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Long-term outcomes of active surveillance for prostate cancer – the Memorial Sloan Kettering Cancer Center experience

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Abstract

Purpose: To report oncologic outcomes for men with Grade Group 1 prostate cancer managed with active surveillance (AS) at a tertiary cancer center.

Materials and Methods: 2,907 patients were managed with AS between 2000–2017 of whom 2,664 were Grade Group 1. Patients were recommended confirmatory biopsy to verify eligibility and were followed semi-annually with prostate-specific antigen (PSA), digital rectal examination (DRE) and review of symptoms. Magnetic resonance imaging (MRI) was increasingly used in recent years. Biopsy was repeated every 2–3 years or after a sustained PSA increase or changes in MRI/DRE. The Kaplan-Meier method was used to estimate probabilities of treatment, progression, and development of metastasis.

Results: The median age at diagnosis was 62 years. For men with Grade Group 1 prostate cancer, the treatment-free probability at 5, 10, and 15 years was 76% (95% CI 74%–78%), 64% (95% CI 61%–68%), and 58% (95% CI 51%–64%), respectively. At 5, 10, and 15 years, there were 1,146, 220, and 25 men at risk for metastasis, respectively. The median follow-up for those without metastasis was 4.3 years (95% CI 2.3, 6.9). Five men developed distant metastasis. Upon case note review, only two of these men were deemed to have disease that could have been cured on immediate treatment. The risk of distant metastasis was 0.6% (95% CI 0.2%–2.0%) at 10 years.

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Conflict of interest: Sigrid Carlsson has received a lecture honorarium and travel support from Astellas Pharma (unrelated to current study). Andrew Vickers is named on a patent for a statistical method to detect prostate cancer that has been commercialized by OPKO Health. Andrew Vickers receives royalties from sales of the test and has stock options in OPKO Health.

Conclusions: AS is a safe strategy over longer follow-up for appropriately selected patients with Grade Group 1 following a well-defined monitoring plan.

INTRODUCTION

Randomized trials comparing observation to radical treatment with surgery or radiation have failed to demonstrate a clear long-term benefit of immediate treatment of low-risk prostate cancer, thus supporting the use of initial conservative management of these men to reduce the risks of overtreatment and side-effects.[1–4] First described in 2002,[5] active surveillance (AS) is a conservative management strategy that involves careful monitoring of disease progression with prostate specific antigen (PSA) and regular biopsy, with the intent to give curative treatment in the event that progression is detected. AS has become increasingly accepted as a primary treatment option for patients with favorable-risk prostate cancer, and is now recommended by a growing body of clinical guidelines worldwide.[6] The 2017 AUA/ASTRO/SUO Guideline recommends AS as the best available care option for very low-risk localized prostate cancer and the preferable care option for most low-risk localized prostate cancer patients.[7] Although the U.S. Cancer of the Prostate Strategic Urologic Research Endeavor registry has documented minimal use of AS from 1990 to 2009 (approximately 10%), there has been a sharp increase in the uptake of AS between 2010 and 2013 (40% [95% CI, 35%–46%]).[8] Several other contemporary population-based registries around the world now report a similar pattern.[9–14] Sweden reports the highest rates of AS, with very high uptake (74%) among men with low-risk prostate cancer and almost complete uptake (91%) among men with very low-risk prostate cancer.[12]

Approximately 10 groups worldwide have now reported outcomes of prospective AS cohorts.[15–17] However, most series are rather small (< 500 patients) and currently have a short median follow-up of approximately 5 years. Only 3 series (Prostate Cancer Research International Active Surveillance, Johns Hopkins, and Toronto) comprise more than 900 patients and have reported follow-up at 10 or 15 years.[15, 17–20] Moreover, because these cohorts used different eligibility criteria and regimens for follow-up, the 15-year prostate cancer mortality risk varies between 0.1% (Hopkins[20]; restrictive criteria) and 5.7% (Toronto[19]; inclusive criteria).[15, 18–21] In order to provide accurate counseling for men considering contemporary AS estimates of oncologic outcomes from large-scale, long-term, contemporary prospective cohorts are needed. We used the long-term experience at our institution to estimate the oncologic safety of AS for men with Grade Group 1 prostate cancer.

