Published in final edited form as:
J Urol. 2008 June ; 179(6): 2212–2217. doi:10.1016/j.juro.2008.01.107.

Surgeon Experience is Strongly Associated with Biochemical Recurrence after Radical Prostatectomy for all Preoperative Risk Categories

Eric A Klein[1,A], **Fernando J Bianco**[2,B], **Angel M Serio**[3,B], **James A Eastham**[2,B], **Michael W Kattan**[4,A], **J. Edson Pontes**[2,C], **Andrew J Vickers**[3,B], and **Peter T Scardino**[2,B]

[1]Glickman Urological and Kidney Institute

[2]Department of Urology

[3]Department of Epidemiology and Biostatistics

[4]Department of Quantitative Health Sciences

Abstract

Background—We have previously demonstrated that there is a learning curve for open radical prostatectomy. In this study we sought to determine whether the effects of the learning curve are modified by patient risk as defined by preoperative tumor characteristics.

Methods—The study included 7,683 eligible prostate cancer patients treated with open radical prostatectomy by one of 72 surgeons. Surgeon experience was coded as the total prior number of radical prostatectomies conducted by the surgeon prior to a patient's surgery. Multivariable survival-time regression models were used to evaluate the association between surgeon experience and biochemical recurrence, separately for each preoperative risk group.

Results—We saw no evidence that patient risk affects the learning curve: there was a statistically significant association between biochemical recurrence and surgeon experience in all analyses. The absolute risk difference for a patient receiving treatment from a surgeon with 10 compared to 250 prior radical prostatectomies was 6.6% (95% C.I. 3.4%, 10.3%), 12.0% (6.9%, 18.2%) and 9.7% (1.2%, 18.2%) for patients at low, medium and high preoperative risk patients. Recurrence-free probability for patients with low risk disease approached 100% for the most experienced surgeons

Conclusions—Cancer control after radical prostatectomy improves with increasing surgeon experience irrespective of patient risk. Excellent rates of cancer control for patients with low risk disease treated by the most experienced surgeons suggests that the primary reason such patients recur is inadequate surgical technique. The results have significant implications for clinical care.

Corresponding author: Eric A, Klein, MD, Desk A100, 9500 Euclid Avenue, Cleveland, OH 44122, 216-444-5591, kleine@ccf.org.
[A]Cleveland Clinic, Cleveland, OH
[B]Memorial Sloan-Kettering Cancer Center, New York, NY
[C]Wayne State University, Detroit, MI

Keywords

Radical prostatectomy; prostate cancer; surgery

Introduction

Radical prostatectomy is a technically challenging operation where outcomes are in part dependent upon surgical experience. For example, prior reports have shown that higher volume surgeons have shorter hospital length of stays, fewer perioperative complications, fewer anastomotic strictures, and better rates of urinary continence.[1,2,3] Furthermore, these studies showed that surgeons who had the best results for one outcome measure also performed better in other measures, that the variation among surgeons in the rate of complications was significantly greater than expected by chance, and that outcomes were independent of hospital volume.[1,2,3]

Other studies have shown that the effects of surgical experience on outcome are not restricted to post-operative complications: for example, surgeon volume has been found to be associated with overall survival after resection of rectal cancers, even though 30-day mortality was no different between high and low volume surgeons.[4] We recently reported a similar finding for radical prostatectomy, observing that a surgeon's lifetime experience with this procedure is strongly associated with the likelihood of biochemical failure that persists even after adjusting for case mix.[5] For a typical patient, we estimated a five-year probability of biochemical recurrence of 17.9% if surgery was performed by an inexperienced surgeon (10 prior cases) compared to 10.7% if performed by a more experienced one (250 prior cases).

In this study we sought to determine whether the learning curve for radical prostatectomy differs depending on preoperative patient risk as defined by pretreatment tumor characteristics. This question is important because choice of surgeon is perhaps the only patient-modifiable factor in determining outcome. The current study differs from our prior work in that in the previously performed analysis risk groups were defined postoperatively by pathological stage rather than by preoperative factors.

