



Association between Literacy, Compliance with Prostate Cancer Screening, and Cancer Aggressiveness: Results from a Brazilian Screening Study

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ABSTRACT

Purpose: Little is known about the effects of literacy levels on prostate cancer screening. This study evaluates the association between literacy, compliance with screening, and biopsy findings in a large Brazilian screening study.

Materials and Methods: We analyzed 17,571 men screened for PCa with digital rectal examination (DRE) and total and free prostate-specific antigen (PSA) from January 2004 to December 2007. Of those, 17,558 men had information regarding literate status. Full urological evaluation in a specialized cancer center was recommended in the case of: a) suspicious DRE, b) PSA > 4.0 ng/mL, or c) PSA 2.5-3.9 ng/mL and free/total PSA (f/tPSA) ratio < 15%. Transrectal ultrasound guided prostate biopsy (14 cores) was performed upon confirmation of these findings after the patient's consent. Patients' compliance with screening recommendations and biopsy results were evaluated according to literacy levels.

Results: an abnormal PSA, a suspicious DRE, or both were present in 73.2%, 19.7%, and 7.1% of those men who underwent biopsy, respectively. PCa was diagnosed in 652 men (3.7%). Previous PSAs or DREs were less common among illiterate men ($p < 0.0001$). Additionally, illiterate men were less prone to attend to further evaluations due to an abnormal PSA or DRE ($p < 0.0001$). PSA levels > 10 mg/mL ($p = 0.03$), clinical stage > T2a ($p = 0.005$), and biopsy Gleason > 7 ($p = 0.02$) were more common among illiterate men.

Conclusions: In a screened population, literacy levels were associated with prior PCa evaluations and with compliance with screening protocols. Illiterate men were at higher risk of being diagnosed with more advanced and aggressive PCa.

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INTRODUCTION

Prostate cancer (PCa) is the most common non-cutaneous cancer and the second cause of

cancer mortality among men, regardless of geographic differences (1). In spite of recent evidence of the association between prostate cancer screening and reduced cancer specific mortality

rates (1,2) data on the effectiveness of screening measures are not uniform and there are important concerns with the magnitude of overdiagnosis (3,4). Therefore, several professional organizations recommend that physicians counsel their patients on the risks and benefits of screening, so that an informed decision about PCa testing can be made (5,6). Few studies discuss literacy levels as a variable that may affect screening efficacy (7,8). Men with low literacy levels may have less knowledge about PCa and may struggle with such complex decisions.

In Latin America, many underprivileged men do not have access to education or to the health care system (9). More specifically, in the Brazilian population, data concerning the relationship between literacy levels and PCa screening are lacking. It is also unknown whether literacy levels correlate with PCa aggressiveness or clinical stage at diagnosis in a screened population. Barretos Cancer Hospital (BCH) is a public institution located in the state of São Paulo, Brazil, which serves a large community of patients from many cities and states. As a tertiary healthcare center specialized in the treatment of cancer, it assists many men whose prostate cancers are suspected or diagnosed elsewhere and who are referred for diagnosis or treatment. Additionally, BCH conducts a study that utilizes five Mobile Cancer Prevention Units (MCPUs) offering opportunistic screening for some of the most common cancers (skin, breast, cervix and prostate) to patients in rural municipalities from six Brazilian states with poor access to specific health care, with the costs of screening, work up and treatment covered by the Brazilian public health system (9).

The purpose of this study was to verify whether illiterate Brazilian at our PCa screening study had higher risk of unfavorable disease, meaning higher PSA levels, more advanced clinical stage and higher Gleason score.

