and a calculated median life expectancy of 17.7–21.1 years [18••, 21]. Her Schonberg index is of six points, which translates into a 5-year risk of mortality of 10–12%, a 10-year risk of mortality of 26–37%, and a 14-year risk of mortality of 42–52% [18••, 24]. Therefore, it seems Ms. P has a long predicted life expectancy, and that she would perhaps benefit from continuing with breast cancer screening.

Ms. F is also 75 years old. She lives with her daughter's family, has diabetes and congestive heart failure, and is being evaluated for a major neurocognitive disorder. Her BMI is 23. She has never smoked. Due to her memory issues, she does not manage her finances or her medications and does not go out of her house by herself. She also has difficulty with pushing or pulling large objects and cannot walk more than two blocks without assistance. She was hospitalized for 2 days 6 months ago due to seasonal influenza. Her daughter points out that she always has her mammography around this time of the year.

For this patient, the Schonberg index translates into a 5-, 10-, and 14-year mortality risk of 47–52%, 74–76%, and 87–88% respectively, while the Lee index shows a 5-year risk of 44–59% and a 10-year risk of 83–91%, with a median life

expectancy of 3.8–5.1 years [18••, 21–23, 24•]. These calculations suggest that stopping screening should be discussed with Ms. F and her family. However, stopping cancer screening on a previously tested patient can sometimes be difficult, and older adults may not completely understand or believe the role of life expectancy in this decision, so this conversation should be approached carefully [36•]. Older adults might be more open to stopping screening within a trusting relationship with their physician, and support using their age and health status to individualize the decision to continue screening [36•].

Initiation of Adjuvant Chemotherapy

The use of chemotherapy carries a significant risk of adverse events, which may be higher in older adults, particularly those with multiple comorbidities or poor performance status. Because of this, the decision to administer chemotherapy in the adjuvant setting requires a thorough assessment of the risks and benefits of treatment, including the risk of recurrence or death due to the cancer, the risk of chemotherapy-related toxicity, the patient's preferences, and competing risks and life expectancy [15••, 37].

Initiation of Adjuvant Chemotherapy: Clinical Vignette

Mr. D is a 79-year-old man. He comes to the clinic after undergoing a left hemi-colectomy for colon cancer. The pathology report showed a stage IIIB (pT3, N1b, M0) tumor, without microsatellite instability. Three weeks after surgery, he feels well and is undertaking his routine activities without assistance. He is hoping to go back to work as a lawyer over the course of the next few weeks. His past medical history includes well-controlled hypertension and benign prostatic hyperplasia. He quit smoking 20 years ago and has a BMI of 25.2. His gait speed is 1.2 m/s, and his SPPB is normal (> 10 points). Mr. D states that he would like to receive the treatment that gives him the best chance to survive longer, since he would like to see his granddaughter, who just entered law school, become a lawyer like him.

Mr. D seems to be relatively healthy. According to the Lee and Schonberg indices, his risk of mortality, without taking his cancer into account, is about 9–15% at 5 years and 34–43% at 10 years [18••, 21–23, 24•]. Considering a 5-year survival from stage III colon cancer of about 60–70%, this most likely represents his highest risk for mortality [38]. The Hurria toxicity tool (available online at www.mycarg.org/Chemo_Toxicity_Calculator) which utilizes clinical, demographic, and geriatric assessment variables to predict the risk of grade 3–5 chemotherapy-related toxicity among older adults shows that his risk of grade 3–5 toxicity is of 59% with poly-chemotherapy, and of 44% with monotherapy [39]. Although older adults with colon cancer seem to have a lower benefit from combination chemotherapy in the adjuvant setting, few patients aged ≥ 70 years were included in the pivotal RCT, and almost none were aged ≥ 75 years [40, 41]. That being said, retrospective evidence shows that older adults with stage III colon cancer may obtain a survival benefit from combination chemotherapy, which may be partially dependent on life expectancy [42, 43].

The calculated risk of clinically significant toxicity for Mr. D is similar to that experienced by younger patients included in RCT evaluating combination regimens [44], so Mr. D would probably be able to tolerate treatment similarly to a younger adult. Furthermore, his noncancer-related life expectancy shows that he might derive benefit from chemotherapy. In this case, all treatment alternatives should be discussed and, if the patient gives a higher value to avoiding toxicity, administering single-drug chemotherapy or a shorter duration of combination therapy [45] would be acceptable options.

End-of-Life Care

Physician assessment of prognosis in patients with incurable disease is not completely accurate, with a tendency to overestimate survival. In a meta-analysis of eight studies, the clinical prediction of survival was accurate to within 4 weeks in only 61% of cases [46]. An accurate assessment of life expectancy utilizing validated tools can be valuable for patients undergoing palliative care, since it can lead to the start of end-of-life discussions, avoid potentially harmful treatments, and provide information that can guide palliative interventions such as radiotherapy.

End-of-Life Care: Clinical Vignette

Mr. K is a 74-year-old man with metastatic pancreatic cancer. He underwent first-line chemotherapy with gemcitabine/nab-paclitaxel, but his 6-month assessment showed progressive disease, with new bone metastases in his right femur and pelvis. Despite treatment, he lost 15 pounds in the last 3 months—he reports that he has almost no appetite and spends most of the day lying down in bed. Physical examination shows ascites and lower extremity edema. He asks directly, "How long do I have left, doctor?"

Mr. K has a PPI of 4.5 points, translating into an estimated survival of between 3 and 6 weeks [19], which means that the benefit of administering further cytotoxic treatments appears very limited. An accurate prediction of prognosis in patients with terminal illnesses permits initiating end-of-life discussions and stopping potentially harmful treatments. In adults with advanced cancer, end-of-life discussions have been

associated with lower rates of aggressive care and earlier hospice enrollment. More aggressive medical care, on the other hand, is associated with worse patient QoL and with a higher risk of depression in bereaved caregivers [47].

During end-of-life discussions, Mr. K mentions some pain in his right leg, which seems to be caused by metastases to his femur. He is referred for a radiotherapy assessment, and a single dose schedule of radiotherapy is recommended after calculating his number of risk factors model (NRF). The NRF is a tool utilized to predict life expectancy which was developed in patients undergoing palliative care referred to a radiation oncology department (median age 68 years). It consists of three risk factors: the primary cancer site (breast vs nonbreast), site of metastases (bone-only vs other sites), and Karnofsky performance score (>60 vs ≤ 60). Median survival in patients with none or one risk factor was 60 weeks, in those with two risk factors 26 weeks, and in those with three risk factors 9 weeks. This score can be useful when recommending a palliative radiation schedule, since it can help tailor treatment and minimize the burden and adverse effects of radiotherapy [48].

Conclusions

The calculation of life expectancy has fundamental implications for the practice of geriatric oncology, and should be a routine part of the assessment of every older adult with cancer. Understanding the relevant factors that determine the life expectancy of an older patient, including socio-demographic data, comorbidities, physical performance, and geriatric assessment variables, as well as how to use existing prognostication tools, is a necessary skill for all oncologists. Considering the patient's noncancer-specific life expectancy when discussing screening cessation, initiation of treatment, and end-of-life care, among others, may lead to better shared decision-making and to improved outcomes for older adults.

Compliance with Ethical Standards

Conflict of Interest Haydee Cristina Verduzco-Aguirre has received travel support from Bristol-Myers Squibb unrelated to the present work.

Carolina Gomez-Moreno declares that she has no conflict of interest.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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