Specifically, we asked whether surgeon experience is important for all patients, or whether experience has important impact on outcome only for certain sub-groups, such as those at highest risk of failure. In this analysis we considered the hypotheses that surgeon technique affects either only favorable risk tumors - perhaps because recurrence for locally advanced disease is related to tumor cells that have spread before surgery – or only unfavorable disease – on the grounds that tumors with favorable pretreatment features are at very low risk for recurrence.

Methods

Patients and outcomes

The study cohort consisted of 9376 patients with clinically localized prostate cancer who were treated by open radical retropubic prostatectomy between January 1987 and December 2003 at one of four participating institutions: Memorial Sloan-Kettering Cancer Center (New York, NY), Baylor College of Medicine (Houston, TX), Wayne State University (Detroit, MI), and the Cleveland Clinic (Cleveland, OH). Patients receiving neoadjuvant therapy (n=1316), adjuvant therapy (n=85) or who had missing data for either surgeon (n=144), prostate specific antigen (PSA; n=66) or clinical stage (n=82), were excluded, leaving a total of 7,683 patients eligible for analysis. All information was obtained with

appropriate Institutional Review Board waivers, and data were de-identified prior to analysis. Patients were treated by one of 72 surgeons, all of whom treated patients only at the study institutions while on staff. Surgeons who conducted their initial radical prostatectomy at a non-study institution were asked to provide their prior caseload. Cancer recurrence was defined as a serum PSA of more than 0.4 ng/mL that was corroborated by a subsequent higher PSA level (i.e., biochemical recurrence).[6] In rare cases (e.g., <1% in the Memorial Sloan-Kettering Cancer Center data set), secondary treatment was initiated for patients who did not meet the criteria for recurrence: such treatment was counted as an event.

Statistical methods

Our research question is whether more experienced surgeons have better results irrespective of patient risk, or whether the association between experience and outcome is found only in certain risk groups. For the preoperative risk analysis, patients were categorized into 3 risk group categories as described by D'Amico et al. based on preoperative variables: low (PSA <10 and biopsy Gleason score ≤ 6 and clinical stage <T2c), high (PSA > 20 or biopsy Gleason score ≥ 8 or clinical stage ≥ T2c) and intermediate (did not meet criteria for high or low risk).[7]

For each patient, surgeon experience was coded as the number of radical prostatectomies conducted by the surgeon prior to the patient's operation. This number reflects total prior experience, including operations conducted at former institutions, and those for patients ineligible for analysis. We first conducted exploratory analyses to see if there were differences in surgical experience by risk group. For these analyses, surgeon experience was entered as an continuous variable in a logistic regression model with clustering by surgeon.

Our main analysis was to evaluate the association between surgeon experience and recurrence after radical prostatectomy within each risk group. To do so, we fitted a multivariable, parametric survival-time regression model; we used a log-logistic survival distribution to model hazard over time as length of follow-up is not independent of surgeon experience. Surgeon experience was entered as a continuous variable. As the relationship between experience and outcome may be non-linear, we used restricted cubic splines with knots at the quartiles. We adjusted for within-surgeon clustering using a generalized estimating equations approach[8] by specifying the *cluster* option in Stata 9.2 (Stata Corp., College Station, TX). As few patients died before experiencing recurrence (5-year overall survival probability of 95%), we did not adjust for competing risk and censored patients at the date of death.