MATERIALS AND METHODS

From January 2004 to December 2007, 17,571 men aged ≥ 45 years voluntarily underwent prostate cancer screening at a mobile cancer prevention unit (MCPU) at least once. Of those, 17,558

men had information regarding literate status. This program included a total of 231 rural municipalities across six Brazilian states. Each MCPU had a general physician trained in performing prostate cancer screening (9). Men were evaluated by clinical history, digital rectal examination (DRE), and serum free and total prostate-specific antigen (PSA) levels. When men entered the MCPU they responded to our own general epidemiologic questionnaire applied by the physician, which included direct questions about urinary symptoms and literacy status. Regarding literacy two groups were defined: illiterate (men who had no formal education or were unable to read and write) and literate (men who had any degree of formal education or were able to read and write). Data regarding educational status were available for 17,558 men, who consisted of our final population. All PSA tests were performed with Hybritech® assays, and were analyzed by the same central laboratory.

Men with a suspicious DRE and/or serum PSA ≥ 4.0 ng/mL were recalled for further evaluation at BCH. From November 2004 onwards, men with serum PSA between 2.5 and 3.9 ng/mL, normal DRE and percentage of free/total PSA (%fPSA) $\leq 15\%$ were also recalled. Upon confirmation of screening data, a 14-core transrectal prostatic biopsy was performed at our center. All biopsies were evaluated at the same pathology laboratory. Cancers were staged according to the TNM system (American Joint Committee on Cancer Staging 2002) and the Gleason score was used for grade classification. The study protocol was reviewed and approved by the BCH ethics committee, and informed consent was obtained from all patients.

We compared variables about clinical data (PSA, clinical stage) and Gleason score in prostate biopsy between illiterate and literate men. Statistical analysis were performed using Epi info 6.02® software. Differences with $p < 0.05$ were considered statistically significant. This study was approved by Ethics Committee - number of protocol: 076/2007.

RESULTS

Mean age at the time of the first screening visit was 61.2 years (range 45 to 98 years), with more than 80% of men with ages between 50 and 74 ye-

ars. Regarding literacy status, of the 17,558 men analyzed, 3,403 (19.4%) were illiterate. Urinary symptoms were present in 1,697 men (9.7%). A total of 5,023 men (28.6%) had performed at least one DRE, and 5,108 men (29.1%) had performed at least one PSA prior to entering the study. Of the 17,558 men evaluated on this study, 2,841 (16.2%) were recalled for further evaluation; of these, 2,291 (80.6%) returned to the hospital appointment, and 1,647 (71.9%) underwent biopsy. Regarding those men with reported literacy status, PCa was diagnosed in 649 men, leading to a cumulative cancer detection rate of 3.7%. Among those biopsied, the main indication was a PSA > 4.0 ng/mL (54.9%), whereas in 19.7% of the men the indication was suspicious DRE findings in the presence of normal PSA levels (< 4.0 ng/mL).

Most prostate cancers (79.3%) were diagnosed in men aged 50 to 74 years. Overall, 285 (43.7%) had a PSA between 4 to 10 ng/mL, and 32.5% of the men had tumors of Gleason score > 7. Most screen-detected tumors (93.4%) were clinically localized (cT1-cT2).

The effect of literacy on the probability of previous screening tests is shown in Table-1. Of all men, 28.9% had received a previous DRE. Whilst 25.2% of illiterate men had undergone a previous DRE evaluation, the proportion of literate men who had undergone a previous DRE was greater (29.4%) ($p < 0.0001$). Likewise, 29.0% of the men had been previously tested for PSA at least once. Illiterate men were less likely to have been tested for PSA (23.4%) than men with higher education levels (30.4%) ($p <$

0.0001). Illiterate men were also less likely to comply with follow-up recommendation (69%) than literate men (87%) ($p < 0.0001$). Of 2,841 men who were recalled for further evaluation due to altered PSA and/or DRE, ten had missing data on literacy status, and were excluded from evaluation. Of 706 illiterate men who were recalled, 482 men (68.3%) complied with the requirements for further evaluation, whereas of 2,125 literate men who required further evaluation, 1,733 (81.6%) returned for reevaluation ($p < 0.01$).

