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ORIGINAL ARTICLE

Time between diagnosis and surgical treatment on pathological and clinical outcomes in prostate cancer: does it matter?

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Abstract

Introduction Prostate cancer (PC) most of the time presents with an indolent course. Thus, delays in treatment due to any causes might not affect long-term survival and may not affect cancer cure rates.

Purpose In this study, we evaluated the effect of delay-time between PC diagnosis and radical prostatectomy regarding oncological outcomes: Gleason score upgrade on surgical specimen, pathologic extracapsular extension (ECE) on surgical specimen, and postoperative biochemical recurrence (BCR) on follow-up.

Methods We evaluated PC patients who underwent radical prostatectomy (RP) regarding clinical and pathological findings and theirs respective interval between diagnosis and surgical treatment measured in days and months. We used univariate and multivariate logistic regression to evaluate the impact of interval-time.

Results A total of 908 PC patients underwent RP between 2006 and 2014. Mean age was 61.5 years, the mean time-to-surgery was 191 days (> 6 months) and 187 (20.5%) patients had BCR, with a mean follow-up of 44 months. According to our analysis, no statistically significant maximum cut-off time interval between diagnostic biopsy and surgery could be established ($p = 0.215$). Regardless of interval-time: ≤ 6 months (56.5%), 6–12 months (38.5%), and > 12 months (5.1%) after biopsy, we found no time interval correlated with poor oncological outcomes. This study has several limitations. It was retrospective and had a mean follow-up of 4 years. Additional follow-up is necessary to determine whether these findings will be maintained over time.

Conclusions We showed that the time between diagnosis and surgical treatment did not affect the oncological outcomes in our study.

Keywords Prostate cancer · Radical prostatectomy · Oncological outcomes · Pathological findings

Introduction

Prostate cancer (PC) is the most common non-cutaneous malignancy of the male adult and a very heterogeneous disease. Many of them present with an indolent course [1]. Thus, delays such as those caused by lack of health insurance coverage, personal reasons, or physician or operating room availability [2, 3] might not affect long-term survival.

Among cancer in general, the effect of treatment delays has diverse results in studies published in the literature. In some reports, treatment delays varied according to type of cancer, and delays in treatment did not affect the survival of patients with breast or colon cancer, for example [4, 5]. Specifically with PC, the effect of treatment delay on long-term survival is unclear [3, 6–10]. In the last decades, lack of conclusive evidence on the detrimental effects of delaying PC treatment prompted clinicians to voluntarily delay initial management of low-risk PC cases in reported active surveillance (AS) cohorts with favorable long-term results [11]. Thus, the timing of surgical treatment for localized PC, whether early or relatively late (up to a certain threshold), may not affect cancer cure rates [12].

Treatment delay studies about PC in developing countries are still lacking, which has racially diverse population and where PC screening is not widespread [13, 14]. In this study, we evaluated the effect of PC treatment delay as measured by the time between PC diagnosis and radical prostatectomy

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Methods and patients

We reviewed medical records of PC patients who underwent radical prostatectomy (RP) from 2006 to 2014. Patients with incomplete clinical data or who underwent neoadjuvant hormone therapy were excluded. We evaluated the following clinical and pathological variables: age, clinical stage, biopsy and specimen Gleason score (GS), D'Amico risk categories, pathologic findings of the surgical specimen, and PSA kinetics. All pathology slides from others localities were reviewed at our institution by experienced uropathologists who used the 2005 Gleason grading system [15]. The interval between diagnosis and surgical treatment was measured in months by subtracting the date of the diagnostic biopsy from the date of the RP procedure.

