Point: The Value of Predicting Life Expectancy in Men with Clinically Localized Prostate Cancer

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Abstract
The prediction of life expectancy in prostate cancer screening and treatment is a controversial topic that evokes various opinions regarding its validity. The authors believe incorporating life expectancy prediction into the treatment algorithms for prostate cancer is important. Using a combination of clinical judgment and specific predictive tools, physicians can estimate the life expectancy of patients with prostate cancer. These estimates can then be used to help guide treatment discussion. Estimating life expectancy benefits older men in whom decisions regarding the best form of treatment may be difficult. (JNCCN 2007;5:703–708)

This article makes a case for predicting life expectancy in men with clinically-localized prostate cancer. The available literature related to this topic is reviewed, including the tables and tools that have been tested and validated for this purpose, and recommendations are made regarding the best ones to use. Readers should learn what evidence exists for predicting life expectancy, what tools and tables are available for this purpose, and limitations. The ultimate decision regarding treatment for prostate cancer in individual patients requires clinical judgment by the physician with consideration of the patient’s overall health and preference for treatment options.

For many patients, a cancer diagnosis is a difficult reality, regardless of age or health status, and it often elicits various expectations on the part of the patient and physician regarding treatment and prognosis.1 Reaching a clinical decision about the most appropriate treatment method for any cancer should be individualized to include patient-related factors, such as health status, life expectancy, treatment tolerance, and preference.2 Tumor-related factors such as pathologic grade, prostate-specific antigen (PSA) elevation, and tumor burden are also important. Prognosis and life expectancy are questions that often arise in treatment discussions. However, both physicians and patients often feel uncomfortable discussing life expectancy, even for terminal illnesses.3 In clinically-localized prostate cancer, however, life expectancy estimations are a key component to the treatment decision process, as shown by the inclusion of a 10-year life expectancy benchmark in the American Urological Association and National Comprehensive Cancer Network (NCCN) guidelines for the treatment of localized prostate cancer.4,5

Screening and Diagnosis
Use of life expectancy has been considered extensively in screening and diagnosis of cancer in the elderly. As the United States population ages, the approach to screening and treating cancer in the elderly must also progress. The United States Census Bureau estimates that the population of Americans older than age 65 will be 61 million in the year 2030, nearly double the number in 2000.6 Deciding to cease screening for cancer in the elderly stirs various ethical and financial debates. An editorial by Lantz and Ubel7 in the Journal of General Internal Medicine highlights several key problems with the current methods of life expectancy prediction in oncology. First, they
assert that the accuracy of current prediction models is poor, citing several examples to support their opinion that the models currently used are “crude and of questionable validity.” Secondly, attempting to predict life expectancy makes current screening guidelines even more cumbersome and time-consuming and may contribute to missed or inappropriate screening. Christakis and Iwashyna found that 60% of internists found predicting life expectancy stressful, 44% waited to be asked by patients before offering life expectancy predictions, and 90% avoided being too specific in making predictions. Many physicians feel underqualified to adequately predict a patient’s life expectancy. Finally, Lantz and Ubel theorize that available life expectancy tools cannot account for the heterogeneity that exists across ethnic and socioeconomic classes, and failing to account for these factors may exclude some racial or financial classes from appropriate screening. Moreover, the nation’s medical schools lack life expectancy training.

**Treatment Decision**

When elderly men have been diagnosed with prostate cancer, they face the daunting task of considering many treatment options, ranging from active surveillance with delayed treatment to immediate treatment with the intent to cure. This cure may be in the form of surgery, radiation, or other options, such as cryotherapy. Despite the criticisms, life expectancy prediction is possible and is an important part of the clinical decision-making process for men with clinically localized prostate cancer.

