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Original article

Learning curve of minimally invasive radical prostatectomy: Comprehensive evaluation and cumulative summation analysis of oncological outcomes

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Abstract

Background and objective: The primary objective was to evaluate the learning curve of minimally invasive radical prostatectomy (MIRP) in our institution and analyze the salient learning curve transition points regarding oncological outcomes.

Methods: Clinical, pathologic, and oncological outcome data were collected from our prospectively collected MIRP database to estimate positive surgical margin (PSM) and biochemical recurrence (BCR) trends during a 15-year period from 1998 to 2013. All the radical prostatectomies (laparoscopic prostatectomy [LRP]/robot-assisted laparoscopic radical prostatectomy [RARP]) were performed by 9 surgeons. PSM was defined as presence of cancer cells at inked margins. BCR was defined as serum prostate-specific antigen >0.2 ng/ml and rising or start of secondary therapy. Surgical learning curve was assessed with the application of Kaplan-Meier curves, Cox regression model, cumulative summation, and logistic model to define the "transition point" of surgical improvement.

Results: We identified 5,547 patients with localized prostate cancer treated with MIRP (3,846 LRP and 1,701 RARP). Patient characteristics of LRP and RARP were similar. The overall risk of PSM in LRP was 25%, 20%, and 17% for the first 50, 50 to 350, and >350 cases, respectively. For the same population, the 5-year BCR rate decreased from 30% to 16.7%. RARP started 3 years after the LRP program (after approximately 250 LRP). The PSM rate for RARP decreased from 21.8% to 20.4% and the corresponding 5-year BCR rate decreased from 17.6% to 7.9%. The cumulative summation analysis showed significantly lower PSM and BCR at 2 years occurred at the transition point of 350 cases for LRP and 100 cases for RARP. In multivariable analysis, predictors of BCR were prostate-specific antigen, Gleason score, extraprostatic disease, seminal vesicle invasion, and number of operations ($P < 0.05$). Patients harboring PSM showed higher BCR risk (23% vs. 8%, $P < 0.05$).

Conclusions: Learning curve trends in our large, single-center experience show correlation between surgical experience and oncological outcomes in MIRP. Significant reduction in PSM and BCR risk at 2 years is noted after the initial 350 cases and 100 cases of LRP and RARP, respectively.

Keywords: Prostate cancer; Laparoscopic prostatectomy; Robotic prostatectomy; CUSUM analysis; Learning curve

1. Introduction

Prostate cancer (PCa) is the most common solid tumor affecting men and second most common cause of cancer-related mortality [1]. PCa pose a significant burden on the healthcare system all over the world [2]. Radical prostatectomy (RP) is the gold standard treatment care for clinically significant, localized PCa with superior cancer control, acceptable complication rates, and functional outcomes [3]. RP is performed as open, laparoscopic, or robot-assisted surgeries depending on the level

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of expertise, patients' preference, and availability of the technology. Surgical robots are widely available in most of the European and United States centers and robot-assisted laparoscopic radical prostatectomy (RARP) is being commonly offered as a primary treatment options in patients eligible for radical treatment [4,5]. With more urologic surgeons gearing up toward mastering the robotic technology, several researchers have shown significant interests in dissecting the anatomy of the learning curve in robot-assisted minimally invasive prostate surgeries [6–10].

Currently, the background surgical experience of the urologists taking up robotic surgery is highly heterogenous. Conventionally, centers performing large-volume laparoscopic surgeries have successfully adopted robotic surgeries [11]. However, the need for laparoscopy experience before robotic surgery is often debated. In large volume centers, surgeons with extensive open prostatectomy experience begin RARP and had shown favorable oncological and functional results [12,13]. More recently, the urology residents are being exposed to various robotic surgeries well ahead of the corresponding open surgical experience. This heterogeneity in the learning population makes it difficult to define a standardized learning curve for robotic prostatectomy [14]. In this study, we evaluated the learning curve of laparoscopic prostatectomy (LRP) and RARP in our high-volume institution for PCa and applied the cumulative summation (CUSUM) analytical technique [15] to identify salient learning curve transition points for LRP and RARP regarding oncological outcomes.

2. Materials and methods

2.1. Patient cohort

We retrospectively reviewed the prospectively maintained RP database of 15 years duration from 1998 to 2013 at our institution with high-volume PCa and identified 6,132 patients who underwent minimally invasive RP—laparoscopic (LRP) or robot-assisted RP (RARP). We excluded 585 patients with insufficient data on follow-up and surgeon information (562 patients) and those who received immediate post-op adjuvant therapy as part of transition from open RP during early part of LRP experience (23 patients). All the patients included in the analysis were restaged systematically to existing pathological classification to maintain uniformity. We started performing RARP 3 years after beginning the LRP program and during the transition from LRP to RARP all the surgeons continued to perform both LRP and RARP until 2008 when all the RPs were exclusively robot assisted. All the RPs (LRP/RARP) were performed by 9 surgeons and the surgery count and the type for each surgeon was continuously maintained in the database. Each individual surgeon started RARP after personally performing approximately 250 cases of LRP.

2.2. Outcomes

The clinical, pathologic, and oncological outcome data were collected from our RP database for each particular surgeon. The learning curve profile for each surgeon was created by categorizing the patients based on the type of RP (LRP/RARP) and also arranging them in a chorological order of performance. Positive surgical margin (PSM) was defined as microscopic identification of cancer cells at inked margins of the RP specimen. Biochemical recurrence (BCR) was defined as serum prostate-specific antigen >0.2 ng/ml and rising or start of secondary therapy after RP.

2.3. Statistical analysis

Wilcoxon signed-rank test was used for comparing matched samples and crosstabs applying chi-square/Fisher's exact tests were used to assess the relationship among continuous variables. Multivariate analysis was used to identify the various risk for BCR. Surgical learning curve was assessed with the application of Kaplan-Meier curves, Cox regression model, CUSUM, and logistic model to define the "transition point" of surgical improvement regarding PSM and BCR outcomes [16]. The analysis was performed using SAS, V 9.2 software.

3. Results

We identified 5,547 patients with localized PCa treated with minimally invasive radical prostatectomy (MIRP) (3,846 LRP and 1,701 RARP). Patient characteristics of LRP and RARP were similar as shown in Table 1.

Table 1
Population's characteristics

Variable (range)	LRP	RARP	*P* value
Number of patients	3,846	1,701	
Mean age in years	62 (58–66)	62 (57–67)	0.9
Mean PSA, ng/ml	7.6 (5.6–10.9)	6.6 (5.2–9.0)	0.11
Mean prostate volume, mm^3	45.3 (33–90)	46.3 (30–86)	0.09
Gleason score			
≤ 5	532 (13.9%)	87 (5.1)	0.83
6	1,964 (51.4%)	932 (55.2%)	
7	1,140 (29.8%)	625 (37%)	
≥ 8	187 (4.9%)	44 (2.6%)	
Pathological stage			
pT3a	711 (18.5%)	366 (21.5%)	0.65
pT3b	312 (8.1%)	100 (5.9%)	
Positive lymph nodes	29 (0.7%)	12 (0.7%)	0.8

PSA = prostate-specific antigen.