Statistical analysis

We developed a time-dependent receiver operating characteristic (ROC) curve for the interval between biopsy and surgery regarding oncological outcomes. We evaluated a cut-off time for delayed treatment [16]. Oncological outcomes were analyzed such as: Gleason score (GS) upgrade on surgical specimen [17], pathologic extracapsular extension (ECE) on surgical specimen, and postoperative biochemical recurrence (BCR) on follow-up. Postoperative biochemical relapse was considered as PSA $\geq$ 0.2 ng/mL in two consecutive measurements [6, 7, 18, 19]. We used Chi-squared test, Fisher's exact test, non-parametric Mann–Whitney test with variables. Univariate and multivariate logistic regression were used for pathological and clinical outcomes. Variables with $p \leq 0.2$ in univariate analyses were included in the adjusted model. We considered in the multivariate analysis a significance level of 0.05. Data were analyzed using IBM SPSS version 21 (Armonk, NY, USA). The Ethics Committee of our Institution approved this study. The researchers were waived of obtaining individual consent forms. We calculated the power of analysis for our study running analyses to cover all of the contingencies for independent proportions in oncological findings. We used the software G*Power to find the goodness of fit tests. This power of analysis in general must be higher than 0.7 [20, 21].

Results

A total of 987 PC patients who underwent RP between 2006 and 2014 were evaluated. Of these, 77 were excluded due to missing data and another two were considered outliers and excluded because their surgery occurred over five years after diagnosis. A total of 908 men were analyzed. Mean age was 61.5 years and mean time-to-surgery was 191 days (> 6 months). Other demographic characteristics before surgery are summarized in Table 1.

In Table 2, we reported the pathologic features of the surgical specimen. Overall, the surgical specimen in 37.1% of patients was classified as an upgrade. Most patients had no positive surgical margins ($n = 603$, 66.3%), no ECE ($n = 809$, 89.1%), or no seminal vesicle invasion ($n = 865$, 95.1%). Vascular infiltration was not observed in 878 patients (96.7%). Most patients had a pathological staging of pT2b.

Mean follow-up period was 44 months. In this study, 187 (20.5%) patients had BCR, with a mean follow-up of 44 months. A total of 224 (24.7%) patients received adjuvant or salvage radiotherapy. Of all 908 patients, only four (0.4%) progressed to metastases. Additionally, 47.4, 40.8, and 11.9% of patients were classified into the low, intermediate and high D'Amico risk classification, respectively.

We evaluated the time interval between diagnostic biopsy and surgery for D'Amico risk groups regarding each clinical variable using an ROC curve, median, simple and multiple logistic regression, which was considered specimen upgrade, pathological ECE, and BCR as oncological outcomes (Table 3). According to our analysis, no statistically significant maximum cut-off time interval between diagnostic biopsy and surgery could be established ($p = 0.215$). Therefore, we categorized the time interval in a similar modus to that found in the literature, [7, 18, 19] i.e., patients underwent surgery within 6 months of the diagnosis date (56.5%), between 6 and 12 months (38.5%), and surgery higher than 12 months after biopsy (5.1%). Additionally, we also analyzed the clinical variables using other time intervals, dividing the group into quartiles, tertiles, and quintiles. No time interval correlated with poor oncological outcomes. To analyze the outcome of BCR-free survival, Kaplan–Meier curves were constructed for the D'Amico categories using temporal division ($\leq$ 6, 6–12, and > 12 months). We observed that delays in performing RP did not affect BCR according to the D'Amico risk categories (Fig. 1a–c). Considering the goodness of tests: contingency tables were found for oncological outcomes regarding our temporal division of time between biopsy and surgery: Upgrade (Effect size 0.105–Power 0.726), ECE (Effect size 0.103–Power 0.714), BQR (Effect size 0.085–Power 0.699).

In addition, we calculated the PSA density (PSAd) at time of biopsy and at time of surgical treatment (0.141 ng/cm^3). None of them was associated with unfavorable outcomes (specimen upgrade, pathological ECE, and BCR).