The natural history of prostate cancer frequently takes an indolent course in older men, even in those with a very long life expectancy. However, recent follow-up data have shown that men with longer life expectancy may still be at risk for aggressive disease when treated conservatively. Accurately predicting life expectancy differentiates the patients with prostate cancer who may benefit from screening and treatment from the population that is at low risk for disease progression because of competing risks of comorbidity. Litwin and Miller state this well: “Clinicians must remain steadfast in their efforts to reduce overtreatment and undertreatment by thoughtfully defining each patient’s unique balance between the natural history of prostate cancer and that individual patient’s life expectancy.” A reasonably accurate life expectancy can be defined for individual patients not only subjectively but also through a model based on prognostic indices in the form of validated self-assessment questionnaires and statistical prognostic indices. Current models can provide reasonable prognostication at treatment decisions and can impact oncologic efficacy by identifying men who would most benefit from prostate cancer therapy. Furthermore, their use may decrease unnecessary screening and reduce the age bias in treating clinically localized prostate cancer.

**Life Expectancy Tables**

The concept of predicting life expectancy is certainly not new. Rogers and Hunt introduced the notion of mortality ratios in 1919 to help life insurance companies predict individuals with higher risk for mortality. Today, this same system is used by insurance actuaries when determining life insurance coverage. The United States Government, through the National Center for Health Statistics and the Social Security Administration, has developed a series of life expectancy tables for every age. The NCCN guidelines advocate using these tables for managing localized prostate cancer in determining men with a 10-year life expectancy. These life tables report the average life expectancy for every age and are used as a starting point for the discussion of life expectancy. The life expectancy average from the table is adjusted up or down by 50% based on the quartile of health status of the patient.

**Comorbid Illness**

An important aspect of the patient-physician treatment discussion is the impact of comorbidity on health status and treatment tolerance. Although chronologic age is readily available, physicians and patients should focus more on physiologic age. Identifying and accounting for comorbidity not only helps clinicians think beyond the chronologic age of a patient but also enhances individualization of life expectancy estimates. Previous work has shown a significant correlation between age and prevalence of comorbid illnesses in patients with cancer. Accounting for the impact of comorbidity certainly affects oncologic treatment options. Recent data have shown that men who actively seek PSA screening are on average healthier than same-age men in the general population who do not seek PSA screening. The true life expectancy dilemma lies in the population of men diagnosed with...
prostate cancer who have increasing age and comorbid illnesses.

How can clinicians identify and account for comorbid illness? Various comorbidity indices and assessment tools have been developed to tackle this question. One of the most well-known validated indices is the Charlson Comorbidity Index (CCI). The original index designed by Charlson was a 4-point scale based on the presence of 19 comorbid conditions and was originally used to predict 1-year mortality in hospitalized patients. The relative risk of 1-year mortality increased by a factor of 2.3 with each increase in point score. Numerous studies encompassing more than 30,000 patients have validated the accuracy of the CCI, and it has been shown to be an independent predictor of long-term survival in patients with various cancers, including lung cancer. Use of the CCI has also been advocated in the multidisciplinary team evaluation of localized prostate cancer, where it was found to be a statistically significant predictor of survival in men with clinically localized prostate cancer. The CCI is a stable comorbidity classification scheme that is less sensitive to change over time. The colon cancer literature has supported the added value of identifying comorbidity and thereby enhancing the prediction of life expectancy.

Other authors have observed the competing risk of comorbidity with life expectancy in treating patients with prostate cancer. Albertsen et al. previously examined a cohort of men treated conservatively for localized prostate cancer in the pre-PSA era and found that 3 commonly used comorbidity indices, the Index of Coexistent Disease (ICED), the CCI, and the Kaplan-Feinstein index predicted all-cause mortality. Moreover, the ICED was a significant predictor of all-cause mortality independent of biopsy Gleason score. Although the task of generating a comprehensive CCI can be time-consuming in a busy clinical practice, shortcuts exist. Hall et al. developed an Excel-based online CCI calculator that allows more rapid calculation of a patient’s CCI, and research has shown that obtaining a comprehensive CCI may not be necessary for the instrument to be effective. Although the original CCI included 19 comorbid illnesses, data by Frohner et al. in patients with prostate cancer showed that the CCI can be reduced to 5 specific conditions and still retain prognostic significance, even in men older than 70 years. These conditions include congestive heart failure, chronic lung disease, peripheral vascular disease, moderate-to-severe renal disease, and diabetes with end-organ damage.