MATERIALS AND METHODS

After institutional review board approval, we retrospectively queried our prospectively maintained database of prostate cancer patients at Memorial Sloan Kettering Cancer Center. Between 2000 and 2017, we identified 2,907 patients diagnosed with low- or intermediate risk prostate cancer who were managed with active surveillance during 2000 to 2017, identified as: either patients with low- or intermediate-risk prostate cancer who had a confirmatory biopsy within 6 months of diagnosis and did not receive treatment within a year, or a review of their medical charts outlining an expectant management strategy. We

performed a chart review of all patients to assess the expectant management strategy employed. As reported previously[22, 23], patients were recommended confirmatory biopsy to confirm eligibility, although this was not standard practice in the earliest years of AS; our protocol was initially to include Gleason Score 6, ≤ 3 cores, with confirmatory biopsy and yearly biopsy, which was changed overtime with the inclusion of MR imaging and newer biopsy techniques as well as developing knowledge about AS, to Gleason Score 6 (Grade Group 1), no core limitations, or Gleason Score 3+4 (Grade Group 2), clinical stage ≤ T2B, confirmatory biopsy and biopsy every 2–3 years. Here we report the outcomes for 2,664 men with Grade Group 1. There was no restriction on number of positive biopsy cores or PSA levels.

Patients were followed semi-annually with digital rectal examination (DRE), total PSA measurement, and a review of general health and symptoms. In more recent years, magnetic resonance imaging (MRI) became increasingly used as an adjunctive tool to confirm eligibility and as part of monitoring every 18 months. Non-targeted systematic biopsy was generally repeated every 2 to 3 years. More recently, MRI/ultrasound fusion targeted biopsy of suspicious lesions on multiparametric (T2-weighted, diffusion-weighted and/or dynamic contrast-enhanced) MRI was more frequently used. Historically, biopsies may have been performed yearly. All cases (diagnostic and surveillance biopsies) were reviewed by subspecialty urologic pathologists at the institution. If there was a change in PSA or MRI, biopsy was performed prior to the 3-year follow-up. Triggers for intervention included patient preference or progression to higher grade (progression was defined as presence of any Gleason grade 4 on biopsy, ie Grade group ≥2) or higher stage (T2c or T3) on DRE or imaging.

Statistics

Time to progression, treatment, distant metastasis, and death were estimated using the Kaplan-Meier method. Because of a small number of deaths from other causes, competing risks analysis was not performed. Patients who did not develop metastasis were censored at the last date of contact with the clinic. Because inclusion criteria for AS have changed over time, we hypothesized that the average age at diagnosis would be lower in more recent study years. To illustrate this, we used locally weighted polynomial regression to plot the relationship between age at diagnosis and calendar year. Similarly, because inclusion criteria for AS were not restricted to very low risk disease (eg included high-volume Grade Group 1), we hypothesized that the oncologic risk would increase over time. We calculated baseline (“preoperative”) risk of non-organ confined disease for all patients using the Memorial Sloan Kettering Cancer Center pre-radical prostatectomy nomogram[24] – a predictive model based on the PSA level, clinical T stage, Gleason grade, and number of positive and negative cores – and plotted the relationship between risk and calendar year using locally weighted polynomial regression. All statistical analyses were performed using Stata 15.0 (StataCorp, College Station, TX, USA).

RESULTS

Between 2000 and 2017, a total of 2,907 patients were monitored by AS at our institution. Here we report the outcomes of men with Grade Group 1 prostate cancer (N=2,664; 92% of our AS population). The number of men in the AS cohort at our center increased sharply over time (Supplementary Figure 1).

Patient and tumor characteristics are described in Table 1. The median age at diagnosis was 62 years (IQR 57, 68). Consistent with the prevalence of PSA screening and early detection during this time period, 89% of men had non-palpable tumors. The majority of patients presented with very low risk disease.