We have performed a correlation analysis using the number of positive cores on biopsy and oncological outcomes (specimen upgrade, pathological ECE, and BCR). Regardless of number of positive cores on biopsy the oncological

Table 1 Clinical characteristics of overall study population and by selected time-to-surgery

	Total ($n=908$)	≤ 6 months ($n=514$)	6–12 months ($n=346$)	> 12 months ($n=48$)
Mean age at surgery, years (SD) range	61.5 (6.3) 39.8–79.5	61.50 (6.53) 39.8–74.6	61.0 (6.06) 43.6–79.5	61.1 (6.2) 46.7–69.3
Mean PSA at diagnosis, ng/ml (SD) range	7.88 (6.09) 0.02–53.55	7.57 (5.69) 0.02–53.5	8.27 (6.55) 0.05–52.08	8.71 (6.79) 0.62–34.03
Mean time-to-surgery, days (SD) range	191.0 (95.0) 30.0–941.0	131 (32) 30–180	233 (44) 181–357	472 (128) 361–941
Ethnicity, no. (%)				
Caucasian	627 (70.0)	364 (71.7)	238 (70.2)	24 (51.1)
Non-caucasian	269 (30.0)	144 (28.3)	101 (29.8)	23 (48.9)
Illiteracy, no. (%)	58 (6.5)	36 (7.1)	18 (5.4)	4 (8.3)
Mean follow-up, months (SD) range	44 (21) 3–132	47 (21) 3–132	42 (20) 6–90	39 (20) 6–78
Biopsy Gleason score, no. (%)				
6	546 (60)	171 (60.9)	127 (58.5)	19 (63.3)
7	311 (34.2)	92 (32.7)	80 (36.9)	11 (36.7)
8–10	53 (5.8)	18 (6.4)	10 (4.6)	0 (0)
Clinical stage, no. (%)				
T1	596 (65.5)	333 (64.8)	228 (65.9)	34 (70.8)
T2	285 (31.3)	165 (32.1)	106 (30.6)	13 (27.1)
T3	29 (3.2)	16 (3.1)	12 (3.5)	1 (2.1)
D'Amico risk groups, no. (%)				
Low-risk	431 (47.4)	251 (48.8)	157 (45.4)	22 (45.8)
Intermediate-risk	371 (40.8)	201 (39.1)	148 (42.8)	21 (43.8)
High-risk	108 (11.9)	62 (12.1)	41 (11.8)	5 (10.4)

PSA prostate-specific antigen, *SD* standard deviation

outcomes have no influence on considering different intervals between diagnosis and surgery in our study.

This analysis revealed the relationship with GS or staging but no differences in the odds ratios considering the time interval. Regardless of delays in surgery, no statistically significant relationship was observed between the time until surgery and the oncological outcomes (Table 4).

Discussion

In this study, no significant differences were found regarding short and intermediate-term oncological outcomes among low-risk, intermediate-risk, and high-risk PC patients considering time interval between diagnosis and surgery. Delays in surgery can occur for various reasons, such as socio-economic or public health problems, delayed decision of the patient who may be unsure of the type of treatment that best suits him or other ones.

Many cases of PC has typically slow-growing behavior. The long natural history of PC was recently demonstrated in two randomized studies that investigated the efficacy of RP. In the last publication of PIVOT trial, which randomized 731 men with localized prostate cancer to radical prostatectomy or observation. During 19.5 years of follow-up (median, 12.7 years), death occurred in 223 of 364 men (61.3%) assigned to surgery and in 245 of 367 (66.8%) assigned to observation. They concluded that after nearly 20 years of follow-up, surgery was not associated with significantly lower all-cause or prostate-cancer mortality than observation [22]. Another randomized (PROTECT trial) study compared active monitoring, radical prostatectomy, and external-beam radiotherapy for the treatment of clinically localized prostate cancer. Total of 1643 agreed to undergo randomization. They observed 17 prostate cancer-specific deaths overall: 8 in the active-monitoring group, 5 in the surgery group, and 4 in the radiotherapy group; the difference among the groups was not significant ($p=0.48$ for the overall comparison). At a median of 10 years, prostate cancer-specific mortality was low irrespective of the treatment assigned, with no significant difference among treatments [23].

