UCSF

UC San Francisco Previously Published Works

Title

Outcomes of men on active surveillance for low-risk prostate cancer at a safety-net hospital.

Permalink

<https://escholarship.org/uc/item/2hf0h8wf>

Journal

Urologic oncology, 35(11)

ISSN

1078-1439

Authors

Osterberg, E Charles
Palmer, Nynikka RA
Harris, Catherine R
et al.

Publication Date

2017-11-01

DOI

10.1016/j.urolonc.2017.07.003

Peer reviewed

Original article

Outcomes of men on active surveillance for low-risk prostate cancer at a safety-net hospital

E. Charles Osterberg, M.D.^{a,c}, Nynikka R.A. Palmer, Dr.P.H., M.P.H.^{a,b},
Catherine R. Harris, M.D., M.P.H.^a, Gregory P. Murphy, M.D.^a, Sarah D. Blaschko, M.D.^a,
Carissa Chu, M.D.^a, Isabel E. Allen, Ph.D.^a, Matthew R. Cooperberg, M.D., M.P.H.^a,
Peter R. Carroll, M.D., M.P.H.^a, Benjamin N. Breyer, M.D., M.A.S.^{a,*}

^a Department of Urology, University of California San Francisco, San Francisco, CA

^b Department of Medicine, University of California San Francisco, San Francisco, CA

^c Department of Surgery, Dell Medical School, University of Texas, San Francisco, CA

Received 27 April 2017; received in revised form 6 June 2017; accepted 1 July 2017

Abstract

Purpose: To characterize demographic, disease, and cancer outcomes of men on active surveillance (AS) at a safety-net hospital and characterize those who were lost to follow-up (LTFU).

Methods: From January 2004 to November 2014, 104 men with low-risk prostate cancer (PCa) were followed with AS at Zuckerberg San Francisco General Hospital (ZSFG). Criteria for AS have evolved over time; however, patients with diagnostic prostate-specific antigen (PSA) 10 ng/mL or less, clinical stage T1/2, biopsy Gleason score 3 + 3 or 3 + 4, 33% or fewer positive cores, and 50% or less tumor in any single core were potentially eligible for AS. Men were longitudinally followed with a PSA or digital rectal examination or both every 3 to 6 months, and repeat prostate biopsy every 1 to 2 years. Clinical staging and grading were based on a physical examination and at least a 12-core biopsy, respectively. LTFU was defined as failure to successfully contact patients with 3 phone calls or any urology visit recorded within 18 months from a prior visit or biopsy. A secondary chart review was performed using the electronic medical record at ZSFG as well as EPIC Systems CareEverywhere which allows access to select non-ZSFG institutions to confirm that patients were truly LTFU.

Results: Among the 104 men on AS at ZSFG, the median age at diagnosis of PCa was 61.5 years (range: 44–81). The median follow-up period was 29 months (range: 0–186 months) during which 18 (17.3%) men were LTFU and 48 (46%) remained on surveillance. Men underwent a median of 7 (1–21) serum PSA measurements and an average of 2 prostate biopsies (1–5). In total, 22 (20.6%) men had definitive treatment with the median time from diagnosis to active treatment being 26 (range: 2–87) months. Radiation therapy was more common than radical prostatectomy (12.5% vs. 7.7%). There was 1 PCa-related death and 3 noncancer deaths. Initial adherence to AS was poor; however, men committed to AS initially were ultimately more compliant over time.

Conclusion: AS for low-risk PCa is challenging among a vulnerable population receiving care in a safety-net hospital, as rates of LTFU were high. Our findings suggest the need for AS support programs to improve adherence and follow-up among vulnerable and underserved populations. © 2017 Elsevier Inc. All rights reserved.

Keywords: Active surveillance; Prostate cancer; Safety-net hospital; Patient compliance

1. Introduction

Differential access to health care for uninsured patients remains challenging owing to financial and nonfinancial barriers [1]. Race/ethnicity, cultural differences, language

barriers, and provider proximity are all important factors for uninsured or Medicaid beneficiaries to ensure appropriate follow-up [2]. After a diagnosis of cancer, routine follow-up is often required. This may present challenges for low-income individuals who have limited resources to prioritize health care [3].

