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Factors Predicting The Return Of Urinary Continence Following Robot-Assisted Laparoscopic Prostatectomy

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Factors predicting the return of urinary continence following robot-assisted laparoscopic prostatectomy

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ABSTRACT

Robot-assisted laparoscopic prostatectomy (RALP) is a potentially curative surgical intervention for men with clinically localized prostate cancer. Although RALP can provide excellent oncological outcomes, it is also associated with detrimental effects to functional outcomes, particularly urinary continence, which negatively impact post-operative quality of life. The purpose of this study is to identify the degree to which pre-operative patient factors, tumor characteristics, and surgical technique influenced the post-operative return of urinary continence in men undergoing RALP performed by a single surgeon for the treatment of clinically localized prostate cancer. We analyzed 182 consecutive patients with clinically localized prostate cancer who were treated with RALP between April 2013 and September 2020. A retrospective chart review was performed to evaluate pre-operative patient and tumor characteristics, as well as post-operative urinary continence. Achievement of urinary continence was defined as wearing no pads or an occasional security pad by patient-reported daily pad usage within 3 (early) and 12 months (late) after RALP. Postoperatively, 68 (37.3%) and 120 (78.9%) men achieved early and late recovery of continence, respectively. Multivariate logistic regression analyses revealed that Retzius sparing approach (OR 2.995; 95% CI 1.265 – 7.089; p = 0.013) and lower BMI (OR 0.823; 95% CI 0.823 – 0.988; p = 0.027) were associated with continence at 3 months post-operatively, while longer pre-operative membranous urethral length (OR 1.205; 95% CI 1.003 – 1.448; p = 0.047) and younger age (OR 0.907; 95% CI 0.824 – 0.998; p = 0.044) were associated with continence at 12 months post-operatively.

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BACKGROUND

Prostate Cancer: Epidemiology and Treatment

Prostate cancer continues to be the most common non-skin malignancy and the second-leading cause of cancer deaths among men in the United States. There will be an estimated 191,930 new cases diagnosed in 2020, representing 21% of new cancer cases in men, and over 33,000 deaths [1]. Fortunately, the majority of cases are slow-growing and low grade with limited aggressiveness. Consequently, the overall 5-year survival rate in the United States is greater than 98%, and the lifetime risk of death from prostate cancer is less than 3% [2]. The true prevalence of prostate cancer is likely substantially higher than reported based on evidence from autopsy studies [3, 4].

The primary risk factors for developing prostate cancer are age, race, and family history of the disease. It is primarily a disease of older men, with 99% of all prostate cancers occurring in men over the age of 50. Incidence is also known to be associated with hereditary and geographic factors previously described as 'race.' In the United States, the rate of new cases per 100,00 in 2017 was 163.8, 96.7, 80.9, and 54.9 among White, Black, Hispanic, and Asian/Pacific Islander men, respectively [5]. Other risk factors include obesity, hypertension, elevated testosterone levels, and certain environmental exposures.

In recent decades, an increasing number of cases have been diagnosed at earlier clinical stages, due primarily to the widespread adoption of prostate-specific antigen (PSA)-based testing [6]. This so-called "stage migration" has significant implications for

treatment counseling. First, a larger proportion of newly diagnosed tumors are confined to the prostate, making them more amenable to localized therapies aimed at removing malignant tissue. Second, a greater number of young, otherwise healthy men are receiving the diagnosis of prostate cancer. This population may have different goals and expectations regarding post-operative quality of life outcomes, namely the preservation of urinary and erectile function, compared to the older cohort of the pre-PSA era.

Patients with localized prostate cancer (clinical stage T1-T2, N0 or NX, M0 or MX) are stratified into risk categories to guide treatment decisions based on clinical stage, PSA, Grade Group, amount of cancer on biopsy (i.e., number of cores involved, maximum involvement of any single core), PSA density, and diagnostic imaging. Current primary treatment modalities include active surveillance (PSA testing, digital rectal exams, surveillance biopsies), external beam radiation therapy (RT), ablative procedures (cryoablation, high-intensity ultrasound, etc.), and radical prostatectomy (RP). According to current AUA guidelines, Level A evidence (strong recommendation) supports the use of RP for patients with intermediate- to high-risk disease. Level B evidence (conditional recommendation) supports its use in low-risk disease in patients who have a high probability of progression on active surveillance, though clinicians should recommend active surveillance for most low-risk localized prostate cancer patients. These conclusions are based on three notable prospective randomized controlled trials investigating the long-term mortality and functional outcomes after RP compared to other interventions.

The Scandinavian Prostate Cancer Study Group number 4 (SPCG-4) randomized 695 men with localized prostate cancer to treatment with RP or watchful waiting between

1989 and 1999. The study found a reduced risk of all-cause and prostate cancer-specific death, a lower rate of prostate cancer metastasis, and less use of palliative androgen-deprivation therapy in the RP group after a median follow-up time of 13.4 years. These effects were more pronounced among men younger than 65 years and in those with intermediate-risk tumors [7]. By contrast, the Prostate Cancer Intervention Versus Observation Trial (PIVOT), which randomized 731 men to treatment with RP or observation between 1994 and 2002, found no significant differences in all-cause and prostate cancer-mortality between groups at ten years of follow up. On sub-group analysis, the PIVOT study found a possible survival benefit to RP in men with intermediate and high-risk tumors only [8]. The generalizability of these studies is limited, however, because they were conducted either completely or partially before the era of PSA screening. Therefore, the cohorts are likely to be poorly representative of the relatively healthier contemporary population of men diagnosed with prostate cancer.

A third study, the Prostate Testing for Cancer and Treatment (ProtecT) trial, compared the long-term oncologic outcomes associated with radiotherapy, surgery, and active surveillance among men diagnosed with PSA-detected prostate cancer. In this study, 82,429 men 50 to 69 years of age were randomized to one of the three treatment arms between 1999 and 2009, with a primary outcome of prostate cancer-specific mortality at a median of 10 years follow-up. While the authors reported that surgery and radiotherapy can reduce the risk of cancer progression and metastasis, they found no significant difference in all-cause or disease-specific deaths between the three groups at

the 10-year median follow-up [9]. These initial findings suggest that there may be minimal benefit to treating prostate cancer within the first decade after diagnosis.

