Perspective

How we use noncancer-specific survival prediction in Geriatric Oncology: A Young International Society of Geriatric Oncology and Nursing & Allied Health Interest Group initiative.

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Keywords: Life expectancy; Survival; Older adults; Cancer; Gait speed; Clinical decision-making

Introduction

An important aspect of the assessment of the health status of an older adult with cancer is estimating noncancer-specific survival, since this can be used to weigh the potential benefits and risks of treatment against the patient's all-cause mortality. Geriatric oncology guidelines issued by the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) recommend the use of validated tools to predict noncancer-specific survival, also labeled "life expectancy calculators", in all patients aged 65 years and older before starting oncological treatment.[1,2] In addition, the estimation of noncancer-specific survival can also be integrated into the decision-making process for other medical interventions relevant for geriatric oncology, such as the decision of stopping screening in an older individual, or for determining the appropriateness of interventions related to the management of comorbidities in older adults with a cancer diagnosis. In this brief report, we outline some of the existing resources for estimating noncancer-specific survival and provide practical information as to how to use them in clinical practice.

How is life expectancy calculated?

Life expectancy calculation requires knowing the survival function in the population of interest that is, usually, obtained from life tables. If the population of interest is the general population, life tables are generally constructed nationally and stratified at on age and sex, although they can also be stratified on race, ethnicity, or socio-economic deprivation, since mortality varies depending on these factors. Life expectancy can be calculated at any age and represents the hypothetical average number of years people can expect to live if age-specific death rates remain constant throughout their lives. The United Nations, for example, provides life tables for 255 geographic areas, which can be accessed online at https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/healthy-life-expectancy-(hale).

To estimate the life expectancy of patients with cancer, tumor-specific life tables stratified on age, sex, race/ethnicity, and socioeconomic deprivation level would be needed. In addition, since survival also depends on stage at diagnosis, life tables should be stratified by stage and possibly by other relevant aspects like comorbidities or lifestyle factors, such as smoking. Furthermore, patients would need to be followed for extended periods of time, which is often not possible. To overcome this barrier, patient and disease-related information obtained from population-based cancer registries could be linked to other administrative databases (including information regarding socioeconomic status, disability, or overall health status) to obtain necessary data to create specific life tables. However, due to the limited availability of data on the overall health status of patients within population-based registries this is possible only in a limited number of high-income countries and even then, long-term survival data is usually missing. An example of this type of life tables are those issued by the United States Social Security Administration, which adjust survival by overall health percentiles, and which are included in the NCCN geriatric oncology guidelines.[2]

While estimating life expectancy using life tables can be useful for the implementation of health policies or for epidemiological purposes, it does not allow for the prediction of life expectancy at the individual level, where other factors like limiting comorbidities come into play. However, there are tools which allow clinicians to predict the noncancer-specific survival of individuals presenting with certain demographic, social, and clinical characteristics.

When should we predict noncancer-specific survival, and what for?

Predicting noncancer-specific survival represents a useful piece of information for decision-making in geriatric oncology. Imagine you are evaluating an 80-year-old patient admitted to the hospital for a urinary tract infection that resolved with antibiotic treatment. At discharge, one of the residents recommends scheduling a screening colonoscopy, while another points out there is no need for colonoscopy because several guidelines recommend offering colorectal cancer

screening in octogenarians at the utmost on an individualized basis. While you acknowledge that guidelines suggest stopping screening at age 75 routinely, you have treated this patient for quite some time, and know that his overall health is excellent, and that he remains independent and is active as a senior consultant in a local firm. Furthermore, you believe that, if cancer was detected through screening, the patient would be fit enough to undergo treatment with acceptable outcomes. On the other hand, you are also aware of the risk an unnecessary intervention could entail.

This situation is common and illustrates one of the many uses of predicting survival to inform clinical decision making across the cancer care continuum, starting with early detection and diagnosis, and moving all the way up to end-of-life care. When balancing the benefits and harms of any intervention, such as stopping screening or administering cancer therapy, determining whether the patient's probability of survival is longer than the "lag time" for a particular outcome is essential. Lag time refers to the period between any given intervention and the moment when you expect to see its benefits reflected in the patient.[3] The average lag time for obtaining benefit from a diagnostic or therapeutic intervention (as well as the magnitude of that benefit) should be balanced both against the potential harms of the intervention and the patient's predicted noncancer-specific mortality risk: interventions providing benefits in a short lag time may still be appropriate in patients with limited survival, while those with longer lag times may not be appropriate in such settings, since death may occur before their benefits are noticeable.