For men with low-risk prostate cancer (PCa), patient compliance, follow-up, and access to care are essential

* Corresponding author. Tel.: +1-415-476-2105; fax: +1-415-476-8849.
E-mail address: Benjamin.breyer@ucsf.edu (B.N. Breyer).

components for active surveillance (AS). Current data support AS as a preferred strategy for most men with low-risk PCa [4,5]. In fact, men with low-risk PCa are urged to strongly consider surveillance, as the risks of immediate surgery or radiation may outweigh any benefits [6]. Under strict surveillance, men will require periodic assessment including prostate biopsies and serial serum prostate-specific antigen (PSA) testing [7]. Compliance with AS presents challenges for some patients as many protocols require quarterly screening and biennial biopsies. In 1 longitudinal AS cohort, 5% of men were lost to follow-up (LTFU) [8].

To date, it is unknown if AS is feasible in a safety-net hospital that serves primarily uninsured and Medicaid beneficiaries. Furthermore, the natural history of men on AS in a safety-net hospital is poorly understood. Our group has previously reported that men presenting to an inner-city, safety-net hospital have higher PSA levels, Gleason scores, Cancer of the Prostate Risk Assessment (CAPRA) scores [9], and ultimately higher burden of disease [10]. As such, these patient populations warrant close follow-up, especially those electing AS.

Our primary objective is to characterize men who initiated AS for PCa at a safety-net, county hospital and describe the natural history of AS in men, specifically the clinical and demographic features. We hypothesize that men on AS within a safety-net hospital represent a unique cohort of men with varying socioeconomic factors and disease-specific factors that may challenge the feasibility of AS.

2. Materials and methods

2.1. Study population

In the state of California, Medi-Cal is the state health care Medicaid benefit program for low-income individuals, serving roughly 12 million beneficiaries [11]. Of the patients enrolled in Medi-Cal, approximately 75% of the population is nonwhite and represent diverse groups including African Americans, Asians/Pacific Islanders, and Hispanics/Latinos. [11] For the uninsured of San Francisco, *Healthy San Francisco* (<http://healthysanfrancisco.org/>) provides an income-based sliding-scale to ensure health care benefits.

Zuckerberg San Francisco General Hospital (ZSFG) is the main public hospital for the City and County of San Francisco, California. It is designated by the Department of Public Health as a safety-net hospital and provides most of the health care services for low-income patients using Medi-Cal or uninsured patients using *Healthy San Francisco*, respectively. It is estimated that roughly 80% of ZSFG's patients use Medi-Cal or are uninsured [12]. ZSFG is vital to northern California, serving a vulnerable population including recent immigrants, elderly, disabled, disadvantaged, or homeless, or all of these.

2.2. Active surveillance at ZSFG

Currently, patients with diagnostic PSA of 10 ng/mL or less, clinical stage T1 or T2, biopsy Gleason scores 3 + 3 or 3 + 4, 33% or fewer positive cores, and 50% or less tumor in any single core are eligible for AS [13]. This has been refined further with the use of PSA density. Confirmatory 12-core prostate biopsy was recommended within 12 to 18 months of a patient's initial diagnostic biopsy to ensure adequate sampling. AS for men with low- or intermediate-risk PCa who agreed to undergo PSA screening every 3 to 6 months and a repeat biopsy every 1 to 2 years were eligible for AS at ZSFG [13–15].

2.3. Definitions of variables

A retrospective review was performed on all patients diagnosed with low-risk PCa at ZSFG who elected for AS after consultation.

Sociodemographic variables collected included age, race/ethnicity, primary language spoken, medical comorbidities, family history of PCa, and history of mental illness. Clinical data included the PSA, biopsy Gleason score, clinical stage at the time of PCa diagnosis, number of biopsy cores, number of positive cores, and CAPRA scores [9].

Variables prospectively collected and retrospectively reviewed included follow-up time, number of PSA tests, and number of follow-up biopsies. Patient outcomes included treatment received (radical prostatectomy, radiation therapy, and androgen deprivation therapy), pathologic upgrading results, and the time from diagnosis to treatment.