A question that may be addressed is whether younger patients could be exposed to a greater risk of disease progression. O'Brien et al. [19] evaluated a sample of PC patients with a mean age of approximately 60 years and found that a higher risk of unfavorable pathological outcomes and BCR was associated with a delay in treatment, even in low-risk patients. However, our study did not find differences between delays in treatment and pathological outcomes and BCR, even in younger patients (mean age of 61.5 years), regardless of the D'Amico risk category. Similar to the results of our study, other studies found no differences in the oncological results for patients with a mean age of

Table 2 Pathologic characteristics of surgical specimen of overall study population and by selected time-to-surgery categories

Total population ($n=908$)	≤ 6 months ($n=514$)	6–12 months ($n=346$)	> 12 months ($n=48$)
Gleason Score, no. (%)			
6 299 (32.9)	179 (34.8)	101 (29.2)	19 (39.6)
7 539 (59.4)	298 (58)	213 (61.6)	28 (58.3)
8–10 70 (7.7)	37 (7.2)	32 (9.2)	1 (2.1)
Positive surgical margins, no. (%)			
Yes 306 (33.7)	175 (34.1)	116 (33.5)	15 (31.2)
No 603 (66.3)	338 (65.9)	230 (66.5)	33 (68.8)
Extracapsular extension, no. (%)			
Yes 99 (10.9)	51 (9.9)	42 (12.1)	5 (10.6)
No 809 (89.1)	462 (90.1)	304 (87.9)	42 43(89.4)
Seminal vesicle invasion, no. (%)			
Yes 45 (4.9)	31 (6.0)	13 (3.8)	1 (2.1)
No 865 (95.1)	483 (94.0)	333 (96.2)	47 (97.9)
Perineural invasion, n. (%)			
Yes 455 (50.1)	254 (49.6)	177 (51.2)	23 (47.9)
No 453 (49.9)	258 (50.4)	169 (48.8)	25 (52.1)
Vascular invasion, n. (%)			
Yes 30 (3.3)	14 (2.7)	15 (4.3)	1 (2.1)
No 878 (96.7)	498 (97.3)	331 (95.7)	47 (97.9)
Lymph node stage (*N*), n. (%)			
pN0 665 (73.1)	511 (99,4)	346 (100)	48 (100)
pN1 236 (25.9)	3 (0,6)	0 (0)	0 (0)
pN2 9 (1.0)	0 (0)	0 (0)	0 (0)
Pathological stage (*T*), n. (%)			
T2a 60 (6.5)	37 (7.2)	22 (6.4)	5 (10.4)
T2b 138 (15.2)	73 (14;2)	56 (16.2)	8 (16.7)
T2c 472 (51.9)	267 (51.9)	182 (52.6)	22 (45.8)
T3a 189 (20.8)	104 (20.2)	73 (21.1)	12 (25.0)
T3b 47 (5.2)	33(6.4)	13 (3.8)	1 (2.1)
T4 4 (0.4)	3 (75)	1 (25)	0 (0)

Table 3 Predictors of Gleason Score upgrade and extracapsular extension in surgical specimen and biochemical recurrence according to time-to-surgery

Outcomes	Total (%)	≤ 6 months (%)	6–12 months (%)	> 12 months (%)	*p* value (%)
Upgrade					
No	571 (62.9)	333 (64.8)	207 (59.8)	31 (64.6)	0.326
Yes	337 (37.1)	181 (35.2)	139 (40.2)	17 (35.4)	
ECE					
No	808 (89.2)	462 (90.1)	304 (87.9)	42 (89.4)	0.594
Yes	98 (10.8)	51 (9.9)	42 (12.1)	5 (10.6)	
BQR					
No	721 (79.4)	401 (78)	281 (81.2)	39 (81.2)	0.497
Yes	187 (20.6)	113 (22.0)	65 (18.8)	9 (18.8)	

PSA prostatic specific antigen, *BQR* biochemical recurrence (*PSA* ≥ 0.2 ng/mL), *ECE* extracapsular extension, *Upgrade* higher Gleason score on surgical specimen

approximately 60 years who experienced delayed surgical treatment [7, 18].

