Variation in Prostate Cancer Detection Rates in a Statewide Quality Improvement Collaborative

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Purpose: There remains significant controversy surrounding the optimal criteria for recommending prostate biopsy. To examine this issue further urologists in MUSIC assessed statewide prostate biopsy practice patterns and variation in prostate cancer detection.

Materials and Methods: MUSIC is a statewide, physician led collaborative designed to improve prostate cancer care. From March 2012 through June 2013 at 17 MUSIC practices standardized clinical and pathological data were collected on a total of 3,015 men undergoing first-time prostate biopsy. We examined pathological biopsy outcomes according to patient characteristics and across MUSIC practices.

Results: The average cancer detection rate was 52% with significant variability across MUSIC practices (range 43% to 70%, $p < 0.0001$). Of all patients biopsied 27% were older than 69 years, ranging from 19% to 36% at individual practices. Men with prostate specific antigen less than 4 ng/ml comprised an average of 26% of the study population (range 10% to 37%). The detection rate in patients older than 69 years ranged from 42% to 86% at individual practices ($p = 0.0008$). In the 793 patients with prostate specific antigen less than 4 ng/ml the cancer detection rate ranged from 22% to 58% across individual practices ($p = 0.0065$). The predicted probability of cancer detection varied significantly across MUSIC practices even after adjusting for patient age, prostate specific antigen, prostate size, family history and digital rectal examination findings ($p < 0.0001$).

Conclusions: While overall detection rates are higher than previously reported, the cancer yield of prostate biopsy varies widely across urology practices in Michigan. These data serve as a foundation for our efforts to understand and improve patient selection for prostate biopsy.

Key Words: prostate, prostatic neoplasms, biopsy, physician's practice patterns, Michigan

Abbreviations and Acronyms

DRE = digital rectal examination

MUSIC = Michigan Urological Surgery Improvement Collaborative

PCa = prostate cancer

PSA = prostate specific antigen

TRUS = transrectal ultrasound guided

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GROWING scrutiny surrounds early detection practices for men at risk for PCa. Reflecting this concern, the AUA (American Urological Association) recently revised its recommendations to limit routine PSA based screening to men 55 to 69 years old after a discussion of risks and benefits.[1] The USPSTF (United States Preventive Services Task Force) entirely recommends against routine screening.[2] Such conflicting

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guidelines are emblematic of the uncertainty surrounding the relative benefits vs harms of PSA based early detection strategies.

At least part of this uncertainty relates to differences in cancer detection rates at initial prostate biopsy. While it is well established that certain patient characteristics (eg PSA and DRE findings) correlate with cancer yield, much less is known about the potential impact of different care settings and providers on the likelihood of cancer diagnosis after prostate biopsy. If present, such variation would suggest the possibility of important differences in practice patterns related to patient selection, biopsy technique and/or pathological interpretation. Accordingly better understanding of this issue could guide ongoing efforts aimed at improving early detection practices in men at risk for PCa.

In this context we examined variation in contemporary cancer detection rates across the diverse academic and community practices participating in MUSIC.

MATERIALS AND METHODS

Michigan Urological Surgery Improvement Collaborative

Established in 2011 with funding from Blue Cross Blue Shield of Michigan, MUSIC is a physician led, statewide collaborative that currently comprises 32 urology practices throughout Michigan, including more than 70% of urologists in the state.[3] These practices represent geographically, socioeconomically and racially diverse regions of Michigan. The goal of this organization is to improve the quality and cost-efficient nature of care provided to men with PCa in Michigan.

Data for this analysis were obtained from 17 participating practices where at least 25 initial prostate biopsies were performed from March 2012 through June 2013. Each practice participates under institutional review board approval. One urologist per practice serves as the clinical champion with responsibilities that include oversight of the local data collection process, regular attendance and participation in tri-annual collaborative-wide meetings, and leadership around local implementation of quality improvement activities. The University of Michigan coordinating center is responsible for overall administration and management of collaborative activities.

