

RESEARCH LETTERS

LESS IS MORE

**Severity of Comorbidity and Non-Prostate Cancer Mortality in Men With Early-Stage Prostate Cancer**

Comorbidity is a key consideration in clinical decision making for prostate cancer. Early-stage prostate cancer often follows an indolent course, with the significant survival advantage of definitive local therapy developing at 8 years after treatment.<sup>1</sup> Men with severe comorbidity may not live long enough to benefit from aggressive therapy and therefore may prefer to treat their disease conservatively. Unfortunately, the lack of a standardized and practical comorbidity assessment tool has limited the application of comorbidity to clinical decision making in this setting.

*See Invited Commentary at the end of this letter*

We have previously reported on the short-term prognostic utility of the Total Illness Burden Index for Prostate Cancer (TIBI-CaP), a patient-reported, questionnaire-based comorbidity assessment tool specifically designed for clinical use in prostate cancer.<sup>2,3</sup> The TIBI-CaP is an 84-item questionnaire in 11 disease subdimensions that measures both presence and severity of comorbid illness and can be completed by a patient in 15 minutes.

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Men with the highest TIBI-CaP scores ( $\geq 12$ ) were 13 times more likely to die of causes other than prostate cancer within 3.5 years of questionnaire administration, compared with men with the lowest scores.<sup>3</sup> We recently fol-

lowed this cohort for a median of 6.2 years after treatment to determine the utility of the TIBI-CaP in predicting long-term survival outcomes.

**Methods.** In 2002, the TIBI-CaP questionnaire was sent to 4635 active participants of the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a national, observational prostate cancer registry.<sup>4</sup> Of the 3389 men who returned the questionnaire, 2900 completed it and were included in the study. The mean time from treatment to TIBI-CaP questionnaire completion was 41.4 months. Our primary outcome was death from causes other than prostate cancer, measured from the time of treatment. We used multivariate Cox proportional hazards regression to assess the association of TIBI-CaP score and nonprostate cancer mortality, while controlling for clinical and demographic factors.

**Results.** After a median follow-up of 6.2 years, overall mortality was 14.5% (420 men), while prostate cancer-specific mortality was only 3% (86 men). Nonprostate cancer-specific mortality was significantly different among comorbidity groups; 41% of patients with the highest TIBI-CaP scores ( $\geq 12$ ) died of causes other than prostate cancer, compared with 6% of those with the lowest scores (0-2) ( $P < .001$ ) (**Table**). In multivariate analysis, higher TIBI-CaP comorbidity scores were significantly associated with elevated risk of non-prostate cancer mortality. Men with the highest TIBI-CaP scores were 10 times more likely to die of causes other than prostate cancer, compared with men with the lowest scores (hazard ratio, 10.3; 95% confidence interval, 5.4-19.5) (Table).

**Comment.** For men considering aggressive vs conservative treatment for clinically localized prostate cancer, comorbidity must be a primary consideration. Our data show that men with significant comorbidity (ie, TIBI-CaP  $\geq 12$ ) have a 41% risk of death from other causes 6 years after treatment, several years before significant

**Table. Survival Rates and Hazard Ratios for Death for Non-Prostate Cancer Mortality by Global TIBI-CaP Score**

TIBI-CaP Score	No. of Men	No. of Nonprostate Deaths Within 6 Years	Non-Prostate Cancer Survival Rate at 6 Years, %	Hazard Ratio (95% CI) <sup>a</sup>
0-2	1178	59	94	1 [Reference]
3-5	1136	134	86	2.19 (1.54-3.11)
6-8	429	93	73	3.68 (2.53-5.39)
9-11	114	34	62	4.81 (2.93-7.88)
$\geq 12$	43	14	59	10.29 (5.44-19.46)

Abbreviations: CI, confidence interval; TIBI-CaP, Total Illness Burden Index for Prostate Cancer.

<sup>a</sup>Hazard ratios were calculated by Cox proportional hazards model controlling for age, education, income, race, and D'Amico tumor risk category.

survival benefits of aggressive local treatment can be realized.<sup>1</sup> Because men with significant comorbidity have a high likelihood of short- to intermediate-term mortality, they may wish to strongly consider conservative over aggressive treatment for their clinically localized prostate cancer.

Although other comorbidity assessment tools such as the Index of Coexistent Disease, Charlson Comorbidity Index, and the Kaplan-Feinstein Index have been validated for use in prostate cancer,<sup>5</sup> their clinical utility is limited by the infeasibility of thorough medical record review during an office visit. The TIBI-CaP, which can be completed by a patient in 15 minutes in the waiting room, offers a practical solution to this problem. Although formal comorbidity assessment may be unwarranted for men with minimal comorbidity, we believe that men with moderate or severe comorbidity ought to be offered this simple questionnaire to inform their decision making.

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## INVITED COMMENTARY

### LESS IS MORE

#### Prostate Cancer: Doing Less Might Be More

The phrase “out of sight, out of mind,” as suggested by Nicolas Bruchofsky,<sup>1</sup> aptly describes the fact that while no other organ causes so much illness in man as the prostate, so little is known about its role in the body. And yet, with our aging population, a lifetime risk of death from prostate cancer of 3%, and dramatic (ie, 2-fold) increase in a lifetime risk of a diagnosis of prostate cancer owing to PSA screening, prostate cancer represents one of the most challenging issues facing physicians today.

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Over the past several decades, PSA screening of asymptomatic men for prostate cancer has come to represent an accepted “truth” in the medical community on the assumption that this test should be innately beneficial, following the concept that, as with other common malignant conditions including colorectal and breast cancer, earlier diagnosis is associated with a lower potential for occult established metastases and a higher potential for cure by local therapeutic means. Though attractive for prostate cancer, this concept frequently does not work out in clinical practice,<sup>2</sup> and unfortunately, the hope of early beneficial diagnosis has contributed to overdiagnosis and overtreatment of prostate cancer with attendant life-altering morbidities including high rates of post-therapeutic bowel, bladder, and sexual dysfunction. Appreciation of these facts and the slow natural history (growth) of many prostate cancers has redirected attention to life expectancy, quality of life considerations, and comorbidities as key factors in clinical decision making for patients with prostate cancer, as considered by Daskivich et al in this issue of the *Archives*. Twenty years ago, even prior to widespread use of PSA testing, life expectancy and comorbidities were shown to be key and independent factors in evaluating clinician decision making among men with prostate cancer.<sup>3</sup>

We would be remiss in attributing the present failure of the potential beneficial effects of PSA screening and the resultant overdiagnosis and overtreatment of prostate cancer to the concept of “screening.” “Screening” is scientifically sound but only if the subsequent use of a single (or multiple) cancer-specific marker(s) can distinguish between the 2 types of prostate cancer: those that will kill you and those that will not. Although the specificity of PSA for the prostate makes it a very useful clinical tool as a harbinger for recurrence of prostate cancer following treatment,<sup>4</sup> because PSA is not cancer specific, it cannot detect prostate cancer and cannot be a screening test for dangerous prostate cancer in the manner the PSA test is currently used, and, ipso facto, it will never be a tool that can distinguish the dangerous from the nondangerous cancers, ergo, the failure of PSA screening.<sup>5</sup>