All prostate biopsies were performed at ZSFG, and pathology review was done internally. Patients were flagged by the electronic medical record (EMR) as LTFU after failure to contact a patient after 3 repeated phone calls, which were prompted after a missed clinic appointment. Among these patients, an in-depth chart review was performed using the EMR at ZSFG as well as EPIC Systems *CareEverywhere* that allows EMR access to non-ZSFG institutions in Northern California (e.g., UCSF, Kaiser Permanente). Following this, we defined LTFU as failure to undergo a repeat examination or a lack of serum PSA evaluation after 18 months either at ZSFG or a participating hospital in *CareEverywhere*. Our primary outcome of interest was the clinicopathologic characteristics of men on AS at ZSFG and the follow-up rates.

2.4. Statistical analysis

We used descriptive statistics to report patients' sociodemographic, clinical, and surveillance outcomes; medians and ranges for continuous variables; and number and percentage for categorical data. Kaplan-Meier curves were constructed to examine the prevalence of adherence to PSA testing every 3 to 6 months and prostate biopsies every 1 to 2 years while on AS. All statistical analyses were performed

Fig. 1. Flow chart of outcomes of patients with low-risk prostate cancer followed on active surveillance.

using IBM SPSS Statistics 23 (SPSS Inc., Chicago, IL). The institutional review board at University of California, San Francisco, approved this study.

3. Results

3.1. Baseline demographics, pathologic characteristics, and outcomes

From January 2004 to November 2014, 386 men were evaluated at ZSFG for low-risk PCa and met criteria for AS. Of these, 104 (27%) chose surveillance, and 48 remained on AS at last follow-up (Fig. 1). The median age at diagnosis of PCa was 61.5 years (range: 44–81) (Table 1). Our study population consisted of 29.8% Asian/Pacific Islander, 28.8% African American/Black, 15% Hispanic/Latino, and 25% White patients.

Almost half of the men had a history of 3 or more comorbidities (46.2%), with the most common being hypertension (68.3%), hyperlipidemia (55.8%), diabetes (26.9%), and mental illness (23.1%). A smaller percentage of patients had a documented history of tobacco use (35%), substance abuse (19.2%), homelessness (5.8%), and a family history of PCa (8.7%). At the time of diagnosis, the median PSA was 6.0 (range: 0.8–14.2). A median of 12 biopsy cores were taken (range: 6–16), with at least 1 core being positive (range: 1–4). Most men had a Gleason score of 3 + 3 (97.1%) and were clinical stage T1c (80.8%) at the time of diagnosis.

In Table 2, we present outcomes of active surveillance. The median follow-up period was 29 months (range: 0–186). There were 5 men who were followed for less than 1 month. Most men (92%) had at least 1 follow-up PSA test, with a median of 7 PSA tests (range: 1–21). On average, men underwent 2 prostate biopsies (range: 1–5).

Upgrading on repeat biopsy occurred in 19 men (18.3%), all of whom underwent treatment. In addition to these men,

Table 1

Sociodemographics and clinical characteristics among men on active surveillance at a public hospital (N = 104)

Demographic characteristics	Median (N)	Range (%)
Age at diagnosis (y)	61.5	44–81
Race/ethnicity		
African American/Black	30	(29)
Asian American/Pacific Islander	31	(30)
Hispanic/Latino	16	(15)
White, non-Hispanic/Latino	26	(25)
Other	1	(1)
Primary language		
English	66	(64)
Spanish	9	(9)
Chinese (Mandarin/Cantonese)	17	(16)
Other	12	(12)
Social history		
History of tobacco use	36	(35)
History of substance abuse	20	(19)
History of homelessness ^a	6	(6)
Medical history		
Comorbidities ^b	2.0	0–7
0	10	(10)
1	20	(19)
2	26	(25)
3 or more	48	(46)
History of mental illness ^b	24	(23)
Family history of prostate cancer	9	(9)
Clinical characteristics ^c		
PSA (ng/mL)	6.0	0.8–14.2
Biopsy cores	12	6–16
Biopsy cores positive	1	1–4
Gleason score		
6 (3 + 3)	101	(97)
7 (3 + 4)	3	(3)
Clinical stage		
T1c	84	(81)
T2a	11	(11)
T2b	3	(3)
T2c	1	(1)
Unknown	4	(4)

^aOne patient incarcerated.

