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Original Article

Retzius-sparing robot-assisted radical prostatectomy: early learning curve experience in three continents

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Objective

To assess the effect of surgical experience on peri-operative, functional and oncological outcomes during the first 50 Retzius-sparing robot-assisted radical prostatectomy (RsRARP) cases performed by surgeons naïve to this novel approach.

Materials and Methods

We retrospectively evaluated the initial cases operated by 14 surgeons in 12 different international centres. Pre-, peri- and postoperative features of the first 50 patients operated by each surgeon in all the participating centres were collected. The effect of surgical experience on peri-operative, functional and oncological outcomes was firstly evaluated after stratification by level of surgical experience (initial [≤25 cases] and expert [>25 cases]) and after using locally weighted scatterplot smoothing to graphically explore the relationship between surgical experience and the outcomes of interest.

Results

We evaluated 626 patients. The median follow-up was 13 months in the initial group and 9 months in the expert group ($P = 0.002$). Preoperative features overlapped between the two groups. Shorter console time (140 vs 120 min; $P = 0.001$) and a trend towards lower complications rates (13 vs 5.5%; $P = 0.038$) were observed in the expert group. The relationship between surgical experience and console time, immediate urinary continence recovery and Clavien–Dindo grade ≥2 complications was linear, without reaching a plateau, after 50 cases. Conversely, a non-linear relationship was observed between surgical experience and positive surgical margins (PSMs).

Conclusions

In this first report of a multicentre experience of RsRARP during the learning curve, we found that console time, immediate urinary continence recovery and postoperative complications are optimal from the beginning and further quickly improve during the learning process, while PSM rates did not clearly improve over the first 50 cases.

Keywords

Retzius-sparing, robot-assisted radical prostatectomy, learning curve, multi-centric, #ProstateCancer, #uroonc

Introduction

In the last 20 years, robot-assisted radical prostatectomy (RARP) has become one of the standard surgical treatments for prostate cancer [1]. The anterior (standard) approach was the most frequently used, replicating open or laparoscopic retropubic surgery, with several different technical variations proposed by different centres (e.g. the Montsouris approach for the seminal vesicles [2], approach directly from the Retzius space [3], lateral approach [4], anterior [5] or

posterior reconstruction [6]). In 2010, our group proposed a posterior trans-Douglas Retzius-sparing (Rs)RARP [7] approach, which had the anatomical advantage of avoiding the Santorini plexus, endopelvic fascia, puboprostatic ligaments, and all other anterior structures. This advantage clinically translated into an improved continence recovery relative to the standard approach, as recently observed in randomized clinical trials [8,9] and in meta-analytical systematic reviews [10,11]. However, several experts are still reluctant to perform RsRARP, asserting that the technique is technically difficult with a higher risk of positive surgical margins (PSMs) compared to the standard approach [12]. Despite recent data [10,11,13] showing conflicting findings in this setting, the technique was adopted by several international centres [14]; however, there is a lack of data assessing peri-operative outcomes improvement during the learning curve for RsRARP-naïve surgeons. To address this, we evaluated the effect of surgical experience on peri-operative, functional and oncological outcomes during the first 50 RsRARP cases performed by surgeons naïve to the Retzius-sparing approach in a multi-institutional setting.

Materials and Methods

Data Source

Using a survey sent via the European Association of Urology (EAU) newsletter at the end of December 2017 to all urologists on the EAU Robotic Urology Society mailing lists, we connected all international centres that perform RsRARP on a regular basis. Surgeons from the 12 international centres identified were invited to send prospectively collected data on their first 50 consecutive cases performed by Retzius-sparing-naïve surgeons. All surgeons except two were expert in standard RARP. Two surgeons had no first-hand RARP experience before their RsRARP experience. All surgeries were performed as described by Galfano et al. [7], with minor variations based on individual surgeon preference [14].

Variable Definition

For each patient, the following clinico-pathological data were prospectively collected: age at surgery; previous prostatic surgery; preoperative total PSA (ng/mL); biopsy Gleason score and International Society of Urological Pathology (ISUP) group; clinical stage (cTNM, 2017); prostatectomy Gleason score and ISUP group; pathological prostate weight; pathological stage (pTNM, 2017); and PSM status. Surgical specimens were evaluated at each centre; no central pathological review was performed. Nevertheless, the specimens were managed and reports compiled according to internationally recognized standards [15].