The Comprehensive Geriatric Assessment (CGA) is another useful tool for assessing the health status of aging patients. The CGA is included in the NCCN guidelines for the care of senior adult oncology patients and goes beyond just evaluating patients based on age and comorbidity. Extermann et al. has shown that comorbidity and functional status are factors that are not always correlative and must be evaluated separately. Thus, the CGA includes not only comorbidity and functional assessments but also information about polypharmacy, geriatric syndromes, emotional conditions, mental status, and nutritional status. The full-length CGA can also be time-consuming, and meta-analysis of this tool has not shown an impact on mortality, although it has been effective in reducing fall risk, preventing disability progression, and decreasing hospitalization rates. The Vulnerable Elders-13 (VES-13), a shorter surrogate tool for the CGA, has been evaluated in patients with advanced prostate cancer. The VES-13 is a 13-question intake form based on the CGA and was found to perform as effectively as the full-length CGA in identifying men at risk for significant short-term health decline.

Subjective Assessment

Subjective life expectancy predictions have been shown to be reliable and accurate, as evidenced by 2 studies in urologic literature. Koch et al. reviewed a series of men believed to have a 10-year life expectancy who underwent radical prostatectomy for localized prostate cancer. When compared with the discriminatory ability of an insurance actuary, the authors were 80% accurate in identifying men with a life expectancy of at least 10 years. Similar results were shown in a study of urologists and radiation oncologists in Canada. With the goal of accurately estimating the 10-year life expectancy benchmark for definitive treatment, simulated patient scenarios of men with localized prostate cancer were mailed to 277 physicians with a 67% response rate. The physicians were asked to determine life expectancy of the simulated patients without accounting for prostate cancer, and the clinicians’ predictions were compared with a Markov life expectancy model. The surveyed clinicians correctly identified men with a life expectancy less or greater than 10 years 82% of the time. These studies show that
clinicians are reasonably accurate in identifying men who meet the 10-year life expectancy benchmark.

**Life Expectancy Estimates**

However, as the medical profession moves toward an evidence-based treatment strategy, completely subjective assessment, although effective, seems less appropriate. Prognostic indices that are accurate, based on randomized data, and applicable to a wide range of individual patients would be ideal. Using retrospective data, Lee et al.10 developed a 4-year mortality index using participants of the Health and Retirement Study (HRS), a telephone-based survey of community dwellers age 50 years or older in all regions of the United States.11 The data collected for the HRS included age, gender, 18 comorbidity variables, and 21 functional variables. The index was reduced to a 12-item questionnaire and each question was given a point value to allow calculation of risk score for 4-year mortality. The model showed good discrimination and calibration in an easy-to-use instrument that could be completed before an office visit. With longer follow-up of these patients, a 10-year mortality index could be developed for prostate cancer discussions.

Albertsen et al.23 introduced the notion of calculating life expectancy in 1996 by developing a mathematical equation for determining life expectancy in patients with clinically localized prostate cancer. The equation was based on the data of 451 men diagnosed with clinically localized prostate cancer in the pre-PSA era with a mean follow-up of 15.5 years. The variables used to create the model included patient age, tumor grade, and ICED score. Although the population used to develop the equation was a narrow cohort of men aged 65 to 75 with lower-grade disease than is seen today, it provides a good starting point for predicting remaining life expectancy. No randomized validation of this model has been performed, but its accuracy has been examined in retrospective data. As a part of their study of age bias in prostate cancer treatment, Alibhai et al.36 validated the Albertsen et al.23 equation by calculating the 8-year survival rate of a hypothetical cohort that was very similar to the cohort in the Scandinavian randomized trial of watchful waiting versus surgery for localized prostate cancer.37 The Albertsen et al.23 equation predicted a 69.7% 8-year survival rate, which compared favorably with the 70% 8-year survival rate seen in the Holmberg et al.38 trial. Validation of this equation using prospective data and broader age range would bolster its application in clinical practice. Tewari et al.37 developed a set of look-up tables for estimating the long-term survival probability in clinically localized prostate cancer. Significant survival predictor variables of the model included age, race, CCI, PSA, year of diagnosis, and Gleason score. Propensity scoring showed the tables to be between 60% and 70% accurate in estimating 10-year survival.