However, longer follow up studies in the SPCG-4 [10] and PIVOT [11] trials have since revealed oncologic benefits associated with the surgical treatment of prostate cancer. At a median follow-up time of 23 years, the authors of the SPCG-4 study reaffirmed that the prostatectomy group had significantly lower rates of overall and prostate cancer-specific mortality, as well as a lower risk of metastasis, when compared to the watchful waiting group. At this longer follow-up time, the absolute benefit associated with surgery increased by a factor of more than 2 for overall and prostate cancer-specific mortality. In the PIVOT trial, surgery was associated with lower all-cause mortality among the 249 patients with intermediate-risk disease at a median follow-up time of 19.5 years (HR = 0.68. 95% CI: 0.50-0.92). This benefit to surgery was not found in low- and high- risk groups at this time-point. Given the time delay between surgery and oncologic outcome improvements, men with longer life expectancies are likely to benefit the most from prostatectomy. It is therefore essential to consider the impact of this treatment on patient quality of life in the years following surgery.

Incontinence after Treatment of Prostate Cancer

It is well documented that each of the common primary therapies for localized prostate cancer can detrimentally affect functional outcomes with a negative impact on patient quality of life, including bowel, sexual, and urinary function. Persistent urinary incontinence has an especially profound negative impact on patient quality of life, causing emotional distress and restrictions to normal physical activity [12, 13]. As such, current AUA guidelines stress the importance of treatment counseling that incorporates shared decision making and considers patient goals and preferences as well as tumor characteristics [14].

Despite an increasing understanding of the etiology of post-prostatectomy incontinence and improvements in surgical technique, incontinence rates are still substantial and vary widely between different studies [15]. The variation in reported continence outcomes stems, in part, from the lack of standardization in the definition of continence. The most common definition of continence in the literature is patient-reported use of 0 urinary pads per day (ppd) or a single safety liner, while others have favored a stricter definition of absolutely no pad usage. A common method to further quantify the degree of urinary incontinence is to document the number of pads used per day. However, several studies have brought the validity of this approach into question, showing that patients may change their pads at different rates based on their individual attitudes and preferences rather than the actual volume of urine leakage [16, 17]. Measurement of pad weight to more accurately assess urine leakage has been employed by some studies, but this method is impractical for large-scale studies. Finally,

standardized questionnaires, such as the International Continence Society Male Short-Form (ICSmaleSF) questionnaire [18, 19], the Expanded Prostate Cancer Index Composite (EPIC) instrument [20, 21], the International Consultation on Incontinence Questionnaire (ICIQ) [22, 23], and International Prostate Symptom Score (IPSS) [24] are commonly used to evaluate urinary function and impact on quality of life.

Data on patient-reported functional outcomes from the ProtecT trial, which incorporated both measurements of pad count and some of the validated questionnaires listed above, demonstrated that RP had a greater negative effect on urinary continence than RT and active surveillance [25]. By year 6 of the study, 17% of men in the RP group were using pads, compared to 8% in the active-monitoring group and 4% in the RT group. The impact of urinary continence on quality of life was worse in the RP group for 2 years, and subsequently became comparable to the other groups. In addition, a large, population-based analysis reported that 6% of men treated with RP had undergone at least 1 procedure to treat post-prostatectomy incontinence, such as urethral sling or artificial urinary sphincter placement, by a median of 20 months after surgery [26].

The Evolution of the Radical Prostatectomy

First performed over a century ago, the RP was traditionally performed via an open, retropubic approach [27]. Over time, several innovations have been developed to improve outcomes toward the RP "trifecta": resection of malignant tissue with negative surgical margins, preservation of urinary continence, and avoidance of erectile dysfunction [28].

The introduction of the Da Vinci surgical system in 2001 prompted a shift from the open RP to a robot-assisted laparoscopic approach (RALP). The enhanced visual field and seven-degree motion provided by the robotic instruments offered the advantage of precise identification of the fascial layers surrounding the prostate. This technology was rapidly adopted despite the absence of conclusive evidence supporting its superiority at the time, and as of 2015, nearly 70% of radical prostatectomies were performed robotically in the United States [29]. In the past two decades, studies comparing the two approaches have generally concluded that RALP leads to better peri-operative and long-term functional outcomes, without compromising oncological outcomes.

Guazzoni et al. [30] performed a prospective, randomized, single-surgeon study comparing intra- and peri-operative outcomes between open RP and laparoscopic RP (LRP), concluding that LRP offers the potential advantages of reduced blood loss, safe early catheter removal, and possibly lower rates of analgesic use. The authors reported no difference in post-operative complications and positive surgical margins (PSM) between groups. In a randomized controlled trial (RCT) comparing early outcomes in 326 patients receiving RALP or open RP, Yaxley et al. [31] did not find significant differences

in oncologic outcomes (positive surgical margin rate) or post-operative complications, nor did they detect any significant differences in urinary and sexual function outcomes between the groups at 6- and 12-weeks post-surgery. Two-year results from the same cohort [32] confirmed the similar functional outcomes between groups, as determined by the urinary and sexual domains of the EPIC questionnaire.

Results from three meta-analyses [33-35] comparing RALP and open RP found that the robotic approach had better intra- and peri-operative outcomes, including estimated blood loss (EBL), transfusion rates, overall complication rate, and duration of hospital stay. Neither Cao et al. [35] nor Basiri et al. [34] found significant differences in oncological or functional outcomes at time points of up to 24 months. Tang et al. [33] found higher 12- month rates of erectile function recovery after RALP (OR: 2.37, p = 0.005) compared to open RP, but failed to find a significant difference with respect to urinary continence.

A more recent innovation to the surgical treatment of prostate cancer is the Retzius sparing approach to RALP (RS-RALP), which preserves several structures thought to play a role in urinary continence. First described by Galfano et al. in 2010, this approach passes through the pouch of Douglas, following an intrafascial plane and avoiding dissection of the anterior compartment, which contains endopelvic fascia, neurovascular bundles, puboprostatic ligaments, and the prostatic venous plexus [36]. Dissection of the bladder neck proceeds in a posterior-to-anterior fashion, preserving the integrity of the detrusor apron at the bladder neck.

An early report of the first 200 patients to undergo RS-RALP demonstrated excellent short-term urinary continence outcomes [37]. Within 7 days of catheter

removal, 90-92% of patients were continent, defined as no pads or one safety liner per day. At 1-year follow-up, the continence rate reached 100%. The patients in this cohort were primarily low to intermediate risk (96% with Gleason score ≤ 7), with relatively small prostates (median prostate volume 43 mL, interquartile range 28-58 mL). Finally, while 89-92% of patients achieved biochemical disease-free survival at one-year follow-up, the authors note that the overall PSM rate was 25.5%.