Peri-operative variables consisted of console time, operating time, nerve-sparing status, bladder neck-sparing status, blood loss, peri-operative transfusion rate, intra-operative and early postoperative complications (within the first 90 days after surgery) classified according to the Clavien–Dindo system [16], time to catheter removal, and hospital stay. Continence recovery was defined as the use of no pads. Immediate continence recovery was defined as the ability to use no pads soon after catheter removal. Complete potency recovery was defined as the ability to achieve penetrative intercourse with or without the use of phosphodiesterase-5 inhibitors. Biochemical recurrence (BCR) was defined as two postoperative PSA readings of 0.2 or above.

Statistical Analysis

Statistical analysis consisted of three steps. First, median and interquartile ranges, as well as frequencies and proportions, were reported for continuous and categorical variables, respectively. The Mann–Whitney *U*-test and chi-squared test were used to compare the distribution of continuous and categorical variables, respectively

Second, the effect of surgical experience on peri-operative, functional and oncological outcomes was firstly evaluated after stratification by surgical experience into an initial (≤25 cases) and an expert group (>25 cases). Surgical experience was also coded as the number of prior RsRARP procedures performed by each surgeon at the time of the index patient's operation. Locally weighted scatter-plot smoothing (LOWESS) [17] was used to explore graphically the relationship between surgical experience and operating time, immediate urinary continence recovery, PSM status, Clavien–Dindo grade ≥2 90-day postoperative complications, after adjustment for case mix (age, any previous surgery, body mass index, previous active surveillance, risk groups and prostate volume) and for clustering at single surgeon level, using generalized estimation equations [18].

Third, the Kaplan–Meier method was used to estimate continence and potency recovery. All the statistical analyses were performed using Statistical Package for Social Sciences software, version 20 (SPSS Inc., Chicago, IL, USA), except the LOWESS curves, which were built using R software v.3.5.1. All tests were two-sided with significance level set at $P < 0.05$.

Results

Overall, we evaluated 626 patients treated using the RsRARP approach by 14 surgeons in 12 centres between 2011 and 2018.

Table 1 summarizes the main features of the series and the differences found during the learning curve improvements. No statistically significant differences were observed for preoperative features between the two surgical experience groups (≤25 and >25 cases), except for a higher percentage of patients exiting an active surveillance programme in the

Table 1 Pre-, peri-, and postoperative characteristics after stratification by surgical experience into an initial (≤25 cases) and expert group (>25 cases).

Characteristic	Overall	≤25 cases	>25 cases	*P*
Median age, years	64	65	64	0.273
Median- BMI, kg/m^2	25.96	25.81	25.99	0.456
Previous prostate surgery, %	15.4	19.7	11	0.329
Previous abdominal surgery, %	23.6	21.5	25.7	0.360
Previous active surveillance, %	3.9	6.5	1.1	0.001
Median PSA, ng/mL	7	7.1	7	0.896
Risk classification, %				
Low	24.9	23.4	26.5	0.447
Intermediate	50.4	52.9	47.6	
High	24.7	23.7	25.8	
Median surgical time, min	187	195	180	0.04
Median console time for prostatectomy, min	130	140	120	0.001
Median catheterization time, days	7	7	7	0.558
Median discharge, days	3	3	3	0.727
Median prostate weight, g	40	40	45	0.502
pT, %				
pT2	62.6	63.6	61.5	0.675
pT3a	26.2	25.1	27.5	
pT3b-4	11.2	11.3	10.6	
pN, %				
pNx	58	58.4	57.5	0.911
pN0	23.1	23.4	22.9	
pN+	18.9	18.2	19.6	
PSM status, %				
Negative	64.7	67	62.2	0.481
Focal	17.8	16.8	18.9	
Positive	17.5	16.2	18.9	
PSMs in pT2, %				
Negative	81.9	82.4	81.4	0.768
Focal	9.3	10.2	8.7	
Positive	8.8	7.4	9.9	
Continence, %				
Immediate	80	77	82.4	0.097
At median follow-up	90.3	87.3	93	0.068
Potency (<65 years, bilateral intrafascial), %	76.3	73.2	79	0.086
Freedom from BCR, %	95.6	95.4	95.7	0.804
Median follow-up, months	12	13	9	0.002

expert group. Shorter console and operating times were observed in the expert group (>25 cases), whereas no statistically significant difference was observed in terms of postoperative complications, PSMs, continence and potency recovery or BCR rates between the two groups (Table 1).

Table 2 shows the 90-day postoperative complication rates stratified according to surgical experience (≤25 vs >25 cases).