We originally intended to use year of surgery as a covariate. However, when first fitting our statistical model to predict recurrence by surgical experience, we observed some implausible results among patients with high preoperative risk: the learning curve increased up to approximately 500 prior cases and then started to decrease such that very highly experienced surgeons appeared to have comparable results to surgeons treating their first case. On analysis, this appeared to be due to our inclusion of year of surgery as a covariate. The learning curve did not decline if we removed year of surgery as a covariate or if we restricted analysis to patients treated after 1995 (either with and without year of surgery), when stage shift in this cohort appeared to be complete[5]. Accordingly, we believe that the apparent decline in the learning curve is a statistical artifact caused by the high correlation between year of surgery and surgeon experience, coupled with the limited number of high risk patients treated by the surgeons with the greatest levels of experience. The learning curves for low and moderate risk patients were unaffected by the inclusion or otherwise of year of surgery as a covariate, whether or not the sample was restricted to patients treated

after 1995. Therefore, all results presented hereafter are without adjustment for year of surgery.

To produce a learning curve for each subgroup of patients, we calculated the five-year recurrence-free probability predicted by the model for each level of surgical experience, using the mean value for covariates in that subgroup. Confidence intervals for the difference in 5-year recurrence rates for 10 vs 250 prior cases were determined using bootstrap methods with 1000 replications. A pre-specified sensitivity analysis was to repeat all analyses in the subgroup of patients treated after 1995, after which stage migration seemed to be largely complete.[5,9]

Results

Clinical and pathological patient characteristics are shown in Table 1. Based on preoperative tumor characteristics, 3422 (45%) patients were categorized as low risk, 2527 (33%) as intermediate risk, and 1734 (23%) as high risk. There was a moderate but statistically significant negative association between risk group and surgeon experience ($P = .011$), for preoperative risk. These results appeared to be due to stage migration: there was no statistically significant association between surgeon experience and preoperative ($P = .2$) risk when the analysis was restricted to patients treated after 1995.

In total, there were 1253 recurrences. The median follow-up for recurrence-free patients was 4.0 years. The learning curve for cancer control after radical prostatectomy, stratified by preoperative risk group, is shown in Figure 1. To illustrate the learning curve, the adjusted 5-year recurrence-free probability for a patient treated by a surgeon with 10 and 250 prior cases are shown in Table 2. Surgeon experience was significantly associated with outcome for all risk groups ($p<0.001$ for low and intermediate risk; $p=0.016$ for high risk). Moreover, the risk difference between more and less experienced surgeons is clinically relevant for all risk categories. The curves for the low and intermediate risk groups continue to increase after 1000 completed cases. This suggests that surgeons continue to improve, even after they are considered to be highly experienced.

Table 3 gives the results of a sensitivity analysis, restricted to patients treated after 1995, when stage migration in our cohort appeared largely complete. These results confirm our main findings that surgeon experience has clinically relevant effects irrespective of risk group. The learning curves for each risk group were also similar (data not shown): in particular, the five-year recurrence free probability was >98% for a patient with low risk disease treated by a surgeon with the greatest levels of experience.

As an additional sensitivity analysis, we used tertiles of the Kattan preoperative nomogram[10] to define risk groups. Five-year recurrence-free survival probabilities were 93.4% to 98.3%; 87.2% to 93.3% and < 87.2% for low, intermediate and high risk groups respectively. Surgeon experience was associated with biochemical recurrence for all three risk groups ($p=0.002$, $p<0.001$ and 0.002). Absolute differences in recurrence probabilities between patients treated by surgeons with 10 and 250 cases were very similar to the main analysis (7.0%, 9.9% and 9.9%).

Discussion

We have found that cancer control after radical prostatectomy improves with increasing surgeon experience irrespective of preoperative risk group. For the overall cohort, the absolute decrease in risk of recurrence at five years for a patient seeing an experienced rather than an inexperienced surgeon varies between 6.6% and 12% (Table 2) depending on risk group. These differences increased for patients treated after 1995 (Table 3), further