Importantly, although the patient's preferences should be prioritized over any calculations, predicting noncancer-specific survival could help provide a clearer perspective regarding the benefits of interventions and lead to more accurate recommendations.

Using personalized geriatric assessment-based noncancer-specific survival calculators

Several personalized noncancer-specific survival calculators exist, such as those collected on the *Eprognosis* website (**www.eprognosis.org**). These calculators, some of which are shown in **Table 1**, include sociodemographic characteristics, comorbidities, laboratory values, and various features which can be obtained through a geriatric assessment, such as activities of daily living, instrumental activities of daily living, and other functional parameters. These models predict the risk of death occurring within a specified period (six months, a year, five years, etc.) or the probability of surviving beyond a certain number of years. The result is given as a percentage: XX% of patients survive beyond five years, or XX% of patients with certain characteristics die within the first year. **Figure 1** shows an example of the use of personalized geriatric assessment-based survival calculators in clinical practice.

Using other methods to predict noncancer-specific survival

The use of functional prognostic factors to predict survival represents an area of ongoing research, since these could potentially provide an objective, reproducible, and practical measure of the global health and fitness of patients across a wide range of diseases. Although many functional measurements have been found to be prognostic of survival, it is important to emphasize that their use has not been compared with the utilization of more complex models in a clinical setting.

An example of a performance-based measure that can predict survival in older adults is gait speed. A pooled analysis of nine cohort studies showed that gait speed was closely associated with survival, and that increments in gait speed were associated with better survival among community-dwelling older adults.[4] In addition, gait speed has been shown to be prognostic of survival among patients with solid and hematologic neoplasms, as well as older cancer survivors.[5-7] Measuring gait speed at usual pace over four meters is relatively easy and feasible in everyday clinical practice, as it can be performed in any corridor in an outpatient or inpatient setting. Patients should be instructed to walk at their normal pace and to use their assistive

device if needed. The measurement gait speed requires patients to have a “rolling start” of one to two meters before the actual start of the four-meter “testing zone”. The timer should be started with the first step within the testing zone and stopped with the first step after it. The total time to walk the four-meter distance should be divided by four to obtain gait speed in meters per second.[8]

Another prognostic measurement which can help predict survival is grip strength. At least three different meta-analyses have found a relationship between weak grip strength and all-cause mortality in community-dwelling older adults, and it also has been shown to be prognostic of mortality in older patients with hematological malignancies.[6,9] In contrast with gait speed, the measuring of grip strength requires using specialized equipment, most commonly a Jamar dynamometer. The technique for grip strength measuring differs between studies, but an accepted protocol is to measure it with the patient sitting down with shoulders neutrally rotated, elbow flexed at 90 degrees, forearm in neutral position and wrist between 0 and 30 degrees of dorsiflexion.[10] Additional indications include conducting up to three trials per hand, with maximal scores utilized.[10]

Using performance-based methods for predicting noncancer-specific survival may not be ideal in all cases, since evaluating physical performance alone without undertaking a geriatric assessment is too general and fails to provide information regarding other outcomes. Furthermore, life events such as a recent surgery might have an acute negative effect on performance-based methods, heavily “penalizing” patient performance and survival and perhaps limiting the options offered based on these results. While data regarding the use of these direct measures of physical function in cancer care is novel, their integration into routine clinical care could improve patient assessment, prognostication, and individualization of care.[6] However, more research is needed before they can be fully integrated into clinical decision-making, and

perhaps a combination of functional assessments and more complex models could represent a future option for better predicting noncancer-specific survival in older patients with cancer.

Conclusions

As illustrated by the clinical vignette presented above, utilizing data obtained from the geriatric assessment to predict the noncancer-specific survival of an older adult facing a cancer diagnosis represents an important piece of information for decision-making, particularly when interventions with small additive gains are considered. Predicting noncancer-specific survival is easy but not without limitations, it is recommended by international geriatric oncology guidelines,[1,2] and can be seamlessly integrated into everyday clinical practice using freely available online calculators or practical physical performance assessments.