Two randomized, single surgeon trials comparing RS-RALP and the standard approach suggested that RS-RALP may provide superior short-term continence outcomes [38, 39]. Menon et al. randomized 120 patients with clinically low-intermediate risk disease to RS-RALP or traditional RALP. While the authors demonstrated significantly higher rates of continence in the RS-RALP group at 3 months, these differences were muted by 1 year after surgery. The PSM rate was noted to be higher in the RS-RALP group, though the difference was not significant (11.7% vs. 8.3%, $p > 0.05$). Asimakopoulos et al. also showed superior continence outcomes (defined as 0 ppd, no safety liner) in the RS-RALP group up to 6 months after surgery, but longer-term data was not available. More recently, Qiu et al. [40] performed a randomized, controlled, single-blind study demonstrating higher rates of immediate continence (pad-free within 1 week after catheter removal) in the RS-RALP group compared to traditional RALP (69.1% vs. 30.9%, $p = 0.000$). Continence outcomes were also better in the RS-RALP group at 1 year (HR= 1.51, log-rank $p = 0.007$), though on sub-group analysis this applied only to patients with low-intermediate risk disease. Oncologic outcomes, including PSM rate, were comparable between the two groups.

Taken together, these studies provide initial evidence that RS-RALP provides swifter return of continence compared to the traditional approach, but further studies are needed to determine whether these differences remain significant at time points up to a year after surgery. They also highlight the importance of appropriate selection of patients for this procedure, given that there is some evidence of higher PSM rates with this technique, particularly in higher risk patients. This potential drawback of RS-RALP follows directly from its 360° intrafascial dissection of the prostate, which preserves key surrounding structures as described above but also risks incomplete tumor resection, particularly in cases where the tumor is located peripherally in the gland.

Another aspect of the surgical technique to consider is preservation of the neurovascular bundle (NVB). Walsh et al. first described the posterolateral location of the NVB relative to the prostate, its relevance to erectile function, and the nerve sparing (NS) technique to improve post-operative erectile function [41, 42]. The relevance of NS approach to preservation of urinary continence has subsequently been recognized [43]. Michl et al. provided insight into the possible mechanism of improved long-term continence rates with NS RP [44]. They retrospectively analyzed patients who underwent NS and non-nerve sparing (NNS) procedures, as well as a third group who had a secondary resection of the NVBs for positive frozen-section results after initial NS dissection (secNNS). Interestingly, they demonstrated increased post-operative continence rates at 1 week, 3 months, and 1 year both among patients in the NS and secNNS groups compared to the NNS group. Continence rates at 1 year did not differ significantly between the NS and secNNS groups (85.4% vs. 87.0%; $p = 0.5$). The authors concluded

that the meticulous apical dissection involved in the NS approach, and not the actual preservation of the NVBs, accounted for the improved continence outcomes in this group.

Patient Characteristics Influencing Return of Continence

Previous studies have found that certain pre-operative patient characteristics also influence post-operative return of continence, including age, body mass index (BMI), comorbidity index, membranous urethral length (MUL), prostate volume, and lower urinary tract symptoms (LUTS) [15, 45].

Several studies have examined the effect of age on functional outcomes after radical prostatectomy. In a large retrospective study, Mandel et al. [46] stratified patients who underwent open RP or RALP into age groups of <65, ≥65 and <70, ≥70 and <75, and ≥75, and showed that continence outcomes (defined as 0-1 ppd) at 3 months (80.3%, 74.0%, 70.3%, and 66.1%, $p < 0.001$) and 1 year (93.3%, 90.8%, 86.0%, and 86.5%, $p < 0.001$) after surgery decreased significantly with increasing age at the time of surgery. It is interesting to note that, although there was a significant difference across age groups in continence rates at both time points, the difference narrowed at 1 year, suggesting that older men who ultimately achieve continence may simply take longer to do so. Similarly, Kundu et al. [47] found significant differences in rates of return of continence (defined as no pads) for patients aged <50, 50-59, 60-69, and ≥70 years (95%, 96%, 93%, and 86%, respectively, $p < 0.001$) among men who underwent open RP. In contrast, Kunz et al. [48] reported an insignificant difference in continence at 24 months (2.01 vs. 2.10, $p = 0.98$)

between patients aged <70 (n = 1,225) and ≥70 (n = 411), using ICSmaleSF questionnaire scores to quantify the degree of continence.

Studies including only RALP procedures have also yielded mixed results with respect to the effect of age on continence. Shikanov et al. [49] demonstrated a significant influence of age on the probability of achieving continence at 12 months (OR = 0.97, p = 0.002) among 1,436 men who underwent RALP. Basto et al. [50] stratified 262 men who underwent RALP into two groups (age <70 and ≥70 years). While they found a trend toward fewer older men being fully continent (no pads) at 4-6 weeks, there were no differences between the groups beyond 3 months. Similarly, Greco et al. [51] performed a single-surgeon retrospective analysis of men who underwent RALP and found that continence (no pads) was significantly lower in men ≥70 years at 6 months after surgery but returned to levels equivalent to those in younger men by 1 year. Finally, in a larger study of 2,000 RALP patients, Labanaris et al. [52] did not find a significant difference in the 12-month continence rate (no pads) between groups aged <75 and ≥75 years (92.8% vs. 86.9%, $p > 0.05$).

Membranous urethral length (MUL), the distance from the prostatic apex to the level of the urethra at the penile bulb, has also been reported to affect post-prostatectomy return of continence. This value can be measured pre-operatively on T2-weighted magnetic resonance imaging (MRI) images. A meta-analysis of studies examining this anatomical factor concluded that MUL had a significant positive effect on the odds of continence recovery at 3-, 6-, and 12-months following surgery [53]. The authors calculated that for every extra millimeter of MUL, the estimated odds of

continence recovery increased by 5-15% (OR: 1.09, 95% CI:1.05-1.15; $p < 0.001$). A recent retrospective study by Ikarashi et al. examined the effect of MUL on continence recovery after RALP [54]. The authors estimated a cutoff point for using MUL to predict return of continence at 3 months after surgery using a receiver operating characteristic (ROC) analysis. They found that using a cutoff point of 12 mm MUL could predict continence at 3 months with 80% sensitivity and 70% specificity.

Prostate volume (or weight) is another anatomical characteristic that may affect continence outcomes, although conflicting evidence exists in the literature. Mandel et al. performed a retrospective study of 5,477 patients who underwent RP and found that large prostate volume (>70 mL) negatively impacted post-operative return of continence, particularly at early (1-week and 3-month) time points [55]. Several other investigators have found similar results regarding the impact of prostate volume on post-operative continence, both in patients receiving open RP and RALP [56-58]. More recently, Galfano et al. investigated the effect of prostate volume on continence specifically after RS-RALP [59]. They evaluated 750 patients with small (<40 g), medium (40-60 g), and large (>60 g) prostates who underwent RS-RALP and found significant differences in the immediate continence rate between groups (88%, 89.5%, 81.3%; $p = 0.045$). However, no differences were observed between the groups after 1 year (93.4%, 94.1%, 94.7%; $p = 0.892$).