^bTotal comorbidities include history of mental illness.

^cAt the time of diagnosis.

3 more men sought active treatment, for a total of 22 (20.6%) men that received definitive treatment. The median time from diagnosis to active treatment was 26 months (range: 2–87). Radiation therapy was more common than radical prostatectomy (12.5% vs. 7.7%), and 2 patients started androgen deprivation therapy as primary therapy for unclear reasons. Pathologic upgrading following radical prostatectomy occurred in 6 men. PSA remained undetectable or without rise in 12 men and increased in 1 patient.

3.2. Natural history and follow-up

The natural history of men on AS in a safety-net hospital yielded 1 cancer-related death and 3 deaths from noncancer

Table 2
Outcomes of patients on active surveillance

Outcomes	Median (N)	Range (%)
Follow-up period (mo)	29	0–186
Number of follow-up PSA tests	7	1–21
Number of follow-up biopsies	2	1–5
Upgraded on repeat biopsy or prostatectomy	19	(18)
Received treatment	22	(21)
Radical prostatectomy	8	(8)
Radiation therapy	13	(13)
Androgen deprivation therapy	2	(2)
Time from diagnosis to treatment (mo)	26	2–87

Note: Radiation therapy includes external beam radiation and brachytherapy. Prostatectomy includes with lymph node dissection and without.

etiologies (cardiopulmonary arrest). The 1 patient who died of disease was LTFU for 30 months after his prostate biopsy. Before this, he had a prebiopsy PSA of 9.6, CAPRA score of 4, and Gleason 3 + 4 cancer in 2 cores. Upon returning for follow-up, the patient had metastatic disease and was started on androgen deprivation therapy. His PSA doubling time was 11.5 months.

Of the 104 men originally enrolled in AS, 18 men transitioned to expectant management. These men were on AS for a median of 6 years before deferring repeated PSA measurements or prostate biopsies or both. At the time of transition off AS, all men were more than 70 years of age (median = 73).

Over the median follow-up period of 29 months, 30 (31%) patients were unable to be reached after 3 attempted phone calls, and thus were flagged by EMR as LTFU. Subsequent chart review using *CareEverywhere* demonstrated that 12 men sought care outside of ZSFG, lowering the number of LTFU to 18 men (17.3%). The median CAPRA score for men who were LTFU previously on AS was 1 (range: 1–4).

Fig. 2 demonstrates a Kaplan-Meier curve for the percentage of men who were adherent to AS screening by PSA testing every 3 to 6 months (Fig. 2A) or prostate biopsy every 12 to 24 months (Fig. 2B). Over time, the rate of repeat PSA and biopsy adherence decreased to under 10% for both at roughly 10 years.

4. Discussion

In a retrospective review of men on AS in a safety-net hospital, we characterize the demographic, social, clinico-pathologic features, and outcomes of men with PCa. Among a vulnerable population with limited resources, we determined that over a median follow-up of 29 months, the median number of serum PSA checks was 7 and the median number of biopsies per patient was 2. Despite this, by approximately 5 years, adherence with serial PSA checks decreased to 20%.

Our reported rates of LTFU were higher than that reported in larger AS cohorts. Klotz et al. [8] report an

LTFU rate of 5% (24/450) among men on a prospective AS program. Similarly, roughly 10% of men were LTFU among the Johns Hopkins Active Surveillance program [16]. In another prospective series of 157 men, the LTFU rate was 22% [17], and unpublished data from the University of Texas and MD Anderson Cancer Center report a 22% LTFU rate among 50 men on AS at Ben Taub Hospital, a safety-net hospital (<http://meetinglibrary.asco.org/content/142099-159>). Most recently, unpublished data from Los Angeles County Hospital describes an LTFU rate of 48% among 116 men on AS (<http://meetinglibrary.asco.org/record/140573/abstract>). On multivariable analysis, patients were more likely to be LTFU if they had a lower household income.

These data corroborate our hypothesis that men within a safety-net hospital present unique challenges for PCa surveillance. Mental illness, homelessness, nonnative English language, and substance abuse may be the contributing factors for LTFU, as noted in our population. Although not measured, literacy and numeracy barriers may further limit patients' understanding of an AS protocol. The direct effect such socioeconomic factors may have on LTFU is unknown.