Acknowledgements: We thank Kah Poh Loh, MBBCh BAO, MS from the Young SIOG Governance and Beatriz Korc-Grodzicki, MD, PhD from the SIOG Publication Committee for their thoughtful reviews and insightful comments on this paper.

Conflicts of interest: The authors have no conflicts of interest to disclose.

Author contributions:

Conception and Design: all authors

Data Collection: all authors

Analysis and Interpretation of Data: all authors

Manuscript Writing: all authors

Approval of Final Article: all authors

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Table 1. Common indices, included items, advantages, and disadvantages					
Included Items	**Gagne Index[11]**	**Lee Index[12]**	**Schonberg Index[13]**	**Suemoto Index[14]**	**Walter Index[15]**
Geographic Location	United States	United States	United States	Outside the United States	Not available
Place of Residence	Living at home	Living at home	Living at home	Living at home	Hospitalized
General Patient Characteristics:					
Gender		x	x	x	x
Body Mass Index		x	x	x	
Subjective rating of patient's health			x		
Hospitalizations in past year			*x*		
Alcohol use	X			x	
Smoking status		x	x	x	
Activities of Daily Living					
Ability to bathe		x		x	
Ability for dressing					x*
Ability for transferring					x*
Ability for toileting					x*
Ability for eating unassisted					x*
Physical activity ≥1x/week				x	
Instrumental Activities of Daily Living					
Ability to do shopping			x		
Ability for handling money/finances		x	x		
Physical function					
Ability to pull large objects		x			
Self-reported health				x	
Ability to walk 1/4 mile/several blocks		x	x	x	
Cognition					

Correct reporting of current date				x	
Comorbidities					
Chronic lung disease	X	x	x	x	x
History of Cancer	x	x	x	x	x
Congestive heart failure	x	x		x	x
Diabetes	X	x	x	x	
Dementia	X				
Weight loss	X				
Hemiplegia	X				
Cardiac arrhythmias	X				
Coagulopathies	X				
Deficiency anemia	X				
Liver disease	X				
Peripheral vascular disorder	X				
Psychosis	X				
Pulmonary circulation disorder	X				
HIV/AIDS	X				
Hypertension	X				
Laboratory values					
Creatinine					x
Albumin	X				x
Fluid and electrolyte disorders	X				
Outputs					
Timeframe	1 year	5- and 10-years	5-, 10-, 14-years	10 years	1 year
Population	Community-dwelling adults aged ≥65	Community dwelling adults aged ≥50	Community-dwelling adults aged ≥65	Community dwelling adults aged ≥65	Hospitalized adults aged ≥70
Advantages	Broad spectrum of comorbidities assessed	5-year mortality is useful as comparator for many cancer entities	5-year mortality is useful as comparator for many cancer entities	Validated outside the United States (Mexico, Brazil, Europe)	Useful in hospitalized patients

Disadvantages	No activities of daily living components included	Very limited selection of comorbidities without grading of severity included	Very limited selection of comorbidities without grading of severity included	No 5-year mortality estimated	No 5-year mortality estimated

Figure Captions

Figure 1: Mrs. S. was recently diagnosed with stage III endometrial cancer. She underwent surgical resection. Now, adjuvant chemotherapy +/- radiotherapy is considered. According to the PORTEC-3 trial, the combination of external beam radiotherapy and two cycles of cisplatin followed by four cycles of carboplatin and paclitaxel would provide a survival benefit after 5 years of ~10% and a failure-free survival benefit of ~12% in comparison to radiotherapy alone.[16] On the other hand, treatment-related morbidity is suspected to be higher with chemoradiotherapy, especially given the higher rates of neuropathy that can increase the risk of recurrent falls and the overall worse treatment tolerability. Her 5-year noncancer-specific survival independent of her endometrial cancer is calculated using the Lee Index. We portray her in three different scenarios to compare the different life expectancies based on clinical variables and geriatric assessment results. If Mrs. S. is considered as fit to receive any type of adjuvant therapy (and these considerations are beyond the scope of this review), the predicted noncancer-specific survival can be weighed against the expected treatment-related survival benefit and the potential life-threatening side-effects of the given treatment modality.

Abbreviations: COPD: chronic obstructive pulmonary disease; BMI: body mass index.