The risk of progression from Grade Group 1 to Grade Group 2 or 3 at 5, 10, and 15 years was 24% (95% CI 22%–26%), 36% (95% CI 33%–39%), and 41% (95% CI 35%–46%), respectively. While reasons for triggers for intervention was not routinely captured in the research database, it can be inferred that the main reason for intervention was grade progression, as it was highly correlated with treatment (Figure 1). Over time, 552 men received treatment. The treatment-free probability at 5, 10, and 15 years after the start of AS was 76% (95% CI 74%–78%), 64% (95% CI 61%–68%), and 58% (95% CI 51%–64%), respectively. Of the 552 men who went on to treatment, the majority underwent radical prostatectomy (66%); the remainder underwent brachytherapy (6%), external beam radiation with or without hormonal therapy (21%), hormonal therapy (2.2%), or focal therapy (4.5%). Of the 363 who underwent radical prostatectomy, 23% were found with Grade group 1 disease in the specimen, 62% displayed Grade Group 2, 10% showed Grade Group 3, and 5% showed Grade Group 4 or 5. At radical prostatectomy, 69% of patients had organ-confined disease, whereas 31% of patients had pT3 or greater disease.

At 5, 10, and 15 years, respectively, there were 1,146, 220, and 25 men at risk (ie, event-free and followed) for metastasis; 885, 145, and 20 men at risk for treatment; and 1,147, 222, and 26 men at risk for death. The median follow-up for those without metastasis was 4.3 years (95% CI 2.3, 6.9). The probability of metastasis in this group was 0.1% (95% CI 0.03%–0.4%) at 5 years, 0.6% (95% CI 0.2%–2.0%) at 10 years, and 1.5% (95% CI 0.4%–5.2%) at 15 years. There were 5 patients who developed distant metastasis in this cohort; 3 (0.1%) of these patients developed distant metastasis while on AS. Clinical information on these 5 patients is described in Table 2.

The overall 10-year survival of men with Grade Group 1 prostate cancer was 94% (95% CI 92%–95%). Out of the 2,664 patients in the cohort, only one patient died of prostate cancer. The 10-year prostate cancer specific survival was 100% (95% CI 99%−100%). The patient had a very unusual course of disease following diagnosis with Grade Group 1 prostate cancer (2/12 positive cores) at age 63. Over a 3-year period, the patient had 3 negative biopsies and 2 negative MRIs; the third MRI had lesions suspicious of osseous metastasis, and the patient developed symptomatic bone metastases consistent with prostatic origin 3 years after his diagnosis. The patient received androgen deprivation therapy and radiation therapy and ultimately died of disease 7 years after his initial diagnosis.

Over time, there was little to no change in the age at diagnosis or baseline risk of locally advanced disease (Figure 2).

DISCUSSION

We have demonstrated that AS is a safe management strategy at a tertiary cancer center when patients are appropriately selected and a well-defined monitoring plan is followed, in particular for men with very low risk prostate cancer. The long-term risk of metastasis is very low. The current study confirms prior reports demonstrating low incidence of oncologic events in men with low-risk prostate cancer on AS.[15, 18–20]