In a more recent series, Cowen et al.39 developed a nomogram for predicting 5-, 10-, and 15-year survival rates in clinically localized prostate cancer. The nomogram was developed using a retrospective cohort of patients with clinically localized prostate cancer diagnosed early in the PSA era, and data were collected on various patient factors, including Eastern Cooperative Oncology Group performance status, demographics, smoking habits, blood pressure, CCI, and angina history. Overall, this was a healthy cohort of men, with 50.5% having a CCI score of 0 and only 25.9% having a CCI of at least 2. The nomogram had a discrimination ability of 73% in determining 5-, 10-, or 15-year life expectancy using the C-statistic, a measure of discrimination ability. Values for the C-statistic range between 0.5 (50%), representing discrimination based on chance alone, and 1.0 (100%), representing discrimination with complete certainty. The nomogram was also used to test the rules of Albertsen et al.23 and Tewari et al.37 and the accuracies of these rules were 70% and 71%, respectively. Thus, the nomograms by Albertsen et al.23, Tewari et al.37, and Cowen et al.39 have reasonable accuracy, with discrimination abilities in the middle range of the C-statistic.

Accurate estimation of life expectancy not only helps to determine the best treatment strategy for prostate cancer patients but also de-emphasizes the importance of age in screening and treatment strategies. Walter et al.39 reported the problem of nondiscriminatory screening in older men. In a cohort of approximately 500,000 men, 56% received at least one PSA measurement for screening purposes, and, as comorbidity increased, no proportionate decrease in screening was seen. In men aged 85 years, health status seemed to have very little effect on screening habits because 34% who were considered in best health and 36% in worst health underwent a screening PSA test. Incorporating a comorbidity intake form into initial clinic visits and educating physicians on the impact
of comorbidity could help reduce much of this unnecessary screening.

Conversely, once prostate cancer has been diagnosed in an older man, an age bias exists regarding the treatment options available. Alibhai et al. examined the factors influencing decisions on treatment of clinically localized prostate cancer. Using the equation published by Albertsen et al. to calculate life expectancy, men aged 70 to 79 years were less likely to receive definitive therapy than their counterparts aged 60 to 69 years despite having similar life expectancy. Identifying older men with long life expectancy may improve the oncologic efficacy of definitive treatment for localized prostate cancer. In a recent review of 20-year outcomes data, Johansson et al. showed that even low-grade, indolent prostate cancer has a propensity for aggressiveness and prostate cancer-specific death in men with long life expectancies at diagnosis. Furthermore, a survival benefit has been seen in older men aged 75 to 80 who undergo definitive treatment. Determining life expectancy in men with advanced age allows clinicians to identify and treat those men who are at risk for prostate cancer morbidity and mortality.

Conclusions

Although the prediction of life expectancy will never be perfectly accurate, incorporating the estimation of life expectancy into the decision to screen and treat localized prostate cancer has merit. Using only clinical judgment and experience, urologists are reasonably accurate in identifying men with a life expectancy of 10 years, which is the benchmark for definitive local therapy. Because of the increasing number of objective means for estimating life expectancy, urologists and physicians can now go beyond subjective methods. Patients must be informed that any prediction of life expectancy is an estimate and that absolute values reported in life expectancy tables represent average values that are adjusted up or down according to health status.

This article attempts to establish the value of predicting or estimating life expectancy in men with localized prostate cancer. The authors recommend using periodic life tables and comorbidity tools, specifically the CCI, to begin a more informed discussion with elderly patients about their life expectancy. Using the CCI in conjunction with life tables helps account for the heterogeneity of health status. The authors recognize a benefit to treating prostate cancer in elderly men because it may affect the quality or length of life in those who live long enough with this cancer. However, the discussions about the benefits of treatment must include the risks and harms to quality of life that may result from overtreatment of men with limited life expectancy. Estimating an individual’s life expectancy is critical to this informed discussion and decision-making process.

The authors believe that new research will eventually result in better prediction methods, particularly around the 10-year benchmark so commonly used in prostate cancer discussions. These methods can be expected to better guide decision-making for elderly men with prostate cancer. However, tools to predict life expectancy are currently available and should be used to guide decision-making for elderly men with prostate cancer.

References


