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Platinum Priority – Prostate Cancer

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Improved Recovery of Erectile Function in Younger Men after Radical Prostatectomy: Does it Justify Immediate Surgery in Low-risk Patients?

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Abstract

Background: Although active surveillance is increasingly used for the management of low-risk prostate cancer, many eligible patients are still nonetheless subject to curative treatment. One argument for considering surgery rather than active surveillance is that the probability of postoperative recovery of erectile function is age dependent, that is, patients who delay surgery may lose the window of opportunity to recover erectile function after surgery.

Objective: To model erectile function over a 10-yr period for immediate surgery versus active surveillance.

Design, setting, and participants: Data from 1103 men who underwent radical prostatectomy at a tertiary referral center were used.

Outcome measurements and statistical analysis: Patients completed the International Index of Erectile Function (IIEF-6) pre- and postoperatively as a routine part of clinical care. Preoperative IIEF-6 scores were plotted against age to assess the natural rate of functional decline due to aging. Reported erectile scores in the 2-yr period following surgery were used to assess post-surgical recovery.

Results and limitations: Each year increase in patient age resulted in a 0.27 reduction in IIEF scores. In addition to IIEF reducing with increased age, the amount of erectile function that is recovered from presurgery to 12-mo postsurgery also decreases (–0.16 IIF points/yr, 95% confidence interval –0.27, –0.05, $p = 0.006$). However, delayed radical prostatectomy increased the mean IIEF-6 score over a 10-yr period compared with immediate surgery ($p = 0.001$), even under the assumption that all men placed on active surveillance are treated within 5 yr.

Conclusions: Small differences in erectile function recovery in younger men are offset by a longer period of time living with decreased postoperative function. Better erectile recovery in younger men should not be a factor used to recommend immediate surgery in patients suitable for active surveillance, even if crossover to surgery is predicted within a short period of time.

Patient summary: Younger men have better recovery of erectile function after surgery for prostate cancer. This has led to the suggestion that delaying surgery for low-risk disease may lead patients to miss a window of opportunity to recover erectile function postoperatively. We conducted a modeling study and found that predicted erectile recovery was far superior on delayed treatment because slightly better recovery in younger men is offset by a longer period of time living with poorer postoperative function in those choosing immediate surgery.

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1. Introduction

There is widespread agreement in the academic community that men with low-risk prostate cancer should be managed by active surveillance. The approach is recommended in guidelines [1] based on evidence that risk of prostate cancer mortality is very low [2] and not improved by treatment [3]. Yet resistance to active surveillance remains, with one recent study demonstrating that while rates of active surveillance have increased, a majority of men with low-risk prostate cancer are nonetheless treated curatively [4].

A key rationale for conservative management is the avoidance of treatment-related morbidities, such as erectile dysfunction. However, an argument can be made that the possibility of such morbidities actually justifies immediate surgery. This argument starts from the premise that many men managed conservatively do end up being treated: in one well-known study, the probability of radical treatment was 57% by 15 yr [2]. Given that the risk of postoperative erectile dysfunction increases with age [5], patients who delay treatment may lose the window of opportunity to recover erectile function after surgery. We have heard this argument expressed as: “I’m probably going to have to operate on you eventually, so I might as well treat you now while you are young and have a good chance of recovery.”

Numerous studies have compared erectile function between men undergoing surgery versus active surveillance, the randomized ProtecT study being a notable example [6]. A challenge of such studies is that functional outcomes in conservatively managed patients depend on the rate of crossover to surgery: a more aggressive approach to monitoring will lead to more treatment and hence poorer functional outcomes. An alternative is to use a statistical modeling approach, which allows the rate of surgery to be varied. At Memorial Sloan Kettering Cancer Center, patients undergoing radical prostatectomy (RP) complete pretreatment and post-treatment patient-reported outcomes as a routine part of clinical care. These data allow us to model a quantitative comparison between immediate and delayed surgery: comparing pretreatment function at different ages gives an estimate of how erectile function would change in an untreated man; comparing postsurgery recovery at different ages allows us to evaluate the marginal benefit of early surgery. Here we report a novel modeling study to compare long-term erectile function comparing immediate surgery versus active surveillance.

