Counterpoint: Prostate Cancer Life Expectancy Can Not Be Accurately Predicted From Currently Available Tools

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What Are the Current Guidelines?
The National Comprehensive Cancer Network (NCCN) guidelines for patients of advanced years with asymptomatic prostate cancer have been modified recently. Current guidelines recommend watchful waiting, rather than potentially curative therapy, in asymptomatic patients with a life expectancy of no more than 5 years and newly diagnosed low- to intermediate-risk prostate cancer. Previously, the NCCN endorsed the 10-year rule, which limits the recommendation for curative therapy to patients with a life expectancy of at least 10 years. This NCCN recommendation was widely accepted among radiation oncologists and urologists. Because these elderly patients are believed to die with, rather than of, their disease, the risk-benefit ratio of treatment had been questioned.
The revised NCCN guidelines state that life expectancy can be estimated using the Social Security Administration tables and then adjusted based on the clinician's estimation of overall health. Clinician's estimate is adjusted as follows: add 50% for men in the best quartile of health; subtract 50% for those in the worst quartile; and make no adjustments for those in the middle 2 quartiles of health.

Is Age Alone Being Used to Guide Treatment Decisions?
In the absence of tools to accurately determine life expectancy, is age alone being used inappropriately to guide treatment decisions? Earlier studies have documented that, compared with younger men, older patients are offered potentially curative therapy less often. Men younger than 60 years with clinically localized disease are 25 times more likely than patients older than 70 years to undergo radical prostatectomy. Donovan et al. surveyed British
clinchists and found that radical prostatectomy was performed in 64%, 24%, and 0% of patients aged 55, 69, and 75 years, respectively. A study of 260,000 men in the U.S. National Cancer Database showed similar findings, with radical prostatectomy performed in 48% of patients aged 50 to 64 years compared with 6% of patients aged 75 years or older. Studies have indicated that grade and comorbidity do not affect the decision to offer curative therapy and that age alone is the deciding factor. Younger men with significant comorbidities and thus limited life expectancy undergo potentially curative therapy more often than older men with minimal comorbidities and significant life expectancy, suggesting an age bias.

How Accurate Are Physician Estimates of Life Expectancy?
Physicians are notoriously poor at predicting life expectancy. Prior studies have shown that life expectancy estimates among physicians for terminally ill patients have been only 20% to 49% accurate. A recent study of survival predictions among radiation oncologists treating patients with metastatic cancer referred for palliative radiation showed these predictions to be inaccurate, with a tendency to overestimate life expectancy. Conversely, a recent study of British physicians’ estimates of life expectancy for hypothetical patients found that physicians routinely underestimated life expectancies. A third study of Australian physicians again documented inaccuracy in physician estimates, with 35% of predictions too optimistic, 39% too pessimistic, and only 29% accurate. Specific to prostate cancer, a Canadian study found that clinicians were able to predict life expectancy among patients with localized prostate cancer with a “modest degree of overall accuracy,” with average prediction errors ranging from 2.4 to 5.2 years.

What Factors Affect Life Expectancy Among Men with Localized Prostate Cancer?
What factors, aside from age, affect life expectancy among men diagnosed with localized prostate cancer? Evidence shows that patient-related factors such as age, comorbidities, and functional status are critical determinants of life expectancy. Equally strong evidence supports tumor-related factors, including Gleason score, tumor stage, prostate-specific antigen (PSA), and efficacy of treatment. Allibhai et al. found that potentially curative therapy results in significantly improved life expectancy and quality of life—adjusted life expectancy in men up to age 80 with few comorbidities and moderately or poorly differentiated prostate cancer. Allibhai et al. thus concluded that age alone should not be a barrier to treatment in older men with localized prostate cancer.

Does a Current Model Accurately Predict Life Expectancy?
Does a current model exist that considers all of these factors to accurately predict life expectancy in individual patients? Common models of life expectancy, such as the Social Security Life Tables, reflect the impact of age alone. Social Security Life Tables are referred to in the literature as “unadjusted life expectancy measures,” meaning that they are probability estimates for the population at large and do not account for individual differences. According to these tables, the elderly population is heterogeneous. An 80-year-old man can have a life expectancy ranging from 3 to 11 years.

Age alone has been repeatedly shown to be unreliable for estimating life expectancy. The NCCN Senior Adult Oncology Panel reviewed data from the Surveillance Epidemiology and End Results study, which examined survival outcomes among cancer patients aged 90 years and older. The data showed that elderly patients have equivalent survival to their younger counterparts after the first year of cancer diagnosis. As a result, the NCCN Senior Adult Oncology Clinical Practice Guidelines in Oncology state that “advanced age alone should not preclude the use of effective cancer treatment that could improve quality of life or extend meaningful survival.” The guidelines conclude that chronologic age alone is not reliable in estimating life expectancy.