PURPOSE

The purpose of this study is to identify the degree to which pre-operative patient factors, tumor characteristics, and surgical technique influenced the post-operative return of urinary continence in men undergoing RALP performed by a single surgeon for the treatment of clinically localized prostate cancer.

METHODS

Patient Population

Between April 2013 and September 2020, 182 men undergoing robotic-assisted laparoscopic prostatectomy (RALP) by a single urologist for clinically localized or locally advanced prostate cancer at our institution (Yale-New Haven Hospital) were included in the final analysis, after exclusion criteria were applied.

Surgical Procedure and Pathology

RALP was performed using the multiple- or single-port da Vinci surgical robot system (Intuitive Surgical, Sunnyvale, CA) via a transperitoneal or extraperitoneal approach. Information on the details of the surgical technique were recorded, namely the presence of pelvic lymph node dissection (PLND), complete or partial nerve sparing, and Retzius sparing approach. Patients without contraindications underwent pelvic MRI pre-operatively. Pathological staging, Gleason score, Grade Group, presence of metastatic lymph nodes, and prostate weight were determined by a board-certified pathologist from whole mount surgical specimens. and retrospectively documented based on pathology reports.

Evaluation of Pre-operative Patient Characteristics and Surgical Approach

Age at the time of surgery, body mass index (BMI), type of surgical approach (nerve sparing, Retzius sparing), preoperative PSA, and serum testosterone level were

retrospectively collected from patient charts. Prostate volume was estimated on pre-operative pelvic MRI by a board-certified radiologist and extracted from image reports. MUL was retrospectively measured on T2-weighted coronal and sagittal sections as the distance from the prostatic apex to the level of the urethra at the penile bulb on pre-operative pelvic MRI. Measurements from the coronal and sagittal sections were averaged for the final estimate of MUL.

Evaluation of Post-operative Urinary Continence

Post-operative recovery of urinary continence was defined as patient-reported use of 0 ppd or an occasional safety liner, as documented in notes from routine post-operative clinic visits. Achievement of continence was defined as early if it occurred within 3 months, and late if it occurred within 12 months after the date of surgery. Catheter removal occurred one week after the date of surgery in most cases. Two patients in our cohort required prolonged catheterization longer than one week due to post-operative complications (1 urine leak, 1 urinary fistula). Patients who underwent salvage RT were excluded from our analysis starting at the date of RT initiation.

Statistical Methods

Kruskal–Wallis test was used for statistical analysis of proportions, and the Mann-Whitney U test was used for continuous variables. Univariable and multivariable logistic regression and ROC curves were used to assess discriminatory ability of membranous urethral length to predict continence following prostatectomy. Two-sided p values <0.05

were statistically significant. SPSS version 27 (IBM SPSS Statistics, Armonk, NY, USA) was utilized to conduct the analysis.

RESULTS

Patient Characteristics and Surgical Approach

We identified a total of 187 patients who underwent radical prostatectomy for the treatment of clinically localized or locally advanced prostate cancer, performed by a single surgeon at our institution between 2013 and 2020. Four patients were excluded from our analysis because the surgical procedure was performed via an open retropubic approach, rather than RALP. Thirty-one patients underwent salvage RT within one year after surgery and were therefore excluded from our analysis at the 12-month timepoint to avoid confounding effects on continence outcomes from radiation exposure. One patient underwent RT within three months after surgery and was therefore excluded from both the 3- and 12-month timepoints. The remaining 30 patients who underwent RT between 3 and 12 months were excluded from the 12-month analysis. The final number of included patients was therefore 182 at the 3-month timepoint, and 152 at the 12-month timepoint. Clinical characteristics of the patients included in the study, as well as details on the surgical approach used, are shown in Table 1. Mean patient age was 62.4 ± 6.4 years, mean BMI was 28.6 ± 4.4 kg/m^2, mean pre-operative PSA was 11.8 ± 16.7 ng/mL, mean prostate weight was 49.4 ± 25.5 g, and mean MUL was 13.7 ± 3.4 mm. All patients included in our analysis were continent prior to surgery. All patients included in our analysis underwent RALP with bilateral pelvic lymph node dissection (BPLND). 57 (31%) patients underwent a complete nerve sparing procedure, 79 (43%) patients underwent a partial nerve sparing procedure, and 46 (25%) underwent a non-nerve sparing procedure.

Retzius sparing was performed in 43 (24%) patients, and a single port procedure was performed in 11 (6%) patients.

Table 1. Patient Characteristics and Details of Surgical Approach

Patient Characteristics	Age (years)		
		Mean ± SD	62.4 ± 6.4
		Min - Max	41.2 - 76.7
		No. (%) <60	55 (30%)
		No. (%) ≥60 and <65	53 (29%)
		No. (%) ≥65 and <70	50 (28%)
		No. (%) ≥70	24 (13%)
	BMI (kg/m²)		
		Mean ± SD	28.6 ± 4.4
		Min - Max	20.1 - 44.9
	Pathological Stage		
		No. (%) Stage II	78 (43%)
		No. (%) Stage III	95 (40%)
		No. (%) Stage IV	31 (17%)
	Grade Group (Surgical Pathology)		
		No. (%) GG 1	3 (2%)
		No. (%) GG 2	109 (60%)
		No. (%) GG 3	49 (27%)
		No. (%) GG ≥4	19 (10%)
		No. (%) Unassigned[1]	2 (1%)
	Pre-operative PSA (ng/mL)		
		Mean ± SD	11.8 ± 16.7
		Min - Max	0.1 - 137
	Prostate weight (g)		
		Mean ± SD	49.4 ± 25.5
		Min-Max	14 - 182
	MUL (average)		
		Mean ± SD	13.7 ± 3.4
		Min-Max	6.4 - 23.3
Surgical approach	Non-nerve sparing	No. (%)	46 (25%)
	Partial nerve sparing	No. (%)	79 (43%)
	Complete nerve sparing	No. (%)	57 (31%)
	Non-Retzius sparing	No. (%)	139 (76%)
	Retzius sparing	No. (%)	43 (24%)
	Single Port	No. (%)	11 (6%)

[1]By convention, a Gleason score is not assigned to patients who received androgen deprivation therapy (ADT) prior to radical prostatectomy.