emphasizing the clinical relevance of surgeon experience in the PSA era. We found no evidence that it is only high risk cases that may need to be treated by highly experienced surgeons and can thus state that the best chance for cure rests in the most experienced hands for patients in all risk groups. These findings corroborate prior studies reporting associations between a surgeon's yearly caseload and decreased perioperative mortality[11], lower rates of surgical complications[1,2,3], and improved overall survival[4], and support calls for regionalization of prostate cancer care at centers of excellence[12] as has been recommended by the National Health Service in the United Kingdom.[13] The learning curves for patients with low risk disease asymptotes towards 0% recurrence with increasing surgeon experience. Conversely, the learning curve for high risk disease flattens at approximately 70% recurrence-free probability at five years, suggesting that about a third of these patients cannot be cured by surgery alone. These findings have important implications for clinical care. Specifically, if a sufficiently experienced surgeon is able to cure all or nearly all patients with low risk disease, the obvious corollary is that recurrence in these patients is primarily a matter of surgical technique. Such a conclusion supports the need for research and changes in surgical education. It is currently unclear exactly what surgical steps the most experienced surgeons use to avoid recurrence; our findings make it clear that systematic research is required to identify the critical aspects of radical prostatectomy that are associated with cancer control. These findings also suggest a need to expand opportunities for training in surgical technique for surgeons in the early years after residency training, encourage less experienced surgeons to look at their own results and get additional training, and to determine if surgical simulators and minimally invasive tools such as robots can shorten the learning curve. It is also clear from these results that surgical experience should be added to nomograms that predict the likelihood of cure based on pre-treatment parameters.

The observation of flattening of the learning curve in patients in the high risk group suggests that surgery alone in not able to cure approximately one-third of those in this group. This most likely reflects that a subset of those with the most unfavorable tumor characteristics have cancer outside the immediate confines of the prostate, and that their chance for cure is not determined by therapy directed at the primary tumor. It is clear that these patients require a multimodality approach to treatment, with the best combination and sequencing of available modalities including surgery, radiation, and systemic therapies yet to be determined.

One possible limitation of our study is that the model is based on patients treated at major academic centers. It is not clear that our results pertain to surgeons practicing in other settings. For example, surgeons in our cohort may have steeper learning curves than those in solo practice in the community because they have protected research time, work in a competitive environment that promotes criticism and self-evaluation and are constantly exposed to new ideas and techniques.

Moreover, one of our findings – that recurrence rates for low risk cancers tend towards zero with increasing surgical experience – is based on a very limited number of surgeons: only two surgeons in our series treated more than 1000 cases. We do not believe that this materially affects our conclusions, on the grounds that even if only one surgeon can achieve near zero recurrence rates, recurrence must be due to inadequate surgical technique. However, caution is advised in applying these results to other surgeons. It seems plausible that outcome may differ between two surgeons with similar levels of experience and, as such, it may not be the case that all highly experienced surgeons have uniformly excellent results with low risk disease.

In conclusion, the surgical learning curve for radical prostatectomy is relevant for all patients, irrespective of preoperative risk. Recurrence rates are close to zero for patients with low risk disease treated by the most experienced surgeons in our data set, suggesting that the primary reason such patients recur is inadequate surgical technique.

Acknowledgments

This research was funded in part by a P50-CA92629 SPORE grant from the National Cancer Institute, the Allbritton Fund, the Koch Foundation, and the Maltz Family Foundation. The funding bodies had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Key for Definitions