Nevertheless, we demonstrate that almost half of our population received regular PSA testing and prostate biopsies within the recommended AS screening period. Over time, the rate of repeat PSA and biopsy adherence decreased. During the initial period on AS, the percentage of men adherent to repeat PSA or biopsies or both were high.

Despite the Affordable Care Act, health care coverage still leaves just under 25 million Americans uninsured [18]. Current studies report that insurance coverage is associated with a lower disease burden, earlier stage of PCa diagnosis, and better outcomes of cancer control [19,20]. However, we have previously shown that men presenting to a county hospital have a higher burden of disease [10]. Current data call into question the safety of AS for African American men [21], of which 29% of our cohort self-identified as African American; however, other studies call into question these findings [22,23].

Understanding the natural history of AS in a safety-net hospital is critical to maximizing high-quality care. Although the future of the Affordable Care Act is unknown, it is clear that this population requires a cohesive health care system that is easy to access.

There are several limitations to this descriptive study. With a short follow-up time, this study was not intended to capture overall survival nor cancer-specific survival; therefore, the safety of AS in a safety-net hospital cannot be concluded. This was a retrospective chart review that has inherent biases. Specifically, patient-reported outcomes and social factors are not universally captured by our EMR and are likely underestimated. Future directions of AS programs in safety-net hospitals should target disease registries whereby long-term follow-up tracking of patients

Fig. 2. Percentage of men adherent to AS by (A) prostate-specific antigen (PSA) testing and (B) prostate biopsy.

is centrally maintained across regional health networks to prevent LTFU. In addition, future directions should focus on standardizing AS programs across both the private and the public health care sectors. Refinements in imaging and advanced genomic PCa markers will greatly benefit vulnerable populations by identifying those who are at low risk for cancer progression.

5. Conclusions

Men on AS in a safety-net hospital present unique challenges. Patient compliance and follow-up care are critical components of PCa surveillance. Proportions of men on AS who were LTFU at ZSFG were greater than

those in large AS cohorts. Safety-net hospitals play a critical role in delivering high-quality care to underserved and vulnerable patient populations.

Author's contributions

Osterberg—protocol/project development, Manuscript writing/editing.

Palmer—data collection or management and data analysis.

Harris—manuscript writing/editing.

Murphy—data collection or management.

Blaschko—data collection or management.

Chu—manuscript writing/editing.

Allen—data collection or management and data analysis.
Cooperberg—protocol/project development and manuscript writing/editing.

Carroll—protocol/project development and manuscript writing/editing.

Breyer—protocol/project development and manuscript writing/editing.

Informed consent

Informed consent was obtained from all individual participants included in the study

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional or national research committee or both, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