Early Recovery of Continence

Early recovery of urinary continence, defined as continence at 3 months after surgery, was achieved in 68 (37.4%) patients. In the univariate analysis for early recovery of continence, lower BMI (27.6 kg/m^2 vs. 29.1 kg/m^2, p = 0.014), lower prostate weight (43.0 g vs. 52.0 g, p = 0.003), and the Retzius sparing approach (60.9% vs. 29.3%, p < 0.001) were significantly associated with continence at this timepoint. Results from the multivariate analysis for early recovery of continence are shown in Table 2. BMI (OR 0.902 per kg/m^2; 95% CI 0.823 – 0.988; p = 0.027) and Retzius sparing surgery (OR 2.995; 95% CI 1.265 – 7.089; p = 0.013) were shown to be significantly and independently associated with continence by 3 months. Prostate weight (OR 0.992; 95% CI 0.971 – 1.013; p = 0.436) was found to be non-significant on multivariate analysis.

Table 2. Multivariate analysis results for the early (3-month) recovery of urinary continence. Significant values are denoted in bold.

Variable	*p* value	Odds Ratio (OR)	95% C.I. for OR
Age (years)	0.159	0.955	0.897 – 1.018
BMI (kg/m^2)	**0.027***	**0.902**	**0.823 – 0.988**
Prostate weight (g)	0.436	0.992	0.971 – 1.013
MUL (mm)	0.094	1.110	0.982 – 1.255
Non-nerve Sparing *(ref)*	0.614		
Unilateral nerve sparing	0.327	1.724	0.581 – 5.117
Bilateral nerve sparing	0.422	1.606	0.506 – 5.097
Retzius sparing	**0.013***	**2.995**	**1.265 – 7.089**

Late Recovery of Continence

Late recovery of urinary continence, defined as continence at 12 months after surgery, was achieved in 120 (78.9%) patients. In the univariate analysis, younger age at the time of surgery (61.7 years vs. 65.0 years, $p = 0.004$) was significantly associated with continence at this time point. The 12-month continence rates for age groups < 60, ≥ 60 and < 65, ≥ 65 and < 70, and ≥ 70 years were 89.3%, 73.8%, 66.0%, and 66.7%, respectively ($p = 0.053$). On multivariate analysis, MUL (OR 1.205 per mm; 95% CI 1.003 – 1.448; $p = 0.047$) and age at the time of surgery (OR 0.907 per year; 95% CI 0.824 – 0.998; p = 0.044)

were shown to be significantly and independently associated with continence at 12 months post-operatively. Results from the analysis are shown in Table 3.

As previously noted, 30 patients included in the 3-month analysis were subsequently excluded at this timepoint due to initiation of salvage radiotherapy within 1 year after surgery. Among this subset of patients, 20 (66.7%) achieved continence prior to the initiation of radiotherapy. Furthermore, a total of 22 (73.3%) of these patients achieved continence within a year after RALP.

Table 3. Multivariate analysis for the late (12-month) recovery of urinary continence. Significant values are denoted in bold.

Variable	*p* value	Odds Ratio (OR)	95% C.I. for OR
Age (years)	**0.044***	**0.907**	**0.824 – 0.998**
BMI (kg/m^2)	0.381	1.057	0.933 – 1.198
Prostate weight (g)	0.225	0.985	0.960 – 1.010
MUL (mm)	**0.047***	**1.205**	**1.003 – 1.448**
Non-nerve Sparing *(ref)*	0.128		
Unilateral nerve sparing	0.321	0.540	0.160 – 1.824
Bilateral nerve sparing	0.384	1.876	0.455 – 7.741
Retzius sparing	0.428	1.624	0.490 – 5.383

The receiver operating characteristic (ROC) curve for MUL measurement as a predictor of continence at 12 months is shown in Figure 1. The area under the curve (AUC) was 0.60. We identified a reasonable cutoff point of MUL > 10.6 mm for recovery of continence at 12 months using the ROC analysis. Using this cutoff point, we were able to predict continence at 12 months after RALP with a sensitivity of 85% and a specificity of 43%.

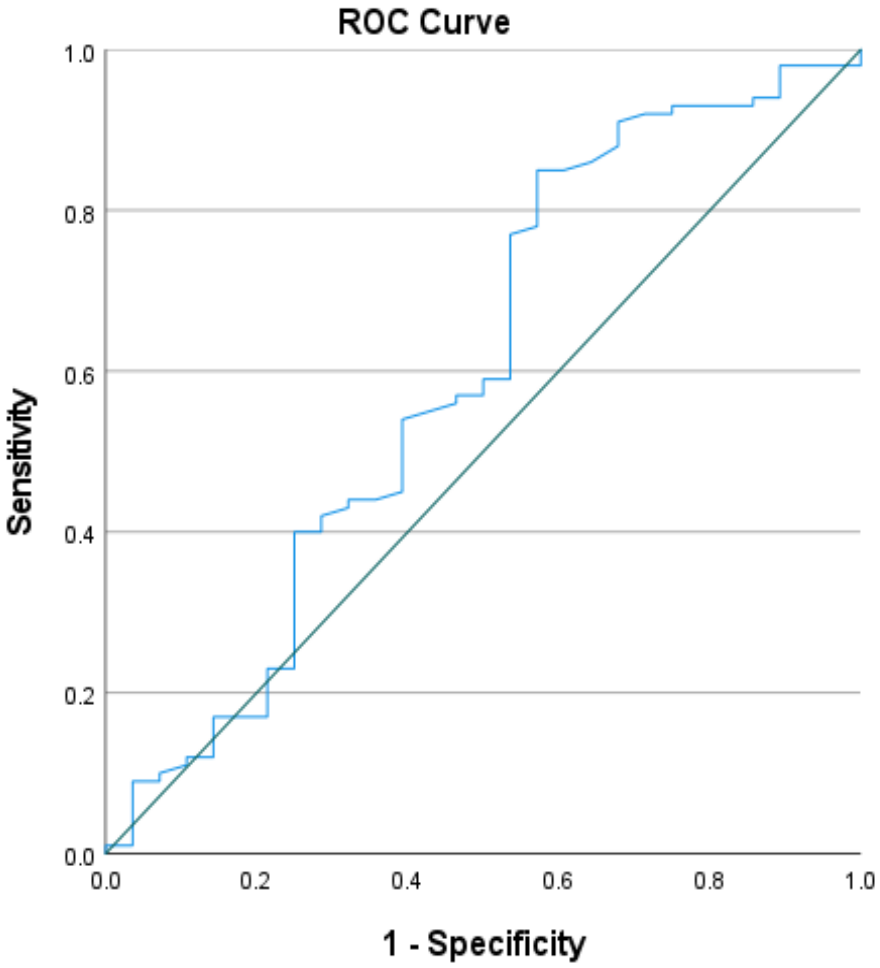

Figure 1. ROC curve for recovery of urinary continence at 12 months after RALP.

