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Evaluation of Risk Factors for Adverse Functional Outcomes after Radical Prostatectomy in Patients with Previous Transurethral Surgery of the Prostate

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Abstract
Introduction: A history of transurethral surgery of the prostate is generally considered as a risk factor of adverse functional outcomes after radical prostatectomy (RP). We tested whether the risk of postoperative urinary incontinence (UIC) and erectile dysfunction (ED) after RP could be further substantiated in such patients. ***Materials and Methods:*** We tested the effect of the following variables on UIC and ED rates 1 year after RP: residual prostate volume after transurethral desobstruction, the time from transurethral desobstruction to RP, the type of transurethral desobstruction (TURP vs. laser enucleation), age, and nerve-sparing surgery (yes vs. no). UIC was defined as usage of any pad except a safety pad. ED was defined as no sexual intercourse possible. ***Results:*** Overall, 216 patients treated with RP between 2010 and 2019 in a tertiary care center were evaluated. All patients had previously undergone transurethral desobstruction. Regarding UIC analyses, only time from transurethral desobstruction to RP significantly influenced UIC rates ($p = 0.003$). Regarding ED rates, none of the tested variables reached statistical significance. ***Conclusion:*** The risk of UIC and ED after RP is substantial in men who had previously undergone transurethral desobstruction. The time from transurethral desobstruction to RP significantly impacts on the postoperative UIC rates. This observation should be further explored in future studies.

Introduction

Radical prostatectomy (RP) is a common surgical procedure for the treatment of localized prostate cancer (PCa). Over the last decades, significant improvements regarding our understanding of prostatic anatomy and further surgical refinements have led to an overall decrease in RP-related morbidity. For example, the description of the neurovascular bundles and surgical techniques enabling nerve-sparing surgery have significantly decreased postoperative erectile dysfunction (ED) rates [1, 2]. Moreover, amelioration of surgical preparation techniques of the urinary sphincter resulted in better postoperative continence rates [3]. Finally, the overall increasing

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usage of robotic-assisted RP might be associated with superior functional outcomes [4]. However, this observation is matter of ongoing discussion. Despite these modifications, however, postoperative urinary incontinence (UIC) and ED rates are still nonnegligible and thus a matter of concern.

Several patient adherent risk factors for adverse functional outcomes after RP have been identified. Among others, obesity, prostate volume, and advanced age are associated with an increased risk of postoperative UIC [5, 6]. Concerning erectile function, advanced age, preoperative erectile function, and comorbidities may among other factors adversely affect postoperative ED rates [7].

Another potential risk factor for increased rates of UIC and ED after RP is previous surgery of the prostate in the medical history. Several reports demonstrated that patients who underwent transurethral resection of the prostate (TURP) or laser enucleation of the prostate before RP are at risk of inferior continence and potency rates [8, 9]. However, not all studies could corroborate these findings [10]. Of note, most of the aforementioned studies used previous TURP or laser enucleation of the prostate as a binary variable (yes vs. no). It is well conceivable that among those patients, further characteristics such as time from TURP to RP or residual prostate volume may further affect functional outcomes.

The aim of the current study was to evaluate the impact of several factors potentially affecting continence and potency rates after RP in patients treated with previous TURP or laser enucleation of the prostate. We aimed at evaluating whether all these patients harbor the same risk of postoperative UIC and ED.

Materials and Methods

The study was approved by the institutional review board. We relied on data of patients with localized PCa treated with RP in a tertiary care center. All patients had previously undergone transurethral desobstruction of the prostate due to benign prostatic enlargement. Previous transurethral desobstruction was performed by classical TURP or by laser surgery. A differentiation between different types of lasers was not performed, since this information was not available. RPs were performed either with an open retropubic approach or with the da Vinci system. The histopathological workup did not differ between patients treated with open RP or robotic-assisted RP. High-volume surgeons performed all RPs. A minimum time interval of 3 months from transurethral desobstruction to RP was generally required prior to RP. We restricted our analyses to RPs performed between 2010 and 2019 to ensure a relatively current assessment.

Patients were excluded from analyses if they received adjuvant or salvage radiation therapy within 1 year after RP ($n = 29$), as this is associated with an increased risk of postoperative ED or UIC [11]. Moreover, patients with evidence of metastases before RP (tumor stage ≥ M1b) were also excluded ($n = 2$), due to the common necessity of leastwise adjuvant androgen deprivation therapy. Finally, patients with unknown data regarding time from TURP to RP were likewise excluded ($n = 4$). This resulted in overall 216 eligible patients for analyses.