The effect of literacy status on some of the most commonly reported independent prognostic variables of progression (PSA, clinical stage, biopsy Gleason) is shown in Table-2. A greater proportion of illiterate men had PSA levels > 10 ng/mL than literate men (36.6% versus 27.6%; $p = 0.03$). The probability of a locally advanced cancer (T3-T4) was also higher among illiterate men than among literates (11% vs. 7.7%; $p < 0.005$). Similarly, illiterate men had a greater proportion of cancers with biopsy Gleason scores > 7 (10.9% versus 5.9%; $p = 0.02$).

DISCUSSION

The introduction of PSA-based screening strategies has led to an increase of prostate cancer incidence in countries where it was adopted (1,10). Screen detected cancers tend to be of lower volume and stage, theoretically more amenable to curative therapies (11,12). Decreasing prostate cancer-specific mortality rates have been reported in countries with more widespread screening policies (1,2,13). Nevertheless, a lack of conclusive

Table 1 - Probability of previous DRE and PSA testing, and compliance with follow-up recommendation, according to literacy status.

Epidemiologic characteristics		Literacy status n total: 17,558		p value
		Illiterate n (%)	Literate n (%)	
Men with previous DRE	No (%)	2,546 (74.8)	9,994 (70.6)	$p < 0.001$
	Yes (%)	857 (25.2)	4,161 (29.4)	
Men with previous PSA	No (%)	2,608 (76.6)	9,849 (69.6)	$p < 0.001$
	Yes (%)	795 (23.4)	4,306 (30.4)	

Table 2 - Distribution of prognostic variables in cases of prostate cancers according to literacy status.

Clinical findings		Literacy Status n = 649		p value
		Illiterate n (%)	Literate n (%)	
PSA	0-10 (%)	99 (63.4)	357 (72.4)	p = 0.03
	> 10 (%)	57 (36.6)	136 (27.6)	
Clinical stage	T1 (%)	100 (64.5)	389 (77.1)	p < 0.005
	T2 (%)	38 (24.5)	75 (15.2)	
	T3-4 (%)	17 (11.0)	30 (7.7)	
Gleason score	≤ 7 (%)	139 (89.1)	464 (94.1)	p = 0.02
	8-10 (%)	17 (10.9)	29 (5.9)	

data from ongoing prospective, randomized trials of prostate cancer screening still poses it as a controversial issue (3,4).

Epidemiological data on prostate cancer in Latin America are still limited (14-16). In Brazil, where PSA-based screening is recommended by most specialty societies, the incidence of prostate cancer is considered intermediate. Due to both economic and demographic disparities, however, healthcare access is problematic for those men entirely dependent on the public health system. A recent report of our comparative data between screened and non-screened patients has shown that screened patients have less aggressive disease at diagnosis (17). However, determinants and motivations for screening are not always well understood.

One of the most widely used measurements of both social and economic status in health studies is the level of education, since it is relatively easy to ascertain, and potentially measurable (9). Education can translate the access to resources that may influence health status and more widespread use of preventive services. It is also recognized that the level of education influences health through the acquisition of certain higher cognitive functions and through effects in the adoption of healthier lifestyles (18,19). It is thus quite possible

that literacy status may influence the results of cancer screening. In fact, low literacy rates affect patient communication, leading to substandard medical care. Illiteracy is associated with poor understanding of written or spoken medical advice, adverse health outcomes, and under utilization of preventive services. In addition, advice on health issues may be ineffectively transmitted due to limited knowledge of cancer screening concepts, human anatomy and specific vocabulary (18,19). Cultural barriers and lack of adequate information have also been identified as potential factors affecting PCa screening, especially concerning DRE, since misconceptions about masculinity may prevent adequate evaluation (20). Men with low levels of information may also opt to leave decisions related to participation on PCa screening to their primary physician (8,21).