A Mayo Clinic study examining survival outcomes among 799 patients aged 90 years or older undergoing major surgery likewise supports that age alone may not determine survival beyond the first year after surgery. In a follow-up of decreased survival in the year immediately after surgery, the study found that survival rates in patients older than 89 years were comparable to rates seen in younger patients beyond the first postoperative year.

Numerous models use comorbidities in estimating life expectancy. A recent review of 13 comorbidity scales found that 4 had sufficient data to confirm
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validity and reliability: the Charlson Comorbidity Index, Index of Coexistent Disease, Kaplan Feinstein Comorbidity Index, and Cumulative Illness Rating Scale. Comorbidity scales that typically assign a numeric value to each comorbid condition and then calculate a total meant to reflect the overall health of individual patients have many acknowledged limitations. One is that the comorbidity indices typically do not account for disease burden but focus on the total number of medical diagnoses. For example, is a patient with mild hypertension, diet-controlled diabetes, and mild asthma necessarily in worse health than a patient with insulin-dependent, poorly controlled diabetes alone? Most comorbidity indices would indicate “yes,” although most clinicians would disagree. Also, comorbidity indices usually do not accurately reflect the conditions that affect mortality and quality of life.

The Comprehensive Geriatric Assessment (CGA) is endorsed by the NCCN Senior Adult Oncology Guidelines. The CGA assesses function, comorbidity, nutrition, polypharmacy, cognition, emotional evaluation, and social support to estimate physiologic age for individual patients. The components of the CGA have been shown to significantly impact life expectancy. Given the impracticality of performing such a thorough assessment in the busy clinical setting, the NCCN guidelines recommend several screening tests to better determine which patients require full CGA. These screening tests include a frailty index, which uses unintentional weight loss, self-reported exhaustion, weakness in grip strength, slow walking speed, and low physical activity to identify frail patients, a measure shown to affect mortality.

The Timed Up and Go (TUG) test is a quick test to assess mobility, also shown to correlate with mortality. A functional assessment developed by Lachs et al. assesses vision, hearing, mobility, urinary incontinence, nutrition, mental status, depression, activities of and instrumental activities of daily living (ADL-IADL), home environment, and social support. The NCCN developed the Distress Thermometer, which is a patient-completed survey used to identify practical, family, emotional, physical, or spiritual problems. Another patient questionnaire is the Vulnerable Elders Survey, which assesses age, self-rated health, and functional limitations and is the official screening tool used by the European Organisation for Research and Treatment of Cancer.

In addition to these screening tests, mounting evidence shows that laboratory tests may soon help predict life expectancy. Elevated levels of inflammatory markers such as interleukin-6 and coagulation markers such as D-dimer have been shown in early studies to predict mortality and cognitive decline.

None of these tools to assess for life expectancy are specific to prostate cancer. However, models that are specific to prostate cancer do exist and account for some of the known determinants of life expectancy discussed earlier. Albertsen et al. published a formula in 1996, based on men treated conservatively, that estimates prostate cancer life expectancy based on age, tumor grade, and comorbidity. Tewari et al. later published 10-year survival probabilities in men with clinically localized prostate cancer based on age, Gleason score, PSA, Charlson comorbidity, and treatment received. Men older than 75 years, however, were not included in this study.

Cowen et al. developed a nomogram for predicting overall survival among men with clinically localized prostate cancer that incorporated clinical staging, Gleason score, PSA, age, body mass index, systolic blood pressure, angina, marital status, Eastern Conference Oncology Group performance status, smoking, ethnicity, treatment received, and Charlson comorbidity. The authors also examined the accuracy of their prediction rule and performed an external validation of the prediction rules published by Albertsen et al. and Tewari et al. The C-statistic for Cowen et al., Albertsen et al., and Tewari et al. were 0.73, 0.71, and 0.70 respectively. Given that a C-statistic of 0.5 represents chance and 1.0 indicates complete certainty, values in the range of 0.7 can be viewed as having only a moderate degree of accuracy in predicting overall life expectancy. The authors themselves concluded that these nomograms were inadequate as the only determinant of an optimal management approach. Probably because of suboptimal accuracy, none of the 3 prostate cancer-specific nomograms for predicting life expectancy are routinely used.

What Is the Goal of Predicting Life Expectancy?

What is the ultimate goal of being able to adequately predict life expectancy among men with localized prostate cancer? The benefit of treating elderly patients with localized prostate cancer will only be
seen when early stage disease, which would otherwise have been lethal before death from other causes, is detected and treated. Whether an elderly patient will benefit from potentially curative therapy depends on the many factors detailed earlier. These factors are patient, disease, and treatment specific. Currently none of the available tools comprehensively account for all these factors in determining life expectancy. Until this tool is developed and validated, clinicians should use caution in recommending against elderly patients undergoing potentially curative therapy based on age alone.

References