In the "National Prostate Cancer Register of Sweden," Holmström et al. assessed outcomes in terms of adverse pathology and prostate cancer-specific mortality in men who underwent primary or deferred radical prostatectomy. They assessed 2344 men who underwent primary radical prostatectomy and 222 who underwent deferred radical

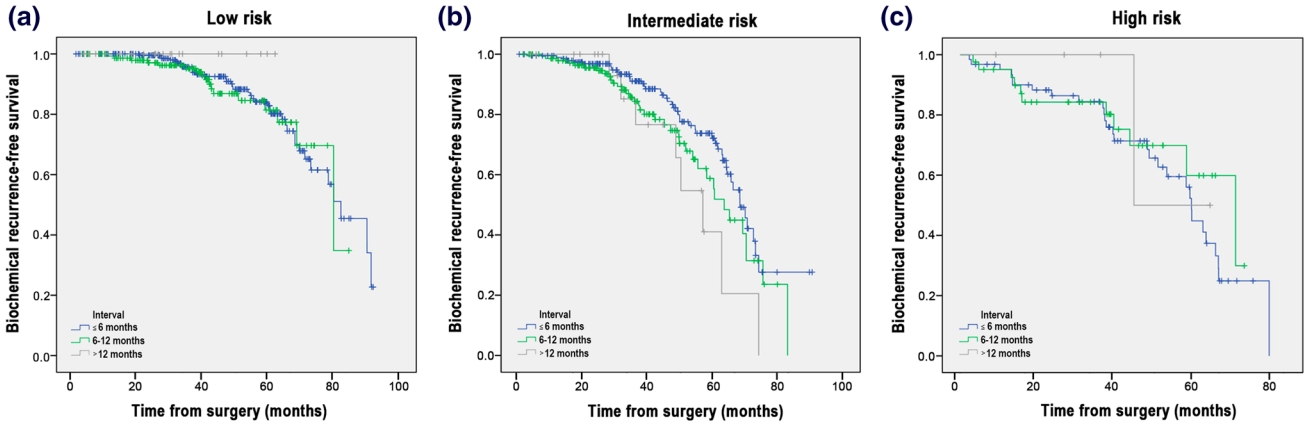

Fig. 1 Kalpan–Meier curve for biochemical recurrence free survival considering time interval between diagnostic biopsy and radical prostatectomy regarding D'Amico risk group

prostatectomy after an initial period of surveillance (less than 19 months). After a median follow-up of 8 years 0.7% of men in the primary radical prostatectomy group and 0.9% in the deferred radical prostatectomy group had died of prostate cancer [22]. Considering deferred RP in AS protocol, in a retrospective cohort of 69 patients on AS for an average of 29 months, van den Bergh et al. found no differences in the frequency of adverse pathological results between the early and late RP groups.

Regarding high-risk cases, the safety of delayed RP is not well established. Khan et al. [9] evaluated 55 men with intermediate- and high-risk PC as a subset of an RP cohort and found no association between delays in surgery greater than 150 days and the development of BCR. Filippou et al. [24] found no differences in BCR-free survival or additional treatment within 3 years (93 vs. 96%) between the immediate RP group and the surgical delay group. However, despite our study had smaller number of cases in high-risk group, we found no significant differences between the occurrence of BCR in patients at low, intermediate, and high risk of PC who experienced surgical delay, irrespective of time. In another study, Abern et al. performed a retrospective analysis of 1561 low and intermediate-risk men treated with RP between 1988 and 2011. Patients were stratified by interval between diagnosis and RP (≤ 3, 3–6, 6–9, or > 9 months) and by risk using the D'Amico classification. For low-risk men, RP delays were unrelated to BCR, ECE, positive surgical margins (PSM), or upgrading (all $p > 0.05$). For intermediate-risk men, however, delays > 9 months were significantly related to BCR (HR: 2.10, $p = 0.01$) and PSM (OR: 4.08, $p < 0.01$). They found for men with intermediate-risk disease, delays > 9 months predicted greater BCR and PSM risk [25].