- [1] Chau S, Chin M, Chang J, Luecha A, Cheng E, Schlesinger J, et al. Cancer risk behaviors and screening rates among homeless adults in Los Angeles County. *Cancer Epidemiol Biomarkers Prev* 2002;11: 431–8.
- [2] Miller DC, Gelberg L, Kwan L, Stepanian S, Fink A, Andersen RM, et al. Racial disparities in access to care for men in a public assistance program for prostate cancer. *J Community Health* 2008;33:318–35.
- [3] Nonzee NJ, Ragas DM, Ha Luu T, Phisuthikul AM, Tom L, Dong X, et al. Delays in cancer care among low-income minorities despite access. *J Womens Health (Larchmt)* 2015;24:506–14.
- [4] Cooperberg MR, Carroll PR. Trends in management for patients with localized prostate cancer, 1990–2013. *J Am Med Assoc* 2015;314:80–2.
- [5] Ganz PA, Barry JM, Burke W, Col NF, Corso PS, Dodson E, et al. National Institutes of Health State-of-the-Science Conference: role of active surveillance in the management of men with localized prostate cancer. *Ann Intern Med* 2012;156:591–5.
- [6] Punnen S, Cowan JE, Chan JM, Carroll PR, Cooperberg MR. Long-term health-related quality of life after primary treatment for localized prostate cancer: results from the CaPSURE registry. *Eur Urol* 2015;68:600–8.
- [7] Dall'Era MA, Albertsen PC, Bangma C, Carroll PR, Carter HB, Cooperberg MR, et al. Active surveillance for prostate cancer: a systematic review of the literature. *Eur Urol* 2012;62:976–83.
- [8] Klotz L, Zhang L, Lam A, Nam R, Mamedov A, Loblaw A. Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. *J Clin Oncol* 2010;28:126–31.
- [9] Cooperberg MR, Pasta DJ, Elkin EP, Litwin MS, Latini DM, Du Chane J, et al. The University of California, San Francisco Cancer of the Prostate Risk Assessment score: a straightforward and reliable preoperative predictor of disease recurrence after radical prostatectomy. *J Urol* 2005;173:1938–42.
- [10] Porten SP, Richardson DA, Odisho AY, McAninch JW, Carroll PR, Cooperberg MR. Disproportionate presentation of high risk prostate cancer in a safety net health system. *J Urol* 2010;184:1931–6.
- [11] Pourat N, Martinez AE, Kominski GF. Californians newly eligible for Medi-Cal under health care reform. *Policy Brief UCLA Cent Health Policy Research*; 2011. p. 1–7.
- [12] Chen AH, Kushel MB, Grumbach K, Yee HF Jr. Practice profile. A safety-net system gains efficiencies through “eReferrals” to specialists. *Health Aff (Millwood)* 2010;29:969–71.
- [13] Welty CJ, Cowan JE, Nguyen H, Shinohara K, Perez N, Greene KL, et al. Extended followup and risk factors for disease reclassification in a large active surveillance cohort for localized prostate cancer. *J Urol* 2015;193:807–11.
- [14] Cooperberg MR, Carroll PR, Klotz L. Active surveillance for prostate cancer: progress and promise. *J Clin Oncol* 2011;29:3669–76.
- [15] Dall'Era MA, Cooperberg MR, Chan JM, Davies BJ, Albertsen PC, Klotz LH, et al. Active surveillance for early-stage prostate cancer: review of the current literature. *Cancer* 2008;112:1650–9.
- [16] Tosoian JJ, Trock BJ, Landis P, Feng Z, Epstein JI, Partin AW, et al. Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. *J Clin Oncol* 2011;29:2185–90.
- [17] Hefermehl LJ, Disteldorf D, Lehmann K. Acknowledging unreported problems with active surveillance for prostate cancer: a prospective single-centre observational study. *BMJ Open* 2016;6: e010191.
- [18] Mahal BA, Aizer AA, Ziehr DR, Hyatt AS, Lago-Hernandez C, Chen YW, et al. The association between insurance status and prostate cancer outcomes: implications for the Affordable Care Act. *Prostate Cancer Prostatic Dis* 2014;17:273–9.
- [19] Fedewa SA, Etzioni R, Flanders WD, Jemal A, Ward EM. Association of insurance and race/ethnicity with disease severity among men diagnosed with prostate cancer, National Cancer Database 2004–2006. *Cancer Epidemiol Biomarkers Prev* 2010;19:2437–44.
- [20] Sadetsky N, Lubeck DP, Pasta DJ, Latini DM, DuChane J, Carroll PR. Insurance and quality of life in men with prostate cancer: data from the Cancer of the Prostate Strategic Urological Research Endeavor. *BJU Int*. 2008;101:691–7.
- [21] Sundi D, Ross AE, Humphreys EB, Han M, Partin AW, Carter HB, et al. African American men with very low-risk prostate cancer exhibit adverse oncologic outcomes after radical prostatectomy: should active surveillance still be an option for them? *J Clin Oncol* 2013;31:2991–7.
- [22] Jalloh M, Myers F, Cowan JE, Carroll PR, Cooperberg MR. Racial variation in prostate cancer upgrading and upstaging among men with low-risk clinical characteristics. *Eur Urol* 2015;67:451–7.
- [23] Leapman MS, Freedland SJ, Aronson WJ, Kane CJ, Terris MK, Walker K, et al. Pathological and biochemical outcomes among African-American and Caucasian men with low risk prostate cancer in the SEARCH database: implications for active surveillance candidacy. *J Urol* 2016;196:1408–14.