DISCUSSION

This study demonstrates that early recovery of continence after RALP is primarily associated with lower BMI and Retzius sparing approach, while younger age and longer pre-operative MUL are the strongest predictors of the return of continence at 12 months post-operatively. The overall rates of continence recovery for the patients in this cohort were 37.3% at 3 months and 78.9% at 12 months. As previously noted, post-operative continence rates vary widely in the literature. The 2012 meta-analysis performed by Ficarra et al. [15] reported 12-month continence rates ranging from 69% to 96%, with a mean value of 84% using a no pad definition. Considering a no pad or safety pad definition, as was done in this study, the authors noted a narrower range of 89% to 92%, with a mean value of 91% at 12 months.

The Retzius sparing approach was strongly associated with continence at the 3-month timepoint, however this association disappeared at the 12-month timepoint. This result is in line with data from a number of similar studies, including the Menon et al. study [38] cited previously, which also found a significant effect at 3 months that was subsequently muted by 12 months post-operatively. In our study at 3 months, the overall continence rate among patients who underwent RS-RALP was 60.9% versus 29.3% among those who underwent conventional RALP. Menon et al. achieved a 3-month continence rate of 95% with the Retzius sparing approach versus 86% with conventional RALP. These remarkably high values may be partially explained by their cohort, which consisted of younger, less obese men with overall lower stage pathology when compared to our

cohort, and also surgeon experience. Nevertheless, our results highlight the relative efficacy of the Retzius sparing approach with respect to achieving earlier restoration of continence, without necessarily affecting long term outcomes. As previously discussed, the mechanistic explanation for earlier continence using this approach is related to better preservation of the bladder neck and structures in the space of Retzius. Further studies with larger scale cohorts are needed to definitively show whether the advantage of this approach truly does not extend past the first 3 to 6 months after surgery.

Similarly, lower BMI was also predictive of higher rates of continence at 3 months after RALP, but this effect was not seen at 1 year post-operatively. This finding is consistent with a 2015 study by Matsushita et al. [60] that examined 2,849 radical prostatectomies to identify predictors of continence. The authors reported that BMI was associated with urinary continence at 6 months (OR 0.97; $p = 0.01$), but not at 12 months ($p = 0.1$). As noted previously, Mandel et al. [46] performed a large study on over 8,000 patients who underwent radical prostatectomy. They showed that BMI was significantly associated with urinary continence at both 3 months (OR 0.97; 95% CI 0.94 – 0.99; $p = 0.002$) and 12 months (OR 0.96; 95% CI 0.94 – 0.99; $p = 0.013$).

When considering the results of our study at 3 versus 12 months after RALP, it should be noted that the later timepoint carried somewhat less power than the earlier timepoint due to our exclusion criteria, which included initiation of salvage radiotherapy. Because we excluded patients from our analysis at the time of salvage therapy initiation, 30 patients were excluded from the 12-month analysis after undergoing radiation between 3 months and 1 year post-operatively. Consequently, it's possible that this

attrition partially explains the loss of the significant associations of BMI and RS-RALP with continence between the two timepoints. Among this subset, 20 (66.7%) achieved continence prior to the initiation of salvage radiotherapy, and 22 (73.3%) were continent within a year after surgery. Therefore, while not included in the final analysis, the continence rates in this subset were similar to the larger cohort.

Our analysis showed that younger age was significantly associated with higher rates of continence at one year after RALP. However, this association was not seen at 3 months. There was a trend toward increasing continence rates at 12 months across age groups < 60, ≥ 60 and < 65, ≥ 65 and < 70, and ≥ 70 years (89.3%, 73.8%, 66.0%, and 66.7%; $p = 0.053$). As discussed previously, Mandel et al. [46] also found that continence rates decreased significantly with increasing age. The 12-month continence rates for age groups < 65, ≥ 65 and < 70, ≥ 70 and < 75, and ≥ 75 years were 93.2%, 90.8%, 86.0%, and 86.5%, respectively. It should be noted that this study's cohort was slightly older than ours (mean age 63.9 years), it stratified patients into different age groups than our study, and it included both open and robotic prostatectomies.

Our results also agree with the Shikanov et al. study [49], which included only robotic procedures. They found that increasing age was associated with decreasing 1-year continence rates (OR 0.92; $p < 0.0001$), which closely matched our results. However, their overall continence rates were somewhat lower due to their use of a stricter (no pad) definition of continence. Interestingly, both Basto et al. [50] and Greco et al. [51] found that younger age was associated with higher continence rates at earlier time points, but this effect did not extend to 1 year after RALP. Our results show the opposite pattern,

with differences in continence between age groups becoming significant only at the 12-month timepoint.

Longer pre-operative MUL was also shown to be predictive of continence at 12 months after surgery, with an OR of 1.205 per millimeter (p=0.047). As previously noted, the meta-analysis conducted by Mungovan et al. [53] yielded similar results. The authors examined 11 studies that reported the OR for restoration of continence at one or more time points and found that MUL had a significantly positive effect on continence at 12 months (OR: 1.12, 95% CI: 1.03–1.22, p = 0.006). In contrast to our results, they also found significant associations of a similar magnitude between MUL and continence at 3 and 6 months. Similarly, the Ikarashi et al. study [54] found a significant association between MUL and lower rates of incontinence at 3 (OR 0.635; 95% CI 0.53 – 0.74; p < 0.0001), 6 (OR 0.699; 95% CI 0.56 – 0.85; p = 0.0002), and 12 (OR 0.743; 95% CI 0.56 – 0.96; p = 0.026) months.

This association is thought to stem from the coordinated function of the smooth muscle fibers within the membranous urethra and the rhabdosphincter that surrounds it, which plays a key role in preventing urinary leakage. Increased MUL is therefore related to a greater number of these muscular components that increase urethral closure pressure that aid in recovery of continence. Paparel et al. [61] showed this with pre- and post-operative measurements of MUL, showing that decreased length of MUL after surgery also predicts incontinence. The authors also suggested that limiting intra-operative trauma to membranous urethra, and therefore peri-urethral fibrosis and

decreased elasticity of the external urinary sphincter, is important to the preservation of continence.

After establishing the association between MUL and the late recovery of continence, we constructed an ROC curve to evaluate the predictive ability of this measurement and identify a reasonable cutoff point for favorable prediction of continence at 12 months after RALP. The results of the ROC analysis yielded a proposed cutoff point of 11 mm, which predicted 12-month recovery of continence with 85% sensitivity. However, the specificity was considerably lower at 43%, which limits its utility as an accurate predictive tool. Comparing these results to the Ikarashi et al. study [54], the authors identified a cutoff point of 12 mm for continence at 3 months, yielding an 80% sensitivity and 70% specificity.