The LOWESS analysis showed a linear relationship between surgical experience and operating time ($P < 0.001$; Fig. 1A) and between surgical experience and immediate continence recovery ($P < 0.001$, odds ratio 0.80; Fig. 1B), without reaching a plateau. Similarly, a linear relationship was observed between surgical experience and Clavien–Dindo grade ≥2 complications ($P = 0.02$, odds ratio 0.95; Fig. 1D). Conversely, a non-linear relationship was observed between surgical experience and PSMs ($P = 0.4$; Fig. 1C).

Figures 2 and 3 show continence and potency Kaplan–Meier curves, respectively.

Discussion

In the present study, we report the first multi-institutional data regarding learning curve outcomes for RsRARP. In 2013, data on the first 200 RsRARP cases were published from a single series [19]. Rather than a genuine learning curve, that experience represented a 'discovery curve', in which the surgeon was standardizing a new surgical technique. During that experience, several technical modifications were performed. For example, at the very beginning the seminal vesicles were cut and removed separately, bladder suspensions and bladder neck stitches were not used and surgery was performed with a three-arm standard Da Vinci model [7]. In the present study, the technique was standardized and the data represent a genuine learning curve report. This explains the initial learning curve median console time of 140 min in this multi-institutional series compared to that of 300 min in the 2013 discovery curve single series [19]. We also recorded a sharp linear decrease in operating time up to 120 min during the last cases performed and no plateau was

Table 2 Ninety-day postoperative complications, stratified according to surgical experience group (initial [≤25 cases] vs expert group [>25 cases]; $P = 0.038$).

	Overall, %	≤25 cases, %	>25 cases, %
Clavien–Dindo grade			
0	90.6	87	94.5
1–2	7.6	10.3	4.7
Bleeding that required transfusions	1.9	3.1	1.1
Deep vein thrombosis	0.7	0.7	0.7
Pulmonary embolism	0.3	0.3	0.4
Fever	1.5	1	2.2
Haematuria	2.1	2.9	1.1
Scrotal swelling	1	1.4	0.4
Acute urinary retention	2	2	1.8
3a	0.7	1.1	0.4
Percutaneous lymphocele drain	0.7	1.1	0.4
Embolization for arterial bleeding	0.2	0.3	0
3b	1.1	1.6	0.4
Rectal lesion	0.2	0.3	0
Ureteric lesion	0.7	1.4	0
Umbilical trocar dehiscence	0.2	0.3	0
Endoscopic catheter replacement	0.2	0	0.4
4–5		0	0

Fig. 1 Locally weighted scatterplot smoothing curves exploring the relationships between surgical experience and console time (**A**), immediate urinary continence (**B**), positive surgical margins (PSMs) (**C**), and Clavien–Dindo grade ≥2 complications (**D**).