To date, 10 groups worldwide have reported the results of prospective AS cohorts. Most cohorts, just like ours, have a median follow-up of approximately 5 years, and only 2 have reported outcomes at 10–15 years. Even in large cohorts (Johns Hopkins and Toronto),[17] the number of men followed for more than 10 years is low. Moreover, because these cohorts used different eligibility criteria and follow-up regimens, just like the present study, the published risks of metastasis and prostate cancer mortality vary. The majority of the men in the Hopkins cohort met the more restrictive very low-risk inclusion criteria (defined by the Epstein criteria as: clinical stage T1c, PSA density < 0.15 ng/mL, biopsy Gleason score ≤ 6, ≤2 positive biopsy cores, and a maximum of 50% involvement of any biopsy core with cancer) and nearly all have low-volume disease[25]. Resultingly, the Hopkins cohort reported a 0.4% risk of metastasis and a 0.1% risk of prostate cancer mortality at 15 years.[20] The Toronto cohort is more heterogeneous and used more inclusive criteria (patients with low- and intermediate-risk prostate cancer, Gleason score ≤ 3+4=7 and PSA ≤ 20 ng/mL) and reported 2.8% risk of metastasis and 5.7% 15-year risk of prostate cancer mortality.[19] In a separate report, the Toronto group analyzed outcomes by grade among men with PSA < 20 ng/mL, showing a 15-year metastasis-free survival of 94% for men with Grade Group 1 (Gleason 6); 84% for men with Grade Group 2 (Gleason 3+4); and 63% for men with Grade Group 3 (Gleason 4+3).[26] In comparison, we here report a 0.6% risk of metastasis (95% CI 0.2%–2.0%) at 10 years and a 1.5% risk (95% CI 0.4%–5.2%) at 15 years – a 4-fold lower rate of distant metastasis for Grade Group 1 at 15 years as compared to the Toronto cohort. While these rates align with those of other AS cohorts and support the oncologic safety of AS over longer-term follow-up, we do note that the upper bound of the confidence interval at 15 years is clinically relevant (5.2% risk of metastasis). However, of the five patients who developed distant metastases, only two might have been cured by early treatment. One man, who later succumbed to the disease, had a very unusual disease course and it is possible that his disease was likely metastatic already at diagnosis; one was non-compliant with a treatment recommendation; one developed metastases after radical prostatectomy for Grade Group 1 disease and it is possible that he would have had a similar outcome if treated immediately.

This study is not devoid of limitations. Because most patients were recruited to our AS program in recent years, the follow-up for metastasis and prostate cancer death is still of intermediate length. As such, we will continue to report longer follow-up as the cohort matures. Furthermore, we acknowledge that this is not a prospective protocol-based AS cohort, but AS criteria were institution-specific: because expectant management in the early

years of our study could entail either AS or watchful waiting, some men with monitoring more resembling watchful waiting have been included. This would have the effect of underestimating the safety of contemporary AS by including these men in our study. Furthermore, our AS program has been adapting to a number of changes overtime. First, a very conservative initial eligibility criteria have expanded to include higher volume disease, integration of MR imaging and subsequent biopsy guidance. As such, there are fewer evaluable patients at 15 years and fewer patients with long established MRI follow up. We did not see evidence of change in median age at diagnosis or baseline risk of locally advanced disease, despite broadening of AS criteria over time.

CONCLUSIONS

Our experience confirms, on a large-scale, prior reports that active surveillance is an oncologically safe management strategy for men diagnosed with low-risk prostate cancer. Active surveillance should be strongly recommended for such patients as it avoids treatment-related morbidity without compromising cancer control.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research presentation: This study was presented as a moderated poster at the American Urological Association annual meeting in San Francisco on May 19, 2018. Abstract published in J Urol 2018:199(4), Suppl, p. e404. The study was also presented at the 19th Annual Meeting of the Society of Urologic Oncology in Phoenix, Arizona on November 30, 2018.

Key abbreviations

ADT	Androgen Deprivation Therapy
AS	Active Surveillance
CI	Confidence Interval
DRE	Digital Rectal Examination
MRI	Magnetic Resonance Imaging
PSA	Prostate-Specific Antigen
RP	Radical Prostatectomy
RT	Radiotherapy