A common problem in analyzing results from PCa screening studies is screening contamination or number of men pre-screened before trial stated: a variable proportion of the participants are previously tested with PSA or DRE, which may give rise to misleading results and conclusions. In the Prostate, Lung, Colorectal and Ovarian (PLCO) trial about half of the patients in the screening group had already been tested at least once with

either PSA or DRE (3). In the European Randomized Study of Screening for Prostate Cancer (ERSPC), contamination was lower (ranging from 8.6% to 36.6%) (4,22). Regarding pre-screened men rates, in our study illiterate men had lower probability to have had a previous prostatic evaluation compared with more educated patients. We believe that the lack of knowledge about the benefits of screening and the poor availability of healthcare access were the most important factors accountable for this finding. The fact that about a third of our illiterate men did not comply to the recommendation of further evaluations at the university hospital (compared to 13% of literate men) may in part be due to the difficulty in understanding the implications of the initial findings.

Pre-treatment PSA is an independent surrogate marker of prognosis for prostate cancer after initial treatment (23-25). Patients with PSA < 4 ng/mL have an 80-90% probability of localized disease compared to 60-70% when PSA is > 10 ng/mL (23,25). In our screen-detected illiterate patients, the probability of having a PSA > 10 ng/mL was 25% higher than that of more educated men.

Stage migration is the most striking and consistent phenomenon associated with PCa screening (1,13,24,26). Data from ERSPC show a significant stage migration with screening, with a 7-fold reduction in the risk of locally advanced disease (4). Skip data from reference centers in the U.S. showed that lower education levels were independent predictors of higher stage at diagnosis (19). In our screening study, the differences in clinical stage among illiterate and literate patients were significant. About thirty-five percent of higher risk T3-4 tumors were observed among illiterate patients. Pre-treatment Gleason score is also considered an important predictor of pathologic features and of biochemical and clinical recurrence after the initial treatment of PCa (27,28). In our series, illiterate men had an almost 2-fold chance of harboring an aggressive tumor. It's difficult to explain these findings of more aggressive and advanced disease in illiterate men based in biological or genetic causes. More probably, the lower rate of previous screenings and the longer period of tumor evolution have contributed to the development of a disease of higher volume and tumor

aggressiveness. However, environmental, behavioral or other intangible factors associated with lower education rates may also be interacting in this clinical scenario.

Our study has several limitations. It was not a randomized, prospective study, and although literate and illiterate men were contemporary and of similar age range, intrinsic differences in their characteristics cannot be fully ascertained. Additionally, data on ethnicity were not available, since such these classifications in the largely multiethnic Brazilian population are difficult to attribute, as previously shown in genetic studies in Brazilian volunteers for prostate screening (29-31). Another limitation is that income data is not available, but the screening program was targeted to an underprivileged, uninsured population living in rural areas, with all work up and treatment performed by the public health system. Moreover, the outcome variables evaluated are at their best prognostic factors or surrogate markers of disease progression, and may not reflect real future reductions in cancer specific and overall mortality rates. This said, we acknowledge that differences associated with literacy status can only be at this point hypothesis-generating findings, and should not be seen as conclusive under this study design. In countries with a limited health budget, it is important to optimize costs and identify a population to which screening efforts may be more beneficial.

CONCLUSIONS

Illiterate screened men are somewhat less amenable to have been previously screened for PCa, and are less likely to follow recommendations of additional follow-up. Illiterate men have a significantly greater risk of harboring a more advanced and aggressive PCa. In our opinion, this is a priority population to whom PCa screening should be strongly considered.

ABBREVIATIONS

CBUG = Cooperative Brazilian Uro-oncology Group
 PCa = Prostate cancer
 BCH = Barretos Cancer Hospital

MCPU = Mobile Cancer Prevention Unit
 DRE = Digital rectal examination
 PSA = prostate-specific antigen
 %f/tPSA = percentage of free/total PSA
 PLCO = Prostate, Colorectal, Lung and Ovarian cancer screening
 ERSPC = European Randomized Study of Screening for Prostate Cancer

CONFLICT OF INTEREST

None declared.

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