Impact of the U.S. Preventive Services Task Force Recommendations against Prostate Specific Antigen Screening on Prostate Biopsy and Cancer Detection Rates

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Purpose: We determined if the USPSTF recommendation against prostate specific antigen screening was associated with a change in biopsy and cancer detection rates.

Materials and Methods: We conducted a time series analysis (October 2008 to June 2013) of prostate biopsies performed at University Health Network (Toronto). Biopsies for active surveillance or solely targeting magnetic resonance imaging detected lesions were excluded from study. Interventional ARIMA models with step functions were used to examine changes in the number of biopsies performed and cancers detected per month. Low risk prostate cancer was defined as no Gleason pattern 4 or greater, 3 or fewer cores involved, or 1/3 or less of the total number of cores involved, and no core with greater than 50% cancer involvement. Intermediate to high grade prostate cancer was defined as Gleason 7-10.

Results: A total of 3,408 biopsies were performed and 1,601 (47.0%) prostate cancers were detected (low risk prostate cancer 563 [16.5%], intermediate to high grade prostate cancer 914 [26.8%]). The median number of biopsies per month decreased from 58.0 (IQR 54.5–63.0) before the recommendations to 35.5 (IQR 27.0–41.0) afterward (p=0.003), while the median number of patients undergoing first-time biopsy decreased from 42.5 (IQR 37.5–45.5) to 24.0 (IQR 19.0–32.5, p=0.025). The median number of low risk prostate cancers detected per month decreased from 8.5 (IQR 6.5–10.5) to 5.5 (IQR 4.0–7.0, p=0.012), while the median number of intermediate to high grade prostate cancers per month decreased from 17.5 (IQR 14.5–21.5) to 10.0 (IQR 9.0–12.0, p <0.001).

Conclusions: After the USPSTF recommendation the number of biopsies performed (total and first-time), based on referrals from our catchment area, has decreased. This is likely due to decreased use of prostate specific antigen screening. Although it is encouraging that fewer low risk prostate cancers are being diagnosed, the sudden decrease in the detection rate of Gleason 7-10 prostate cancers is concerning.

Key Words: early detection of cancer, prostate, biopsy, prostatic neoplasms

Abbreviations and Acronyms

ARIMA = autoregressive integrated moving average

DRE = digital rectal examination

I-HGPC = intermediate to high grade prostate cancer

LRPC = low risk prostate cancer

PC = prostate cancer

PCP = primary care practitioner

PSA = prostate specific antigen

USPSTF = U.S. Preventive Services Task Force

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Study received institutional research ethics approval.

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For another article on a related topic see page 1669.

Editor's Note: This article is the fourth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1732 and 1733.

SINCE its rapid uptake approximately 25 years ago, controversy has surrounded the use of serum PSA for the early detection of prostate cancer.[1,2] With the aim of resolving the controversy, 3 large randomized PC

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screening trials were recently reported.[3–5] The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial failed to detect a difference in PC related mortality between men randomized to annual PSA based screening and controls receiving usual care, although high rates of PSA screening in the control arm may have biased results toward the null.[3,6] Conversely, the European Randomized Study of Screening for Prostate Cancer (ERSPC)[4,7] and Goteborg[5] screening trials (which shared a considerable number of patients) reported a reduction in PC related mortality with screening, although the number needed to screen (ERSPC 1,055; Goteborg 293) and number needed to detect (ie manage expectantly or treat actively, ERSPC 37, Goteborg 12) to prevent 1 PC related death were high.

After appraisal of the evidence, the USPSTF released a recommendation statement in May 2012 against PSA based screening for PC. This statement carried a Grade D recommendation, conveying that according to their assessment, "there is moderate to high certainty that the service has no net benefit or that the harms outweigh the benefits."[8] Along with extensive media coverage that captured the attention of the lay public and health care practitioners, the release of this recommendation was met with polarized opinions and criticisms, emphasizing the lack of agreement in the interpretation of the trials.[9–12] Based on diverging opinions regarding the relative benefits and harms of PC screening, the impact of the USPSTF recommendation statement on clinical practice remains unclear. Therefore, we evaluated whether our prostate biopsy rates and cancer detection rates (based on referrals from our catchment area) changed after the USPSTF recommendation statement using a time series analysis.

METHODS

Study Design, Patients and Data Collection

Patients who underwent transrectal ultrasound guided prostate biopsy from October 1, 2008 to June 30, 2013 were identified from our institutional Genitourinary BioBank Project at University Health Network in Toronto, Canada (census metropolitan area population 5.58 million). All biopsy referrals to our network of academic hospitals are centralized and performed by 2 high volume radiologists. The BioBank approaches all men before prostate biopsy and has a 94.7% consent rate for inclusion. Institutional research ethics approval was obtained and patient consent was sought for inclusion in the database.

The majority of men (approximately 60%) were referred by the 13 academic urologists in our network while the remainder was referred by community urologists (approximately 30%) or directly by PCPs (approximately 10%) in our catchment area. Of note, the Canadian health care system requires referral from another physician (usually a PCP) before specialist consultation. Therefore, screening is conventionally performed by PCPs and urologist consultation is only sought if they are concerned (eg elevated PSA or abnormal DRE).

First-time biopsies generally involved 10 to 12 cores while repeat biopsies involved 13 to 18 cores. All biopsies were read by genitourinary pathologists. Biopsies for active surveillance (1,140) or biopsies solely targeting lesions detected on magnetic resonance imaging (22) were excluded from analysis. Clinical data were obtained through patient questionnaires (patient reported ethnicity, family history of PC, use of certain medications) and electronic chart review (serum PSA, DRE findings and biopsy pathology results).

Exposure and Outcome Measures

The event of interest (ie the intervention) was the release of the USPSTF recommendation statement on May 22, 2012. Taking into account slight delays between the referral and the actual biopsy date, June 2012 was considered the first month after intervention.

To evaluate the impact of the USPSTF recommendations on the monthly biopsy rate, we evaluated the total number of prostate biopsies performed per month (primary outcome) and the number of first-time biopsies performed per month (secondary outcome). The former was chosen because it is thought to reflect overall rates of ongoing PSA based PC screening. The latter was chosen because patients without prior biopsy are most likely to be newly referred by PCPs and, thus, this measure likely reflects the rates of PSA screening among PCPs.

We then evaluated the impact of the USPSTF recommendations on absolute (number of cancers per month) and relative (number of cancers per month per 100 biopsies performed) cancer detection rates as additional secondary outcomes (see supplementary figure, http://jurology.com/). The absolute and relative numbers of low risk PCs detected per month were evaluated. Low risk PC was defined as no Gleason pattern 4 or greater, 3 or fewer cores involved, or 1/3 or less of the total number of cores involved, and no core with more than 50% cancer involvement, representing cancers that are generally most appropriate for surveillance rather than radical therapy.[13] Then the absolute and relative numbers of I-HGPC (defined as Gleason score 7-10) detected per month were evaluated. These cancers represent potential threats to survival[14] and are most likely to benefit from early intervention.[15,16]

Statistical Analysis

Statistical analyses were performed using SAS® v9.3 with the Time Series Forecasting System. Characteristics were compared between biopsies performed in the months before vs after the release of the USPSTF recommendations using standardized differences.

To assess for significant changes after the release of the USPSTF recommendations, interventional ARIMA models with step functions were used.[17,18] This technique offers several advantages compared to simpler before vs after comparisons. Most notably, the model intrinsically