There are several limitations which may have influenced the validity of this study's results. First, the retrospective design of the study introduced several sources of bias. Most notably, some patient records were missing or incomplete, especially with respect to consistent documentation of patient pad count in post-operative clinic notes. A prospective study with a standardized method of collecting pad count data or the use of a validated incontinence questionnaire would be a more reliable method of evaluating urinary continence outcomes. Furthermore, even among patients with complete records, self-reported pad count is an inherently imperfect measure of incontinence due to recall bias, different activity levels between patients requiring different needs for protection against urinary leakage, and different patient preferences with respect to their tolerance for urinary leakage and therefore the number of pad changes per day. Another key

limitation of the study is its relatively small size (*N*=182), which limits the study's power. Finally, the study's single-surgeon design may limit the ability to generalize the results to the entire population of men undergoing RALP.

In summary, these results add to the existing literature examining the factors, related to both pre-operative patient characteristics and surgical technique, that affect the probability of a patient recovering urinary continence in their first year after RALP. Identifying the relative importance of these influences on continence is critical to the appropriate counseling of patients considering their treatment options for prostate cancer. An understanding of the primary risk factors for post-operative incontinence presented here and elsewhere in the literature, combined with a firm understanding of each patient's specific goals and expectations, will allow physicians to provide better guidance to patients as they navigate these difficult decisions.

REFERENCES

1. Siegel, R.L., K.D. Miller, and A. Jemal, *Cancer statistics, 2020.* CA: A Cancer Journal for Clinicians, 2020. **70**(1): p. 7-30.
2. Howlader N., N.A.M., Krapcho M., Miller D., Brest A., et al. *SEER Cancer Statistics Review, 1975-2016*. 2019; based on November 2018 SEER data submission, posted to the SEER web site, April 2019.]. Available from: https://seer.cancer.gov/archive/csr/1975_2016/.
3. Jahn, J.L., E.L. Giovannucci, and M.J. Stampfer, *The high prevalence of undiagnosed prostate cancer at autopsy: implications for epidemiology and treatment of prostate cancer in the Prostate-specific Antigen-era.* Int J Cancer, 2015. **137**(12): p. 2795-802.
4. Bell, K.J., et al., *Prevalence of incidental prostate cancer: A systematic review of autopsy studies.* Int J Cancer, 2015. **137**(7): p. 1749-57.
5. *U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2019 submission data (1999-2017): U.S. Department of Health and Human Services*. 2020; Available from: www.cdc.gov/cancer/dataviz.
6. Sebesta, E.M. and C.B. Anderson, *The Surgical Management of Prostate Cancer.* Semin Oncol, 2017. **44**(5): p. 347-357.
7. Bill-Axelson, A., et al., *Radical prostatectomy or watchful waiting in early prostate cancer.* N Engl J Med, 2014. **370**(10): p. 932-42.
8. Wilt, T.J., et al., *Follow-up of Prostatectomy versus Observation for Early Prostate Cancer.* N Engl J Med, 2017. **377**(2): p. 132-142.
9. Hamdy, F.C., et al., *10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer.* N Engl J Med, 2016. **375**(15): p. 1415-1424.
10. Bill-Axelson, A., et al., *Radical Prostatectomy or Watchful Waiting in Prostate Cancer - 29-Year Follow-up.* N Engl J Med, 2018. **379**(24): p. 2319-2329.
11. Wilt, T.J., G.L. Andriole, and M.K. Brawer, *Prostatectomy versus Observation for Early Prostate Cancer.* N Engl J Med, 2017. **377**(13): p. 1302-3.
12. Fowler, F.J., Jr., et al., *Effect of radical prostatectomy for prostate cancer on patient quality of life: results from a Medicare survey.* Urology, 1995. **45**(6): p. 1007-13; discussion 1013-5.
13. da Mata, L.R., et al., *Postoperative self-efficacy and psychological morbidity in radical prostatectomy.* Rev Lat Am Enfermagem, 2015. **23**(5): p. 806-13.
14. Sanda, M.G., et al., *Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I: Risk Stratification, Shared Decision Making, and Care Options.* J Urol, 2018. **199**(3): p. 683-690.
15. Ficarra, V., et al., *Systematic review and meta-analysis of studies reporting urinary continence recovery after robot-assisted radical prostatectomy.* Eur Urol, 2012. **62**(3): p. 405-17.
16. Tsui, J.F., et al., *Pad count is a poor measure of the severity of urinary incontinence.* J Urol, 2013. **190**(5): p. 1787-90.

17. Dylewski, D.A., et al., *A statistical comparison of pad numbers versus pad weights in the quantification of urinary incontinence.* Neurourol Urodyn, 2007. **26**(1): p. 3-7.
18. Donovan, J.L., et al., *The ICS-'BPH' Study: the psychometric validity and reliability of the ICSmale questionnaire.* Br J Urol, 1996. **77**(4): p. 554-62.
19. Donovan, J.L., et al., *The responsiveness of the ICSmale questionnaire to outcome: evidence from the ICS-'BPH' study.* BJU Int, 1999. **83**(3): p. 243-8.
20. Lee, T.K., et al., *A systematic review of expanded prostate cancer index composite (EPIC) quality of life after surgery or radiation treatment.* Can J Urol, 2015. **22**(1): p. 7599-606.
21. Crump, R.T., et al., *Evaluating the measurement properties of the 26-item Expanded Prostate Cancer Index Composite (EPIC-26) with a multicenter cohort.* Can Urol Assoc J, 2020. **14**(4): p. 111-117.
22. Wein, A.J., *ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence.* J Urol, 2005. **173**(3): p. 908-9.
23. Novara, G., et al., *Evaluating urinary continence and preoperative predictors of urinary continence after robot assisted laparoscopic radical prostatectomy.* J Urol, 2010. **184**(3): p. 1028-33.
24. Bayoud, Y., et al., *International Prostate Symptom Score is a predictive factor of lower urinary tract symptoms after radical prostatectomy.* Int J Urol, 2015. **22**(3): p. 283-7.
25. Donovan, J.L., et al., *Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer.* N Engl J Med, 2016. **375**(15): p. 1425-1437.
26. Kim, P.H., et al., *Trends in the use of incontinence procedures after radical prostatectomy: a population based analysis.* J Urol, 2013. **189**(2): p. 602-8.
27. Young, H.H., *The early diagnosis and radical cure of carcinoma of the prostate. Being a study of 40 cases and presentation of a radical operation which was carried out in four cases. 1905.* J Urol, 2002. **167**(2 Pt 2): p. 939-46; discussion 947.
28. Bianco, F.J., Jr., P.T. Scardino, and J.A. Eastham, *Radical prostatectomy: long-term cancer control and recovery of sexual and urinary function ("trifecta").* Urology, 2005. **66**(5 Suppl): p. 83-94.
29. Gandaglia, G., et al., *Robot-assisted radical prostatectomy in prostate cancer.* Future Oncol, 2015. **11**(20): p. 2767-73.
30. Guazzoni, G., et al., *Intra- and peri-operative outcomes comparing radical retropubic and laparoscopic radical prostatectomy: results from a prospective, randomised, single-surgeon study.* Eur Urol, 2006. **50**(1): p. 98-104.
31. Yaxley, J.W., et al., *Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study.* Lancet, 2016. **388**(10049): p. 1057-1066.
32. Coughlin, G.D., et al., *Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: 24-month outcomes from a randomised controlled study.* Lancet Oncol, 2018. **19**(8): p. 1051-1060.