Vickers et al. [18] evaluated 3149 consecutive patients who underwent RP and the time between diagnosis and surgery was entered as a predictor in a multivariate logistic regression model predicting BCR. The authors found no clear evidence of a significant effect of delay to diagnosis on BCR and they concluded that the time between biopsy and surgery does not appear to have a large effect on the risk of disease recurrence [18]. Our cohort of low- and intermediate-risk patients was sufficiently large ($n = 910$) and our data suggest that men at low or intermediate-risk of PC did not have unfavorable clinical or pathological outcomes when RP is performed even over 15 months after diagnosis. We had in our study less number of patients in high-risk group in comparison with other ones and this can reduce the statistical power. However, considering the goodness of tests: contingency tables were found for oncological outcomes regarding our groups power of tests around 0.7, and it is considered reasonable.

Our follow-up period was not long enough to include data from cases of metastasis or mortality data. We used BCR as a long-term oncological outcome because the literature has evidence of association between shorter time for development of BCR after RP with higher cancer-specific mortality and overall mortality [26–28].

In our database, two outlier patients who underwent surgery for more than 5 years after a PC diagnosis were excluded from the analysis. Despite that both patients had a biopsy with a GS 6 but did not have an upgrade in the surgical specimen or BCR during follow-up, even with this increased time between diagnosis and surgery. This study has several limitations. It was retrospective and had a mean follow-up of 4 years. Another limitation is the high-risk group had fewer numbers of patients.

Conclusion

In this study, we have shown that the time between diagnosis and surgical treatment does not affect the oncological outcomes of patients at low-, intermediate-risk group according

Table 4 Association of time-to-surgery and other predicting variables with Gleason Score upgrade and extracapsular extension on final surgical specimen, and with biochemical recurrence in uni- and multivariate models

Variable	Univariate OR (95% CI)	*p* value	Multivariate OR (95% CI)	*p* value
Outcome of Gleason Upgrade on surgical specimen				
Age, years	0.982 (0.962–1.003)	0.087	0.985 (0.964–1.006)	0.166
Preoperative PSA	0.990 (0.967–1.013)	0.372	0.990 (0.967–1.013)	0.394
Time-to-surgery				
≤ 6 months	–	0.326	–	0.395
6–12 months	1.235 (0.933–1.636)	0.140	1.229 (0.912–1.655)	0.175
> 12 months	1.009 (0.544–1.873)	0.978	1.138 (0.593–2.184)	0.698
Outcome of extracapsular extension on surgical specimen				
Age, years	0.988 (0.957–1.019)	0.444	0.989 (0.955–1.024)	0.542
Preoperative PSA	1.050 (1.023–1.079)	0.000	1.050 (1.023–1.079)	0.000
Time-to-surgery				
≤ 6 months	–	0.597	–	0.712
6–12 months	1.252 (0.811–1.930)	0.310	1.145 (0.711–1.844)	0.578
> 12 months	1.078 (0.811–2.848)	0.879	0.728 (0.214–2.473)	0.611
Outcome of biochemical recurrence				
Age, years	1.028 (1.002–1.054)	0.038	1.025 (0.995–1.055)	0.102
Preoperative PSA	1.056 (1.031–1.082)	0.000	1.037 (1.009–1.066)	0.009
Time-to-surgery				
≤ 6 months	–	0.497	–	0.075
6–12 months	0.821 (0.584–1.155)	0.257	0.691 (0.466–1.026)	0.067
> 12 months	0.819 (0.385–1.741)	0.604	0.416 (0.139–1.243)	0.116
Other variables				
Specimen Gleason Score				
6	–	0.000	–	0.000
7	3.105 (1.995–4.835)	0.000	2.655 (1.618–4.358)	0.000
8–10	8.985 (4.864–16.598)	0.000	5.065 (2.402–10.678)	0.000
Positive surgical margins	3.077 (2.210–4.285)	0.000	2.707 (1.838–3.985)	0.729
Extracapsular extension	1.659 (1.035–2.658)	0.035	0.675 (0.365–1.248)	0.211
Seminal vesicle invasion	1.609 (0.827–3.130)	0.162	0.564 (0.240–1.327)	0.190
Perineural invasion	2.041 (1.463–2.849)	0.000	1.261 (0.846–1.879)	0.255
Vascular invasion	1.692 (0.762–3.760)	0.196	1.065 (0.412–2.753)	0.897
Lymph node invasion				
pN0	–	0.002	–	0.651
pN1	1.536 (0.357–6.611)	0.564	1.205 (0.232–6.252)	0.824
pN2	0.548 (0.387–0.775)	0.001	0.830 (0.546–1.262)	0.385