PSA prostate specific antigen

References

1. Hu JC, Gold KF, Pashos CL, Mehta SS, Litwin MS. Role of surgeon volume in radical prostatectomy outcomes. J Clin Oncol. 2003; 21:401–5. [PubMed: 12560426]
2. Bianco FJ Jr, Riedel ER, Begg CB, Kattan MW, Scardino PT. Variations among high volume surgeons in the rate of complications after radical prostatectomy: further evidence that technique matters. J Urol. 2005; 173:2099–103. [PubMed: 15879851]
3. Begg CB, Riedel ER, Bach PB, Kattan MW, Schrag D, Warren JL, et al. Variations in morbidity after radical prostatectomy. N Engl J Med. 2002; 346:1138–44. [PubMed: 11948274]
4. Schrag D, Panageas KS, Riedel E, Cramer LD, Guillem JG, Bach PB, et al. Hospital and surgeon procedure volume as predictors of outcome following rectal cancer resection. Ann Surg. 2002; 236:583–92. [PubMed: 12409664]
5. Vickers AJ, Bianco FJ, Serio AM, Eastham JA, Schrag D, Klein EA, et al. The surgical learning curve for prostate cancer control after radical prostatectomy. J Natl Cancer Inst. 2007; 99:1171–7. [PubMed: 17652279]
6. Stephenson AJ, Kattan MW, Eastham JA, Dotan ZA, Bianco FJ Jr, Lilja H, et al. Defining biochemical recurrence of prostate cancer after radical prostatectomy: a proposal for a standardized definition. J Clin Oncol. 2006; 24:3973–8. [PubMed: 16921049]
7. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. J Amer Med Assn. 1998; 280:969–74.
8. Lee, EW.; Amato, D. Survival Analysis, State of the Art. Dordrecht: Kluwer; 1992. Cox-type regression analysis for large number of small groups of correlated failure time observations.
9. Dong F, Reuther AM, Magi-Galluzzi C, Zhou M, Kupelian PA, Klein EA. Pathological Stage Migration Has Slowed in the Late PSA Era. Urology. 2007; 70:839–42. [PubMed: 18068435]
10. Stephenson AJ, Scardino PT, Eastham JA, Bianco FJ Jr, Dotan ZA, Fearn PA, et al. Preoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. J Natl Cancer Inst. 2007; 98:715–7. [PubMed: 16705126]
11. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med. 2003; 349:2117–27. [PubMed: 14645640]
12. Lipscomb J. Transcending the volume-outcome relationship in cancer care. J Natl Cancer. 2006; 98:151–4.
13. [accessed on September 1, 2007] Making Progress on Prostate Cancer, report of the National Health Service. Nov. 2004 www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4093866

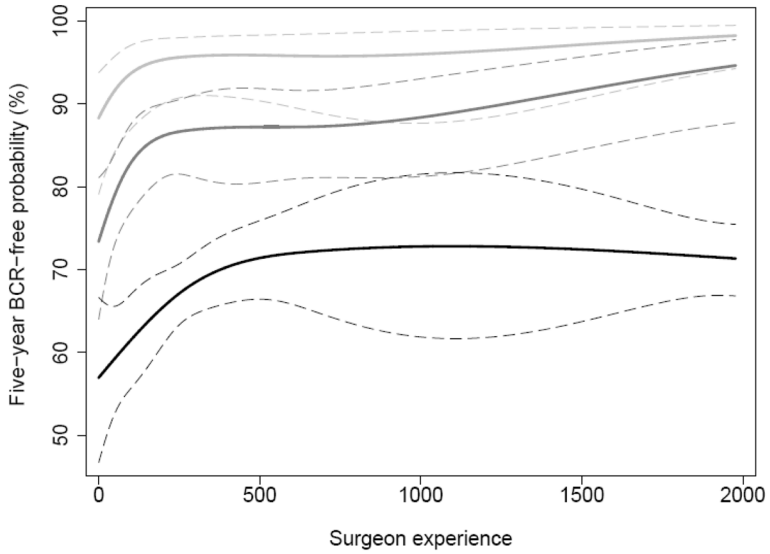

Figure 1.

The learning curve for cancer control after radical prostatectomy, stratified by pre-operative risk group. Predicted probability of freedom of biochemical recurrence (BCR) at 5 years with increasing surgeon experience. Probabilities are for a patient with typical cancer severity in the risk group (mean PSA, pathological stage and grade) within each group. Light grey lines: low risk; Medium grey lines: intermediate risk; Black lines: high risk. Dotted lines are 95% C.I.