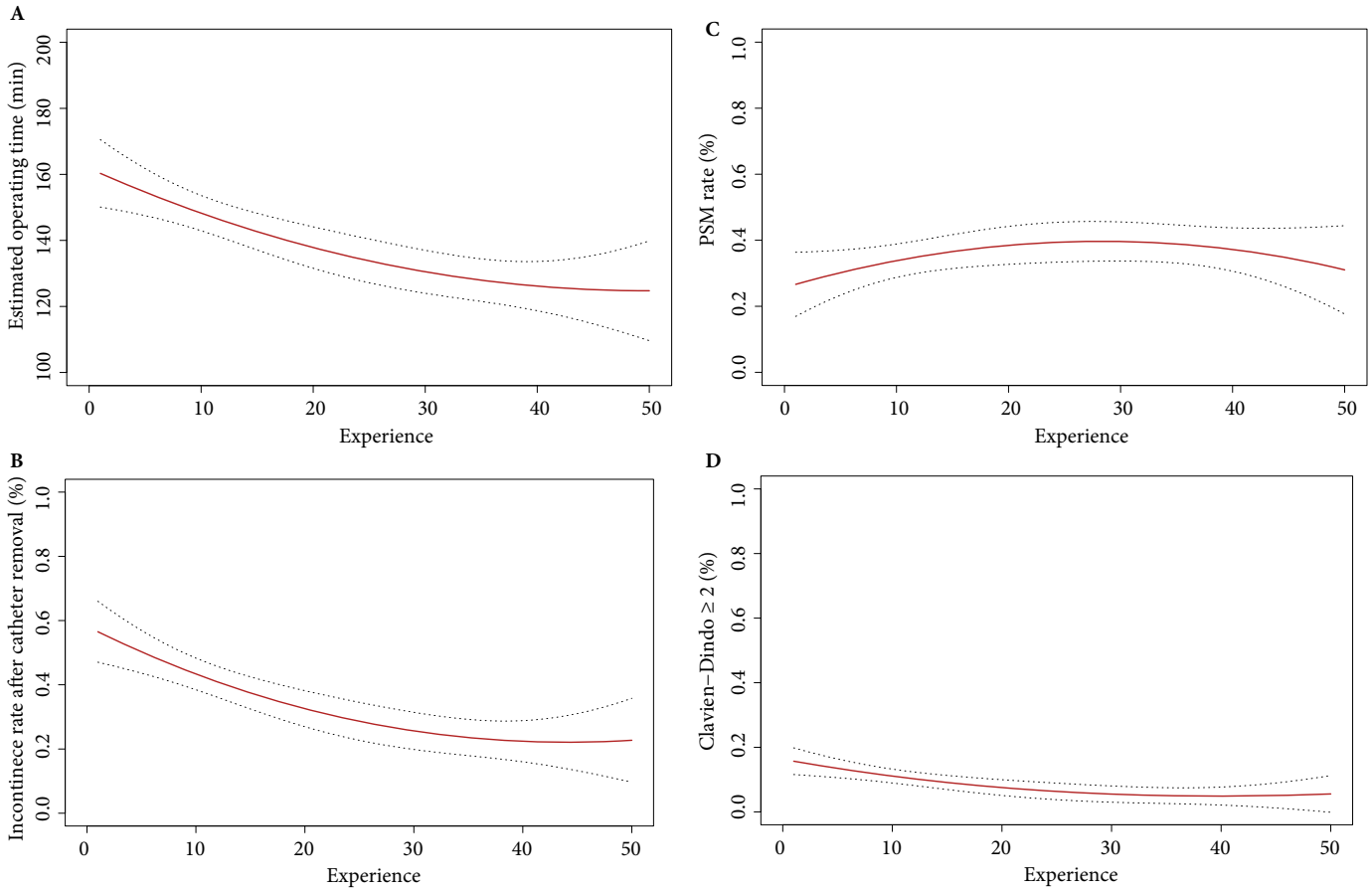


Fig. 2 Kaplan–Meier curve for urinary continence recovery ($P = 0.892$).

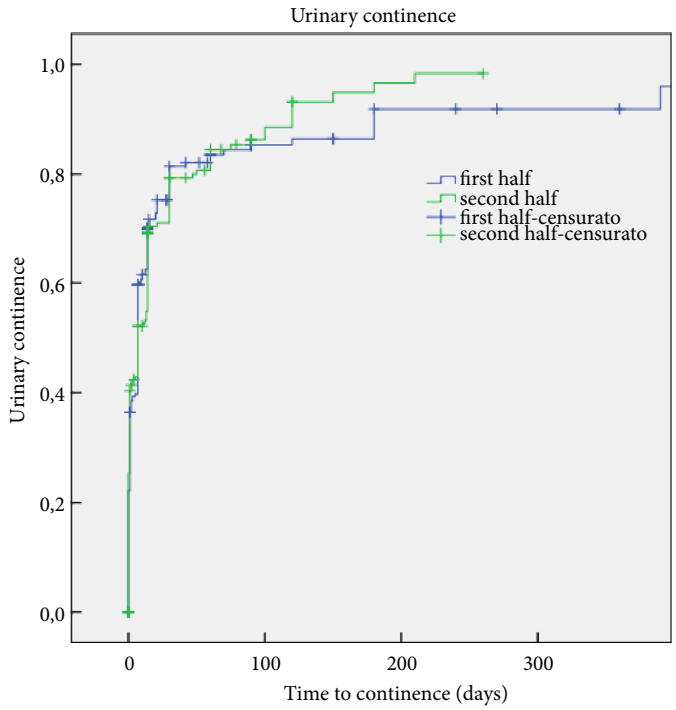
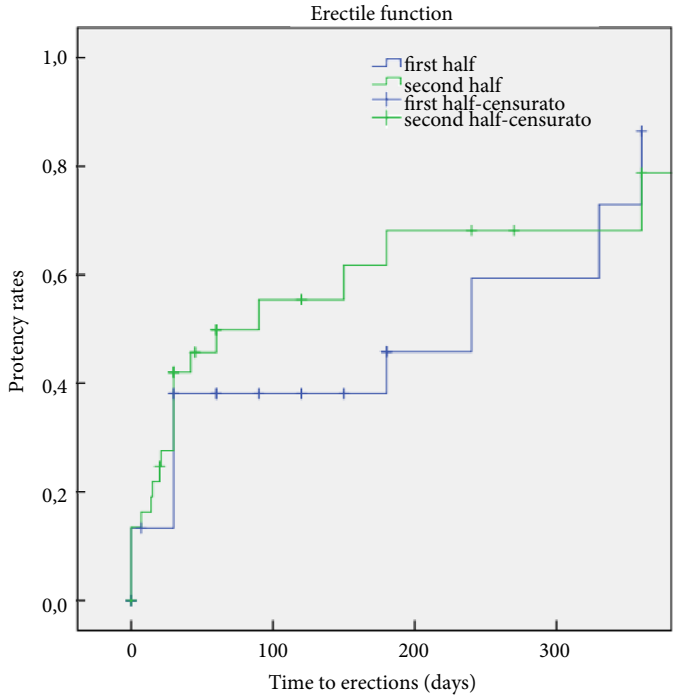