to the D'Amico classification. The impact of delayed treatment on high-risk group is still under debate. Additional follow-up is necessary to determine whether these findings will be maintained over time.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval For this type of study formal consent is not required.

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

References

1. Johansson JE, Andren O, Andersson SO, Dickman PW, Holmberg L, Magnuson A et al (2004) Natural history of early, localized prostate cancer. JAMA 291(22):2713–2719
2. Korets R, Seager CM, Pitman MS, Hruby GW, Benson MC, McKiernan JM (2012) Effect of delaying surgery on radical prostatectomy outcomes: a contemporary analysis. BJU Int 110(2):211–216
3. van den Bergh RC, Steyerberg EW, Khatami A, Aus G, Pihl CG, Wolters T et al (2010) Is delayed radical prostatectomy in men

with low-risk screen-detected prostate cancer associated with a higher risk of unfavorable outcomes? Cancer 116(5):1281–1290
4. Sainsbury R, Johnston C, Haward B (1999) Effect on survival of delays in referral of patients with breast-cancer symptoms: a retrospective analysis. Lancet 353(9159):1132–1135
5. Roncoroni L, Pietra N, Violi V, Sarli L, Choua O, Peracchia A (1999) Delay in the diagnosis and outcome of colorectal cancer: a prospective study. Eur J Surg Oncol 25(2):173–178
6. Nam RK, Jewett MA, Krahn MD, Robinette MA, Tsihlias J, Toi A et al (2003) Delay in surgical therapy for clinically localized prostate cancer and biochemical recurrence after radical prostatectomy. Can J Urol 10(3):1891–1898
7. Freedland SJ, Kane CJ, Amling CL, Aronson WJ, Presti JC Jr, Terris MK (2006) Delay of radical prostatectomy and risk of biochemical progression in men with low risk prostate cancer. J Urol 175(4):1298–12302 **(discussion 302–303)**
8. Boorjian S, Ng C, Munver R, Palese MA, Vaughan ED Jr, Sosa RE et al (2005) Impact of delay to nephroureterectomy for patients undergoing ureteroscopic biopsy and laser tumor ablation of upper tract transitional cell carcinoma. Urology 66(2):283–287
9. Khan MA, Mangold LA, Epstein JI, Boitnott JK, Walsh PC, Partin AW (2004) Impact of surgical delay on long-term cancer control for clinically localized prostate cancer. J Urol 172(5 Pt 1):1835–1839
10. Graefen M, Walz J, Chun KH, Schlomm T, Haese A, Huland H (2005) Reasonable delay of surgical treatment in men with localized prostate cancer-impact on prognosis? Eur Urol 47(6):756–760
11. Klotz L, Vesprini D, Sethukavalan P, Jethava V, Zhang L, Jain S et al (2015) Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol 33(3):272–277
12. Harris R, Lohr KN (2002) Screening for prostate cancer: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 137(11):917–929
13. Faria EF, Carvalhal GF, Vieira RA, Silva TB, Mauad EC, Tobias-Machado M et al (2011) Comparison of clinical and pathologic findings of prostate cancers detected through screening versus conventional referral in Brazil. Clin Genitourin Cancer 9(2):104–108