REFERENCES

1. Moschini M, Carroll PR, Eggener SE et al.: Low-risk Prostate Cancer: Identification, Management, and Outcomes. Eur Urol, 72: 238, 2017 [PubMed: 28318726]
2. Wilt TJ, Andriole GL, Brawer MK: Prostatectomy versus Observation for Early Prostate Cancer. N Engl J Med, 377: 1302, 2017
3. Hamdy FC, Donovan JL, Lane JA et al.: 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med, 375: 1415, 2016 [PubMed: 27626136]
4. Bill-Axelson A, Holmberg L, Garmo H. et al.: Radical prostatectomy or watchful waiting in early prostate cancer. N Engl J Med, 370: 932, 2014 [PubMed: 24597866]
5. Choo R, Klotz L, Danjoux C. et al.: Feasibility study: watchful waiting for localized low to intermediate grade prostate carcinoma with selective delayed intervention based on prostate specific antigen, histological and/or clinical progression. J Urol, 167: 1664, 2002 [PubMed: 11912384]
6. Bruinsma SM, Bangma CH, Carroll PR et al.: Active surveillance for prostate cancer: a narrative review of clinical guidelines. Nat Rev Urol, 13: 151, 2016 [PubMed: 26813955]
7. Sanda MG, Cadeddu JA, Kirkby E. et al.: Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I: Risk Stratification, Shared Decision Making, and Care Options. J Urol, 199: 683, 2018 [PubMed: 29203269]
8. Cooperberg MR, Carroll PR: Trends in Management for Patients With Localized Prostate Cancer, 1990–2013. JAMA, 314: 80, 2015 [PubMed: 26151271]
9. Ingimarsson JP, Celaya MO, Laviolette M. et al.: Trends in initial management of prostate cancer in New Hampshire. Cancer Causes Control, 26: 923, 2015 [PubMed: 25840558]
10. Weerakoon M, Papa N, Lawrentschuk N. et al.: The current use of active surveillance in an Australian cohort of men: a pattern of care analysis from the Victorian Prostate Cancer Registry. BJU Int, 115 Suppl 5: 50, 2015
11. Womble PR, Montie JE, Ye Z. et al.: Contemporary use of initial active surveillance among men in Michigan with low-risk prostate cancer. Eur Urol, 67: 44, 2015 [PubMed: 25159890]
12. Loeb S, Folkvaljon Y, Curnyn C. et al.: Uptake of Active Surveillance for Very-Low-Risk Prostate Cancer in Sweden. JAMA Oncol, 3: 1393, 2017 [PubMed: 27768168]
13. Timilshina N, Ouellet V, Alibhai SM et al.: Analysis of active surveillance uptake for low-risk localized prostate cancer in Canada: a Canadian multi-institutional study. World J Urol, 35: 595, 2017 [PubMed: 27447989]
14. Mahal BA, Butler S, Franco I. et al.: Use of Active Surveillance or Watchful Waiting for Low-Risk Prostate Cancer and Management Trends Across Risk Groups in the United States, 2010–2015Trends in Use of Active Surveillance and Watchful Waiting for Management of Low-Risk Prostate CancerLetters. JAMA, 321: 704, 2019 [PubMed: 30743264]
15. Klotz L: Active surveillance for low-risk prostate cancer. Curr Opin Urol, 27: 225, 2017 [PubMed: 28267056]
16. Dall'Era MA, Albertsen PC, Bangma C. et al.: Active surveillance for prostate cancer: a systematic review of the literature. Eur Urol, 62: 976, 2012 [PubMed: 22698574]
17. Tosoian JJ, Carter HB, Lepor A. et al.: Active surveillance for prostate cancer: current evidence and contemporary state of practice. Nat Rev Urol, 13: 205, 2016 [PubMed: 26954332]
18. Bul M, Zhu X, Valdagni R. et al.: Active surveillance for low-risk prostate cancer worldwide: the PRIAS study. Eur Urol, 63: 597, 2013 [PubMed: 23159452]
19. Klotz L, Vesprini D, Sethukavalan P. et al.: Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol, 33: 272, 2015 [PubMed: 25512465]
20. Tosoian JJ, Mamawala M, Epstein JI et al.: Intermediate and Longer-Term Outcomes From a Prospective Active-Surveillance Program for Favorable-Risk Prostate Cancer. J Clin Oncol, 33: 3379, 2015 [PubMed: 26324359]
21. Kinsella N, Helleman J, Bruinsma S. et al.: Active surveillance for prostate cancer: a systematic review of contemporary worldwide practices. Transl Androl Urol, 7: 83, 2018 [PubMed: 29594023]