Fig. 3 Kaplan–Meier curve for erectile function recovery ($P = 0.441$).



reached (Fig. 1A), suggesting that there is still a margin of improvement. Indeed, more recent series reported median console time of <90 min [20].

Postoperative complications were very uncommon in the present multi-institutional experience. Indeed, after the first RsRARP cases were performed, the overall rate of complications observed was very low. Moreover, when we evaluated the relationship between surgical experience and Clavien–Dindo grade ≥2 complications, we demonstrated a significant decrease in complications through the surgical experience progression. It is also noteworthy that very few patients developed major (Clavien–Dindo grade ≥3) complications, and most complications occurred in the first 25 cases of the learning curve. All these findings strongly underline that the technique is safe also in RsRARP-naïve surgeons.

The PSM rate was approximately 17% in the first pT2 patients, in line with the rate for standard RARP learning curves [21]. No difference was found between the first 25 and the second 25 patients operated on by the different surgeons. Similarly, the LOWESS curve concerning PSMs (Fig. 1C) turned out not to be significantly improved by the surgeon's experience, suggesting that 50 cases are not enough to reduce the PSM rates. Nevertheless, it should be noted that the rate of PSMs reported in the present study is still more than acceptable for a learning curve series. New imaging technologies and tools for image-guided surgical navigation are promising and will allow real-time understanding of surgical anatomy, which will probably help in lowering the PSM rates during the learning curve process [22].

Moreover, when immediate continence recovery was analysed, we observed that in this multi-institutional series urinary continence recovered 1 week after surgery in more than 80% of cases. It should also be noted that a sharp decrease in immediate incontinence at catheter removal was observed through surgical experience progression, without reaching a plateau. Specifically, the rates of immediate incontinence at catheter removal decreased from 58% to 22% between case 1 and case 50 (Fig. 1B). The optimal early urinary continence recovery observed in the present study is in line with the recent systematic review [23] that confirmed the benefit of RsRARP in terms of continence recovery relative to the standard RARP. However, the reader could argue that in this systematic review no distinction was provided between studies with standard anastomosis vs posterior reconstruction of the rhabdosphincter. Considering the promising findings observed for RARP series with posterior reconstruction of the rhabdosphincter in terms of early functional recovery [24,25], future comparative studies with RsRARP are needed to satisfy this unmet need.

Moreover, when considering nerve-sparing surgery, erectile function recovered well and quickly in most cases. These figures definitely compare favourably with reports from standard RARP [21]. We chose not to perform LOWESS to assess long-term urinary continence, erectile function, or freedom from BCR because the median follow-up of the series was too short for this type of analysis and our findings

would be biased by the shorter follow-up of the patients treated at the end of the surgical experience.

The present study has some limitations. First, it was a retrospective analysis with the limitations inherent to such an approach. Second, no comparison with standard RARP was made. Third, the baseline experience of the surgeons was heterogeneous. Lastly, cases were not subjected to central pathological review and standardized assessment of outcomes. Nevertheless, the study was multi-institutional and pragmatic, and in this sense represents 'real-life' data, involving both referral and local centres, thus increasing its generalizability.

In conclusion, we have provided the first report of multi-institutional experience of the RsRARP learning curve. We found that console time, immediate urinary continence recovery and postoperative complications were optimal from the beginning, and further quickly improve during the learning process, while PSM rates did not clearly improve over the first 50 cases.

Conflicts of Interest

None declared.

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Abbreviations: BCR, biochemical recurrence; EAU, European Association of Urology; ISUP, International Society of Urological Pathology; LOWESS, locally weighted scatterplot smoothing; PSM, positive surgical margin; RsRARP, Retzius-sparing robot-assisted radical prostatectomy.