Trained clinical abstractors in each participating practice submit data to a web based clinical registry developed in conjunction with a private software vendor. The MUSIC registry includes data on all patients who undergo prostate biopsy in participating practices as well as all seen for newly diagnosed PCa. The registry includes approximately 150 unique variables with information on patient demographics, laboratory, imaging and pathology results, comorbid conditions, PCa treatments and patient outcomes, including complications and mortality, among others. Data collection is guided by standard variable definitions and collaborative-wide operating procedures. Each abstractor also completes a formal training session before commencing data collection and participates in quarterly educational webinars developed and administered by the coordinating center staff. In terms of quality assurance coordinating center members perform quality audits on site to ensure proper case identification and data integrity. This process involves direct review of sample cases from each participating practice, collaboration between administrators and data abstractors to reconcile missing and erroneous data, and database review to identify and resolve incomplete or missing information.

Primary Outcome

The primary outcome of this analysis was the pathological finding of prostate adenocarcinoma on initial prostate biopsy in patients with no PCa history. Pathology services are provided to MUSIC practices by a mixture of community based general pathologists, genitourinary pathology specialists employed by large groups, academic genitourinary pathologists and large commercial pathology laboratories. After reviewing pathology reports the results of prostate biopsies (ie presence or absence of cancer and other relevant pathological findings) are entered in the registry by data abstractors with any discrepancies or uncertainties in pathological interpretation adjudicated by the local clinical champion. There is no central pathology review. In addition, the prostate biopsy technique is not standardized across MUSIC practices. Because our study was restricted to patients who underwent initial prostate biopsy, all except 1 biopsy was TRUS. The number of cores sampled was only available for patients diagnosed with PCa. In those patients the mean and median number of cores were 12 (72.5% of all patients underwent 12-core TRUS biopsy). The 10th percentile was 11 cores and the 90th percentile was 14.

Data Analysis

We first generated descriptive summary statistics for all patients in the analytical sample. We then used appropriate univariate statistical tests to compare the proportion of biopsies positive for cancer (ie the cancer detection rate) across MUSIC practices and according to patient characteristics (eg age, PSA, TRUS prostate volume and DRE results). We fit a multivariate logistic regression model to examine the association between specific patient characteristics and positive biopsy. From this model we also generated and compared the predicted cancer detection rate for each MUSIC practice, adjusting for differences in patient characteristics (age, family history, PSA, DRE findings and prostate size) across participating sites. All statistical testing was 2-sided, performed at the 5% significance level and completed using SAS®, version 9.2. The chi-square test was used for all univariate analysis of categorical variables and the nonparametric Wilcoxon rank test was applied to compare medians.

RESULTS

From March 2012 through June 2013 a total of 3,015 men underwent initial prostate biopsy at 1 of 17 MUSIC practices (table 1). The average patient

Table 1. *Patient characteristics, PCa detection rate variability, and lowest and highest values among 17 practices*

	Values/17 Practices			% PCa Pos Biopsy			
	Overall	Lowest	Highest	Overall	Lowest	Highest	p Value
No. pts	3,015	37	473	52	43	70	
Age:							
Median (IQR)	64 (58–70)	61 (54–66)	67 (60–71)	—	—	—	—
No. less than 55 (%)	434 (14)	(7)	(26)	45	18	73	0.1303
No. 55–69 (%)	1,766 (59)	(52)	(68)	50	32	67	0.0001
No. greater than 69 (%)	814 (27)	(19)	(36)	59	42	86	0.0008
PSA (ng/ml):							
Median (IQR)	5.1 (3.9–7.0)	4.5 (3.4–6.5)	5.8 (4.5–9.1)	—	—	—	—
No. less than 4 (%)	793 (26)	(10)	(37)	38	22	58	0.0065
No. 4–10 (%)	1,853 (61)	(48)	(77)	54	47	63	0.24
No. greater than 10 (%)	362 (12)	(4)	(25)	71	44	83	0.0526
Estimated prostate vol (cc):*							
Median (IQR)	40 (30–55)	32 (24–42)	55 (44–72)	—	—	—	—
No. less than 30 (%)	596 (20)	(8)	(42)	62	49	100	0.0022
No. 30–60 (%)	1,641 (55)	(43)	(67)	52	33	75	<0.0001
No. greater than 60 (%)	736 (25)	(5)	(45)	39	14	50	0.92
Family history (%):†							
Neg	2,134	—	—	50	41	71	<0.0001
Pos	676 (22)	(17)	(31)	58	42	82	0.26
No. DRE findings (%):‡							
Neg	2,085 (69)	(34)	(92)	49	40	66	<0.0001
Pos	755 (25)	(7)	(40)	59	36	90	0.0005