22. Adamy A, Yee DS, Matsushita K. et al.: Role of prostate specific antigen and immediate confirmatory biopsy in predicting progression during active surveillance for low risk prostate cancer. J Urol, 185: 477, 2011 [PubMed: 21167529]

23. Berglund RK, Masterson TA, Vora KC et al.: Pathological upgrading and up staging with immediate repeat biopsy in patients eligible for active surveillance. J Urol, 180: 1964, 2008 [PubMed: 18801515]

24. Memorial Sloan Kettering Cancer Center. Prediction Tools - Prostate Cancer Nomograms - Pre-Radical Prostatectomy. Available at: https://www.mskcc.org/nomograms/prostate/pre_op.

25. Tosoian JJ, Mamawala M, Patel HD et al.: Tumor Volume on Biopsy of Low Risk Prostate Cancer Managed with Active Surveillance. J Urol, 199: 954, 2018 [PubMed: 29074222]

26. Musunuru HB, Yamamoto T, Klotz L. et al.: Active Surveillance for Intermediate Risk Prostate Cancer: Survival Outcomes in the Sunnybrook Experience. J Urol, 196: 1651, 2016 [PubMed: 27569437]

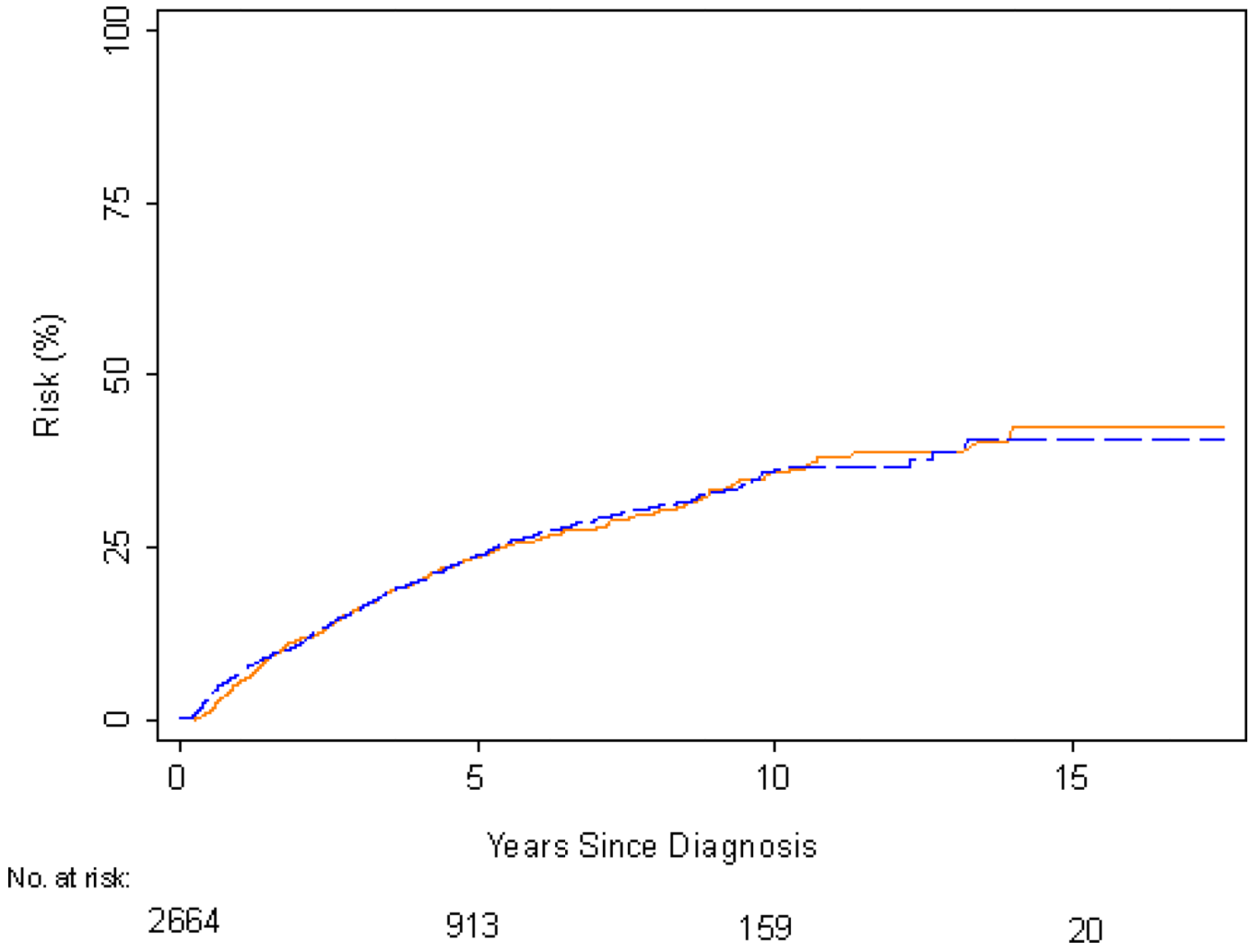

Figure 1. Risk of treatment and grade progression among Grade Group 1 patients

Dashed blue line represents risk of grade progression and solid orange line represents risk of treatment.