33. Tang, K., et al., *Robotic vs. Retropubic radical prostatectomy in prostate cancer: A systematic review and an meta-analysis update.* Oncotarget, 2017. **8**(19): p. 32237-32257.
34. Basiri, A., et al., *Comparison of retropubic, laparoscopic and robotic radical prostatectomy: who is the winner?* World J Urol, 2018. **36**(4): p. 609-621.
35. Cao, L., et al., *Robot-assisted and laparoscopic vs open radical prostatectomy in clinically localized prostate cancer: perioperative, functional, and oncological outcomes: A Systematic review and meta-analysis.* Medicine (Baltimore), 2019. **98**(22): p. e15770.
36. Galfano, A., et al., *A new anatomic approach for robot-assisted laparoscopic prostatectomy: a feasibility study for completely intrafascial surgery.* Eur Urol, 2010. **58**(3): p. 457-61.
37. Galfano, A., et al., *Beyond the learning curve of the Retzius-sparing approach for robot-assisted laparoscopic radical prostatectomy: oncologic and functional results of the first 200 patients with >/= 1 year of follow-up.* Eur Urol, 2013. **64**(6): p. 974-80.
38. Menon, M., et al., *Functional Recovery, Oncologic Outcomes and Postoperative Complications after Robot-Assisted Radical Prostatectomy: An Evidence-Based Analysis Comparing the Retzius Sparing and Standard Approaches.* J Urol, 2018. **199**(5): p. 1210-1217.
39. Asimakopoulos, A.D., et al., *Retzius-sparing versus standard robot-assisted radical prostatectomy: a prospective randomized comparison on immediate continence rates.* Surg Endosc, 2019. **33**(7): p. 2187-2196.
40. Qiu, X., et al., *Retzius-sparing robot-assisted radical prostatectomy improves early recovery of urinary continence: a randomized, controlled, single-blind trial with a 1-year follow-up.* BJU Int, 2020. **126**(5): p. 633-640.
41. Walsh, P.C. and P.J. Donker, *Impotence following radical prostatectomy: insight into etiology and prevention.* J Urol, 1982. **128**(3): p. 492-7.
42. Walsh, P.C., *Anatomic radical prostatectomy: evolution of the surgical technique.* J Urol, 1998. **160**(6 Pt 2): p. 2418-24.
43. Suardi, N., et al., *Nerve-sparing approach during radical prostatectomy is strongly associated with the rate of postoperative urinary continence recovery.* BJU Int, 2013. **111**(5): p. 717-22.
44. Michl, U., et al., *Nerve-sparing Surgery Technique, Not the Preservation of the Neurovascular Bundles, Leads to Improved Long-term Continence Rates After Radical Prostatectomy.* Eur Urol, 2016. **69**(4): p. 584-589.
45. Qin, H., et al., *Predictors for immediate recovery of continence following Retzius-sparing robot-assisted radical prostatectomy: a case-control study.* Int Urol Nephrol, 2019. **51**(5): p. 825-830.
46. Mandel, P., et al., *The effect of age on functional outcomes after radical prostatectomy.* Urol Oncol, 2015. **33**(5): p. 203 e11-8.
47. Kundu, S.D., et al., *Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies.* J Urol, 2004. **172**(6 Pt 1): p. 2227-31.

48. Kunz, I., et al., *Tumour characteristics, oncological and functional outcomes in patients aged >/= 70 years undergoing radical prostatectomy.* BJU Int, 2013. **111**(3 Pt B): p. E24-9.
49. Shikanov, S., et al., *Robotic radical prostatectomy for elderly patients: probability of achieving continence and potency 1 year after surgery.* J Urol, 2010. **183**(5): p. 1803-7.
50. Basto, M.Y., et al., *Early urinary continence recovery after robot-assisted radical prostatectomy in older Australian men.* BJU Int, 2014. **114 Suppl 1**: p. 29-33.
51. Greco, K.A., et al., *Robot-assisted radical prostatectomy in men aged > or =70 years.* BJU Int, 2009. **104**(10): p. 1492-5.
52. Labanaris, A.P., J.H. Witt, and V. Zugor, *Robotic-assisted radical prostatectomy in men >/=75 years of age. Surgical, oncological and functional outcomes.* Anticancer Res, 2012. **32**(5): p. 2085-9.
53. Mungovan, S.F., et al., *Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis.* Eur Urol, 2017. **71**(3): p. 368-378.
54. Ikarashi, D., et al., *Appropriate preoperative membranous urethral length predicts recovery of urinary continence after robot-assisted laparoscopic prostatectomy.* World J Surg Oncol, 2018. **16**(1): p. 224.
55. Mandel, P., et al., *Impact of prostate volume on oncologic, perioperative, and functional outcomes after radical prostatectomy.* Prostate, 2015. **75**(13): p. 1436-46.
56. Konety, B.R., et al., *Recovery of urinary continence following radical prostatectomy: the impact of prostate volume--analysis of data from the CaPSURE Database.* J Urol, 2007. **177**(4): p. 1423-5; discussion 1425-6.
57. Boczko, J., et al., *Impact of prostate size in robot-assisted radical prostatectomy.* J Endourol, 2007. **21**(2): p. 184-8.
58. Oefelein, M.G., *Prospective predictors of urinary continence after anatomical radical retropubic prostatectomy: a multivariate analysis.* World J Urol, 2004. **22**(4): p. 267-71.
59. Galfano, A., et al., *Does prostate volume have an impact on the functional and oncological results of Retzius-sparing robot-assisted radical prostatectomy?* Minerva Urol Nefrol, 2018. **70**(4): p. 408-413.
60. Matsushita, K., et al., *Preoperative predictive model of recovery of urinary continence after radical prostatectomy.* BJU Int, 2015. **116**(4): p. 577-83.
61. Paparel, P., et al., *Recovery of urinary continence after radical prostatectomy: association with urethral length and urethral fibrosis measured by preoperative and postoperative endorectal magnetic resonance imaging.* Eur Urol, 2009. **55**(3): p. 629-37.