* Unknown in 42 patients (1.4%).
† Unknown in 205 patients (7%).
‡ Unknown in 175 patients (6%).

was 64 years old and had PSA 5.1 ng/ml, a 40 cc prostate, no PCa family history and no abnormalities detected on DRE. Patient characteristics and risk strata varied considerably by practice. For example, across all practices 26% of men undergoing initial prostate biopsy had PSA less than 4 ng/ml and the range was 10% to 37% across individual MUSIC sites. The incidence of men older than 69 years at biopsy was 19% to 36% across individual practices and 5% to 45% of men undergoing biopsy had a transrectal ultrasound prostate volume of greater than 60 cc.

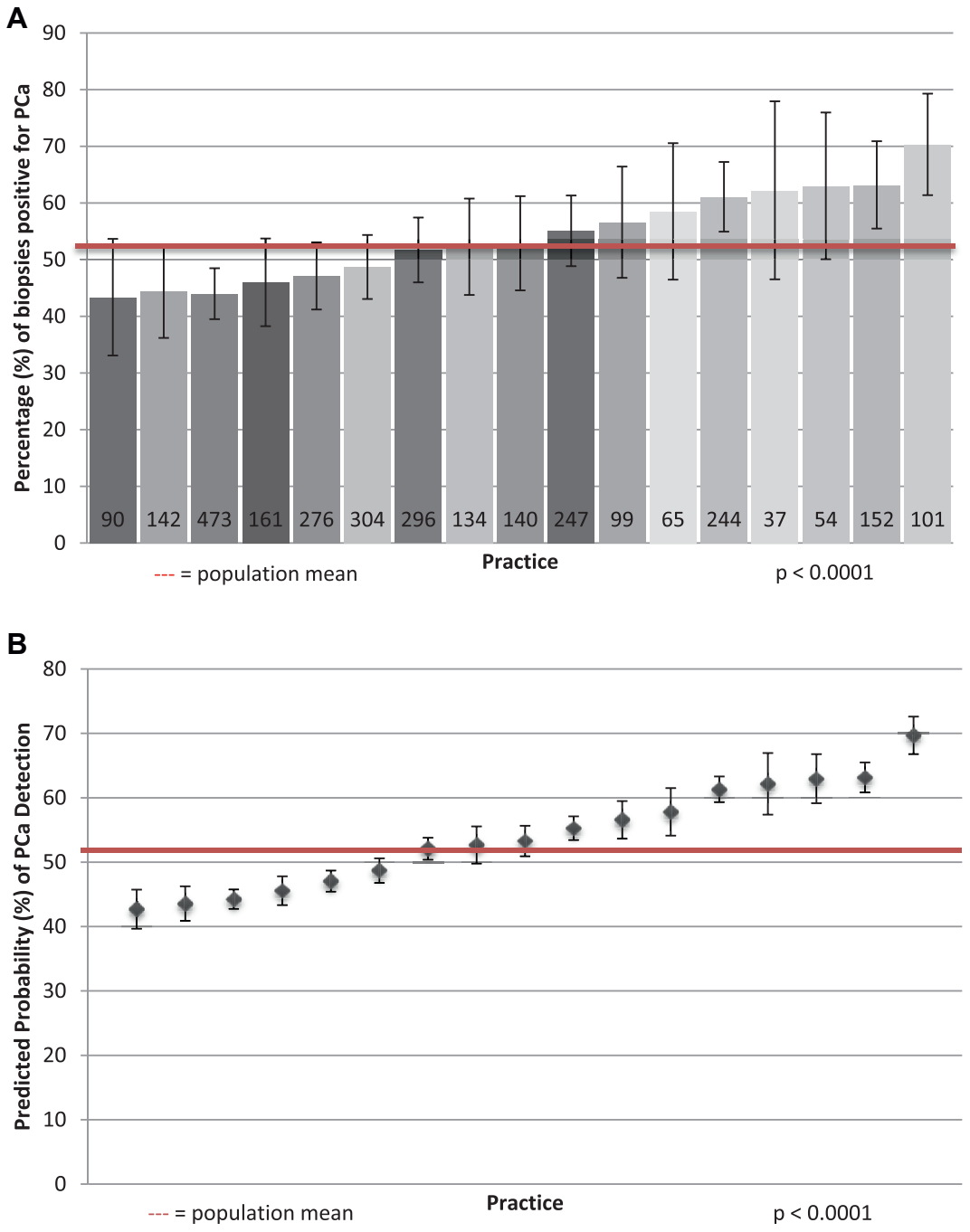
Overall 1,562 of these initial prostate biopsies (52%) were positive for PCa. In terms of patient characteristics PCa detection rates were associated with greater patient age, higher PSA, a smaller prostate, family history of PCa and abnormalities on DRE (tables 1 and 2). PCa was detected in 62% of biopsies in patients with a prostate of less than 30 cc compared to 39% in those with a prostate volume of greater than 60 cc. On multivariate analysis increasing age and PSA, smaller prostate size, positive family history and positive DRE findings were independently associated with cancer detection (table 2).