14. Faria EF, Carvalhal GF, Vieira RA, Silva TB, Mauad EC, Carvalho AL (2010) Program for prostate cancer screening using a mobile unit: results from Brazil. Urology 76(5):1052–1057
15. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL (2005) The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. Am J Surg Pathol 29(9):1228–1242
16. D'Amico AV, Whittington R, Malkowicz SB, Weinstein M, Tomaszewski JE, Schultz D et al (2001) Predicting prostate specific antigen outcome preoperatively in the prostate specific antigen era. J Urol 166(6):2185–2188
17. Corcoran NM, Hong MK, Casey RG, Hurtado-Coll A, Peters J, Harewood L et al (2011) Upgrade in Gleason score between prostate biopsies and pathology following radical prostatectomy significantly impacts upon the risk of biochemical recurrence. BJU Int 108(8 Pt 2):E202–E210
18. Vickers AJ, Bianco FJ Jr, Boorjian S, Scardino PT, Eastham JA (2006) Does a delay between diagnosis and radical prostatectomy increase the risk of disease recurrence? Cancer 106(3):576–580
19. O'Brien D, Loeb S, Carvalhal GF, McGuire BB, Kan D, Hofer MD et al (2011) Delay of surgery in men with low risk prostate cancer. J Urol 185(6):2143–2147
20. Hsieh FY, Bloch DA, Larsen MD (1998) A simple method of sample size calculation for linear and logistic regression. Stat Med 17(14):1623–1634
21. Borm GF, Bloem BR, Munneke M, Teerenstra S (2010) A simple method for calculating power based on a prior trial. J Clin Epidemiol 63(9):992–997
22. Wilt TJ, Jones KM, Barry MJ, Andriole GL, Culkin D, Wheeler T et al (2017) Follow-up of prostatectomy versus observation for early prostate cancer. N Engl J Med 377(2):132–142
23. Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P et al (2016) 10-Year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 375(15):1415–1424
24. Filippou P, Welty CJ, Cowan JE, Perez N, Shinohara K, Carroll PR (2015) Immediate versus delayed radical prostatectomy: updated outcomes following active surveillance of prostate cancer. Eur Urol 68(3):458–463
25. Abern MR, Aronson WJ, Terris MK, Kane CJ, Presti JC Jr, Amling CL et al (2013) Delayed radical prostatectomy for intermediate-risk prostate cancer is associated with biochemical recurrence: possible implications for active surveillance from the SEARCH database. Prostate 73(4):409–417
26. Freedland SJ, Humphreys EB, Mangold LA, Eisenberger M, Dorey FJ, Walsh PC et al (2005) Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. JAMA 294(4):433–439
27. Choueiri TK, Chen MH, D'Amico AV, Sun L, Nguyen PL, Hayes JH et al (2010) Impact of postoperative prostate-specific antigen disease recurrence and the use of salvage therapy on the risk of death. Cancer 116(8):1887–1892
28. Freedland SJ, Humphreys EB, Mangold LA, Eisenberger M, Dorey FJ, Walsh PC et al (2007) Death in patients with recurrent prostate cancer after radical prostatectomy: prostate-specific antigen doubling time subgroups and their associated contributions to all-cause mortality. J Clin Oncol 25(13):1765–1771