2. Materials and methods

2.1. Patients and outcomes

Following institutional review board approval, we identified 5865 patients through our prospectively maintained database who underwent open or minimally-invasive nerve-sparing RP from an experienced attending surgeon from 2009 through 2013, and who did not receive adjuvant therapy. Given that we were interested in patients potentially eligible for active surveillance, we excluded men with any clinical features of high-risk prostate cancer, including prostate-specific antigen ≥ 20 ng/ml, biopsy Gleason grade group ≥ 3 , and clinical tumor

stage $>cT2b$. Men who did not undergo bilateral nerve-sparing surgery were also omitted, leaving a cohort of 1581. Note that although we included some patients (eg, Gleason grade group 2) who are not considered eligible for active surveillance in some institutions, this does not affect our findings, as functional outcomes are not importantly different in these patients compared with those with lower risk disease. Four hundred and fifty men without preoperative erectile function scores were excluded, as well as 28 men without a postoperative score (final cohort $n = 1103$). There were no significant differences in patient age, preoperative prostate-specific antigen, comorbidities, number of positive biopsy cores, surgical margin status, extracapsular extension, seminal vesical invasion, lymph node invasion, pathology Gleason, or pathology stage between the men with and without preoperative erectile data (all $p > 0.05$).

Patient-reported erectile function was electronically collected through our web-based platform using the International Index of Erectile Function 6 (IIEF-6; range, 1–30). The surveys are administered at baseline (preoperative period) and postoperatively at 3 mo, 6 mo, 9 mo, 12 mo, 18 mo, and 24 mo or shortly before any postoperative appointments. As is standard, patients were asked to report function on oral medication—if they took Viagra or other phosphodiesterase type 5 inhibitors—but without the use of injection therapy or other erectile function aids.

2.2. Statistical analysis

Our primary aim was to model the effects of immediate surgery versus active surveillance on long-term erectile function. We plotted preoperative IIEF-6 scores against age to assess the natural rate of functional decline due to aging. Reported erectile scores in the 2-yr period following surgery were used to assess postsurgical recovery. Due to more limited data on erectile function by age after 2 yr, we assumed that recovery plateaus after 2 yr, and thereafter function declines with age at the same rate as for preoperative function.

It is well known that comorbidities have an adverse effect on erectile function. We sought to assess whether function declined at a faster rate due to aging for men with more comorbidities. Using linear regression models, we investigated the effect of patient age and comorbidity status on baseline and postoperative IIEF-6 scores, with an interaction term in the model to examine the effect of patient comorbidities on the rate of decline of erectile function with increasing age. Data on major comorbidities known to affect erectile function (cardiovascular disease, hypertension requiring medical therapy, diabetes mellitus, and peripheral vascular disease) were captured and included in the model categorized as none, one, two, or three or more major comorbidities. A significant interaction between age and the number of comorbidities would indicate that function declines faster for unhealthy patients as they age, and that the above analyses investigating the effects of delayed RP would need to be stratified by comorbidity status.

Using patient age, baseline, and postoperative IIEF-6 scores from the study cohort, we estimated the expected postoperative erectile function recovery using locally weighted scatterplot smoothing for immediate surgery versus surgery after varying periods of observation. An average IIEF-6 score over 10-yr duration was calculated for the two scenarios by calculating the area under the erectile function curve. Bootstrap resampling was used to 95% confidence intervals (CIs). Our plan was to use prior data [2] on the distribution of time to treatment to give expected erectile function on active surveillance. In brief, the predicted IIEF score over 10 yr for a patient undergoing surgery after n yr would be multiplied by the actuarial probability of surgery at n yr with results then summed over all n . However, this analysis was found not to be warranted. All statistical analyses were conducted using Stata 13 (Stata Corp., College Station, TX, USA).

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