The cancer detection rate varied significantly across MUSIC practices (range 43% to 70%, $p < 0.0001$, part *A* of figure). Differences were due in part to different patient characteristics in each MUSIC practice (table 1). However, after accounting for patient age, PSA, prostate size, family history and DRE findings the overall predicted probability of detecting PCa at individual MUSIC practices ranged from 43% to 70% ($p < 0.0001$, part *B* of figure). In addition, variation in the proportion of positive biopsies across MUSIC practices was observed in almost every patient subgroup when stratified by known PCa risk factors (table 1). Taken together these data suggest that practice specific and/or provider specific factors may contribute to the PCa detection rate. For example, practice size correlated with PCa detection. The average PCa detection rate was 55.2%, 53.5% and 47.4% at practices with 1 to 4, 5 to 10 and more than 10 urologists, respectively

Table 2. *Multivariate analysis of association of risk factors with PCa detection*

	OR (95% CI)	
	Unadjusted	Adjusted*
Age:		
Less than 55	1	1
55–69	1.21 (0.98, 1.50)	1.32 (1.06, 1.67)
Greater than 69	1.76 (1.39, 2.23)	2.03 (1.56, 2.63)
PSA (ng/ml):		
Less than 4	1	1
4–10	1.98 (1.67, 2.34)	2.47 (2.04, 2.98)
Greater than 10	4.01 (3.07, 5.25)	4.93 (3.66, 6.63)
Median prostate vol (cc):		
Less than 30	1	1
30–60	0.67 (0.56, 0.80)	0.53 (0.44, 0.64)
Greater than 60	0.40 (0.32, 0.50)	0.23 (0.18, 0.29)
Family history:		
Neg	1	1
Pos	1.48 (1.25, 1.75)	1.44 (1.20, 1.74)
DRE findings:		
Neg	1	1
Pos	1.36 (1.15, 1.62)	1.54 (1.28, 1.87)

* Also adjusted for practice site.



PCa detection rates at initial prostate biopsy in 17 MUSIC practices. *A*, unadjusted. X-axis indicates number of initial biopsies performed at corresponding practice during study period. Variability was assessed by chi-square test. *B*, adjusted. Predicted probabilities of practice specific rates were derived from multivariate logistic regression models adjusting for patient age, family history, PSA, DRE findings and prostate size.

($p = 0.001$). The PCa detection rate of the highest and lowest volume practices was 61.2% and 48.12%, respectively ($p = 0.0122$).

DISCUSSION

Across Michigan 52% of men who undergo initial prostate biopsy are diagnosed with PCa. This proportion differs according to established clinical risk factors for PCa, including greater age, higher PSA, abnormal DRE findings and a smaller prostate, among other factors. Notably the cancer detection rate also varies significantly across diverse urology practices in the state even after adjusting for differences in patient characteristics. This observation suggests that provider and practice specific factors

are likely determinants of prostate biopsy pathology outcomes.

Generally speaking our findings are consistent with existing literature demonstrating that PCa detection rates in the PSA screening era are strongly influenced by a well-defined set of patient characteristics, including age, PSA, family history and abnormalities detected on prostate examination.[4–19] However, our results add to this literature in 2 important ways. The overall cancer detection rate in Michigan is higher than in previous reports showing that slightly less than a third of initial prostate biopsies are positive for cancer.[5–12,16,20–23] There are several potential explanations for this discrepancy. A possibility is that publication bias contributed to the difference with prior estimates. Namely in contrast to the population based data in the current study, prior reports were done largely at single institution academic centers. Alternatively the higher cancer rates that we report may indicate that more recent practice patterns involve better selection of candidates for prostate biopsy, particularly given heightened concern regarding false-positive and false-negative PSA tests, and potentially unnecessary prostate biopsies.