Table 1

Clinical and pathological patient characteristics by preoperative risk category

	Risk Category		
	Low* N=3422	**Intermediate** N=2527**	**High*** N=1734**
Age at surgery (years)	60 (55, 65)	62 (57, 66)	63 (58, 67)
Total PSA (ng/ml)	5.7 (4.4, 7.0)	8.4 (5.6, 12.0)	10.6 (6.0, 22.8)
Clinical Stage			
T1	2279 (67%)	1124 (44%)	268 (15%)
T2a	1143 (33%)	794 (31%)	234 (13%)
T2b	0 (0%)	609 (24%)	175 (10%)
T2c/T3/T4	0 (0%)	0 (0%)	1057 (61%)
Biopsy Gleason score			
≤ 6	3422 (100%)	1012 (40%)	831 (48%)
7	0 (0%)	1515 (60%)	489 (28%)
≥ 8	0 (0%)	0 (0%)	414 (24%)
Pathology Gleason score			
≤ 5	242 (7%)	99 (4%)	87 (5%)
6	1906 (56%)	677 (27%)	414 (24%)
7	1235 (36%)	1603 (63%)	924 (53%)
8	32 (1%)	116 (5%)	198 (11%)
≥ 9	7 (0%)	32 (1%)	111 (6%)
Extracapsular extension	524 (15%)	875 (35%)	840 (48%)
Seminal vesicle invasion	52 (2%)	270 (11%)	368 (21%)
Lymph node metastasis	22 (1%)	82 (3%)	184 (11%)
Surgeon experience			
0–49	570 (17%)	494 (20%)	327 (19%)
50–99	296 (9%)	239 (9%)	160 (9%)
100–249	594 (17%)	518 (20%)	439 (25%)
250–999	1336 (39%)	938 (37%)	624 (36%)
≥ 1000	626 (18%)	338 (13%)	184 (11%)
Positive surgical margins	670 (20%)	745 (29%)	633 (37%)

* PSA < 10ng/ml and biopsy Gleason score ≤ 6 and clinical stage ≤ T2a

** Does not meet the criteria for either high or low risk

*** PSA > 20ng/ml or clinical stage ≥ T2c or biopsy Gleason score ≥ 8.

Table 2

Effects of surgeon experience on outcome, separately by preoperative risk group. Probabilities are for a patient with typical cancer severity within each group (mean PSA, stage and grade) treated at the midpoint of the series. 95% confidence intervals for the absolute and relative differences are given in parentheses.

Analysis	Adjusted P value for surgeon experience	Adjusted 5-year probability of recurrence		10 vs 250 prior cases	
		10 prior cases	250 prior cases	Absolute difference	Relative difference
Low risk	<0.001	11.0%	4.4%	6.6% (3.4%, 10.3%)	2.5 (1.7, 4.0)
Intermediate risk	<0.001	25.4%	13.4%	12.0% (6.9%, 18.2%)	1.9 (1.5, 2.6)
High risk	0.016	42.6%	32.9%	9.7% (1.2%, 18.2%)	1.3 (1.03, 1.6)

Table 3

Effects of surgeon experience on outcome, separately by preoperative risk group: analysis restricted to patients treated after 1995 (n=5038). Probabilities are for a patient with typical cancer severity within each group (mean PSA, stage and grade) treated at the midpoint of the series. 95% confidence intervals for the absolute and relative differences are given in parentheses.

Analysis	Adjusted P value for surgeon experience	Adjusted 5-year probability of recurrence		10 vs 250 prior cases	
		10 prior cases	250 prior cases	Absolute difference	Relative difference
Low risk	0.008	10.3%	2.2%	8.1% (2.7%, 12.8%)	4.7 (2.2, 11.8)
Intermediate risk	<0.001	27.1%	10.4%	16.7% (7.6%, 25.1%)	2.6 (1.7, 4.3)
High risk	0.001	46.3%	19.5%	26.8% (11.6%, 43.4%)	2.4 (1.5, 3.8)