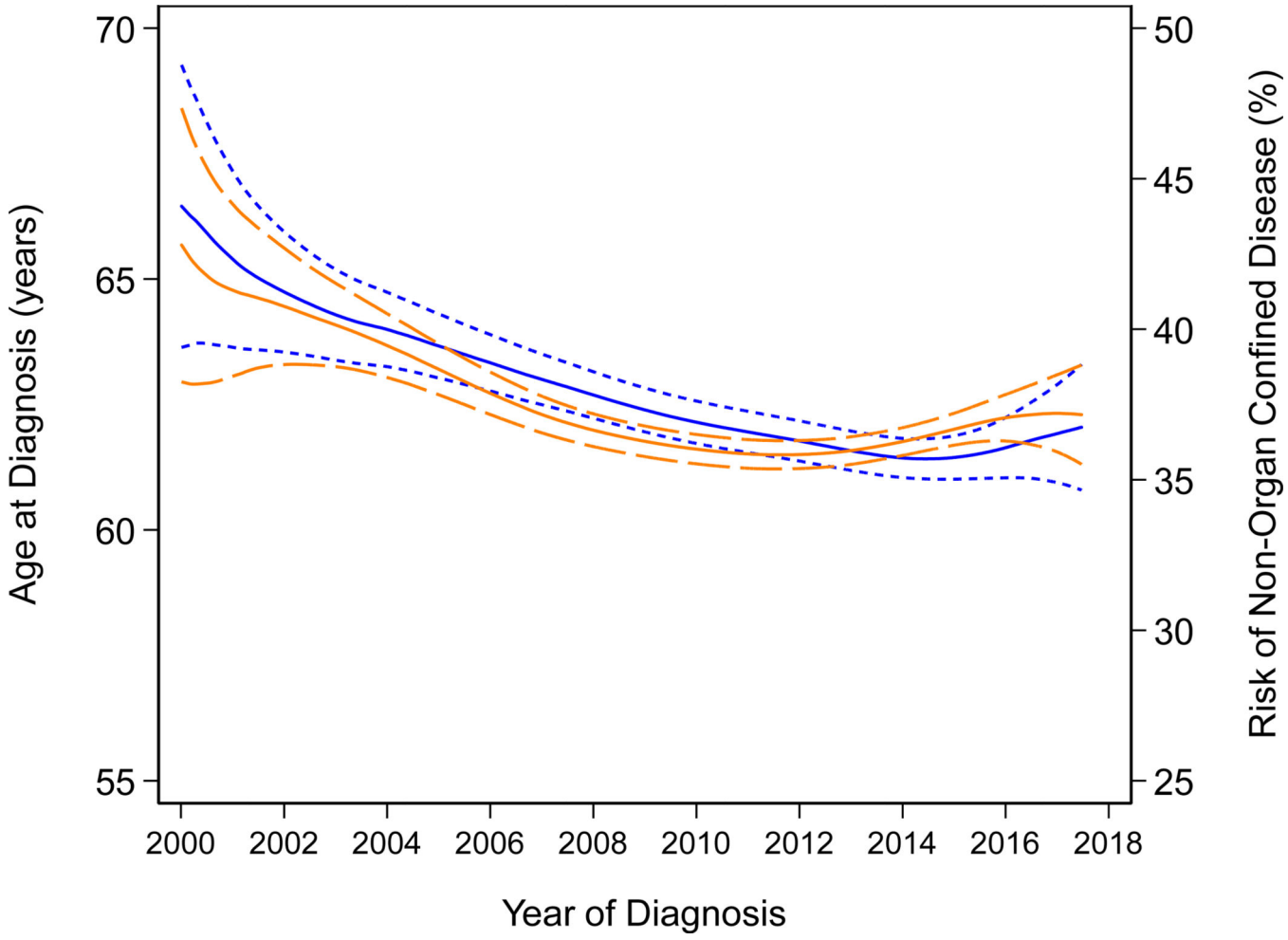

Figure 2. Age and risk of non-organ confined disease at diagnosis over time for men with Grade Group 1

The blue line with the short-dash confidence interval represents the change in age at diagnosis over time. The orange line with long-dash confidence interval represents the change in risk of non-organ confined disease at diagnosis over time.

Table 1.

Patient and tumor characteristics

Values are displayed as median (interquartile range) or frequency (percentage). Biopsy data are based on diagnostic biopsy.

	N=2,664
Age at Diagnosis, years	62 (57, 68)
Diagnostic PSA (N=2,400), ng/mL	5 (4, 6)
Number of Positive Cores at Diagnosis (N=2,547)	1 (1, 2)
Number of Total Cores at Diagnosis (N=2,483)	12 (6, 13)
Percent Cancer at Diagnosis * (N=2,259)	8% (5%, 20%)
Total Cancer Length at Diagnosis (N=1,998), millimeters	1 (1, 3)
Nomogram Risk of Locally Advanced Disease (N=2,090)	35% (31%, 42%)
Year of Diagnosis	
2000–2004	221 (8.3%)
2005–2009	656 (25%)
2010–2014	1293 (49%)
2015–2017	494 (19%)
Clinical stage at diagnosis	
≤T1C	2,359 (89%)
T2A	248 (9.3%)
T2B	34 (1.3%)
T2C	23 (0.9%)

Abbreviations: PSA=prostate-specific antigen, MRI=magnetic resonance imaging

* The highest reported percentage of cancer in any biopsy core

Table 2.

Clinical characteristics of the patients who developed metastasis following active surveillance

Patient	Age at diagnosis	Time to Metastasis from Diagnosis (Years)	Time to Metastasis from Treatment (Years)	First Treatment	Grade Group at RP	Current Status	Comments
1	76	8.8	Pre-treatment metastasis	ADT	-	Alive with disease	Patient decision to remain on AS after upgrade to Grade Group 3; treated with ADT after metastatic diagnosis.
2	45	7.6	0.6	RP	5	Alive with disease	Treated with prostatectomy after local progression; nodal and osseous metastasis post prostatectomy.
3	58	11.8	8.7	RP	1	Alive with disease	Neuroendocrine differentiation on lumbar spine biopsy.
4	63	3.5	Pre-treatment metastasis	RT + ADT	-	Died of disease	Three negative biopsies and 2 negative MRIs; back pain and osseous metastasis on third MRI.
5	60	1.8	Pre-treatment metastasis	ADT	-	Alive with disease	Back pain and widespread osseous metastasis on MRI.

Abbreviations: ADT=androgen deprivation therapy, RP=radical prostatectomy, RT=radiotherapy, AS=active surveillance, MRI=magnetic resonance imaging.