The other novel finding is the wide variation in cancer detection rates across urology practices. Such variation implies that local factors may strongly influence prostate biopsy outcomes. This observation may reflect important but less easily measured differences in biopsy selection criteria, divergent techniques and/or technology used during biopsy, and/or dissimilarities in pathological technique or expertise. Better understanding of these issues will prove crucial to ongoing efforts aimed at optimizing cancer detection by prostate biopsy.

This study has several limitations. 1) MUSIC data are currently reported at the practice level. This may have decreased our ability to understand how much variation was actually due to the selection criteria and techniques of individual providers.

2) There is no gold standard PCa detection rate. It is implied that higher PCa detection rates are a positive result but it is certainly plausible that an excessively high rate may indicate that screening is not done early enough in the disease course or lower risk tumors that may be better left undiscovered are over detected. Future studies of associations between positive biopsy rates and adverse pathological features, such as higher Gleason score and/or extraprostatic extension in radical prostatectomy specimens, may help us better understand this issue.

3) The prostate biopsy method is not standardized across MUSIC practices. Real world variability in technique is present in the current study and may have influenced the reported cancer detection rates. Although more than 99.9% of biopsies in this study were performed via a TRUS approach, there was some variation in sampling strategy with a 12-core approach documented for 72.5% of biopsies showing PCa. The number of biopsy cores was only recorded in men diagnosed with PCa, currently preventing us from correlating the detection rate with the number of cores. After recognizing this the MUSIC registry now collects the number of cores for all patients who undergo prostate biopsy, allowing future analysis of this factor.

4) Patient race was documented incompletely during the initial months of data collection in MUSIC. As a consequence, our analysis did not account for potential differences in cancer detection according to this risk factor. Because the demographics of patient panels is quite variable across MUSIC practices, this may account for some observed differences in the positive biopsy rate.[24] Importantly patient race is now collected routinely and will be available for followup analysis.

5) A final limitation is the lack of central pathological review in MUSIC. However, the MUSIC registry provides data on and analysis of the practice pattern of urologists across the state, which can be readily and realistically applied to providers nationally.

These limitations notwithstanding, our findings have important clinical and policy implications. The higher cancer detection rates reported are directly relevant to current controversies surrounding early detection practices for PCa. Namely achieving a higher cancer yield, particularly for high grade tumors, with prostate biopsy arguably alters the risk-benefit analysis that underlies recommendations for and against early detection policies. Also relevant to this debate are our findings in men 70 years old or older in whom evidence supporting benefits of early detection and treatment is less apparent. While cancer detection rates in Michigan are higher in this patient population, these men are also at greatest risk for overtreatment since they often have more significant competing health risks than younger men. Accordingly an important next step is to better understand the rationale for biopsy and subsequent treatment decisions in this group of patients.

Moving forward this study serves as the foundation for ongoing quality improvement efforts in MUSIC. In particular we are more deeply examining practice and provider specific selection criteria and biopsy techniques that may contribute to the variability in this study. Ultimately we hope to better define the role of each clinical factor in the decision to perform biopsy. Correlating this information with the likelihood of detecting PCa may

allow us to identify specific practice patterns that achieve a better yield with the first prostate biopsy. Quality improvement initiatives based on these findings have the potential to improve cancer detection rates further while also decreasing the frequency of biopsies that are likely to be low yield in terms of the likelihood of detecting cancer and the likelihood that the patient would benefit from treatment if cancer were found. Such study will prove essential to achieving an optimal balance between the detection of clinically relevant disease and the over diagnosis of tumors unlikely to lead to morbidity or mortality.

CONCLUSIONS

The average cancer detection rate at initial biopsy was 52% in Michigan with significant variability across individual practices. This heterogeneity in biopsy yield is likely related to the selection criteria used to recommend patients for prostate biopsy as well as other practice and potentially provider specific factors. Nonetheless, the extent to which different patient populations, referral patterns and equipment or technique contribute to this variability remains unclear. In the future better understanding of these issues will help urologists achieve an optimal balance between the detection of clinically relevant PCa and the over diagnosis of tumors unlikely to cause harm.

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