We assessed the rates of UIC and ED 12 months after RP. Data were retrieved from our prospectively collected database. In this database, data from all patients who underwent RP in our institution are collected (written informed content required) and follow-up questionnaires regarding oncologic and functional parameters are implemented 1 week, 6 months, 12 months, and every other

Table 1. Characteristics of the entire patient cohort ($N = 216$)

Variable	*N* (%)
Age at radical prostatectomy	
Median (IQR)	68 (63–71)
Surgical treatment	
Open retropubic prostatectomy	151 (69.9)
da Vinci prostatectomy	65 (30.1)
TRUS-derived prostate volume, cm^3	
Median (IQR)	24 (18–32)
Time from transurethral desobstruction to radical prostatectomy, months	
Median (IQR)	53 (11–96)
Transurethral desobstructive surgery	
TURP	187 (86.6)
Laser surgery	29 (13.4)
Tumor stage after radical prostatectomy	
pT2	137 (63.4)
pT3a	56 (25.9)
pT3b	23 (10.6)
pN-stage	
pN0	180 (83.3)
pN1	7 (3.2)
pNx	29 (13.4)
Gleason grade group of the radical prostatectomy specimen	
1	22 (10.2)
2	136 (63.0)
3	49 (22.7)
4	1 (0.5)
5	8 (3.7)
Surgical margins	
Positive	25 (11.6)
Negative	189 (87.5)
Unknown	2 (0.9)
Full continence 1 year after prostatectomy	
No	55 (25.5)
Yes	161 (74.5)
Rates of erectile dysfunction 1 year after prostatectomy with nerve-sparing surgery in preoperatively known potent patients ($n = 63$)	
No erectile dysfunction (sexual intercourse possible)	25 (38.5)

Table 2. Logistic regression analysis for the prediction of urinary incontinence (usage of ≥1 pads per day) 1 year after radical prostatectomy

	Odds ratio	95% CI	*p* value
Age	0.99	0.94–1.05	0.81
TRUS volume	0.99	0.98–1.02	0.86
Time from transurethral desobstruction to radical prostatectomy	0.99	0.985–0.997	0.003

year after RP. For both endpoints, we tested the impact of the following parameters: age (continuously coded and categorized), TRUS-derived prostate volume (continuously coded and categorized), time from transurethral desobstruction to RP (continuously coded and categorized), and the surgical approach of transurethral desobstruction (TURP vs. laser surgery). The impact of nerve-sparing surgery (no vs. unilateral or bilateral) was only tested for the prediction of UIC.

For assessment of UIC, we defined incontinence as usage of any pad. Patients using a safety pad were considered continent. For analyses of ED, we only relied on patients who had no evidence of ED prior to RP (sexual intercourse possible) and underwent nerve-sparing surgery (unilateral or bilateral). A patient was considered as postoperatively potent if sexual intercourse (assisted or unassisted) was possible. Of note, the categorization of the aforementioned predictor variables was not entirely similar for assessment of ED and UIC rates, since the number of patients available for ED analyses was substantially smaller than for UIC analyses.

For all statistical analyses, the Statistical Package for Social Sciences (SPSS) version 19 was used. Univariable logistic regression models were used to test the impact of continuously coded variables on continence and potency rates 12 months after RP. For comparisons between categorized variables, the χ^2 test was applied. A p value of ≤0.05 was considered as statistically significant.

Table 3. Assessment of categorized variables for the prediction of urinary incontinence (usage of ≥1 pads per day) 1 year after radical prostatectomy

	Incontinence, % (*n*/*N*)	*p* value
Age, years		
≤70	24.5 (37/151)	0.24
≥71	27.7 (18/65)	
Nerve-sparing		
Yes (uni- or bilateral)	24.3 (49/202)	0.26
No	40 (4/10)	
Prostate volume, cm^3		
≤15	26.7 (8/30)	
16–29	27.8 (32/115)	0.59
≥30	21.1 (15/71)	
Surgical desobstruction		
TURP	24.1 (45/181)	0.23
Laser surgery	34.5 (10/29)	
Time from transurethral desobstruction to radical prostatectomy, months		
≤12	32.7 (18/55)	
13–60	31.3 (21/67)	0.04
≥61	17.0 (16/94)	

Results

The descriptive data of our patient cohort are shown in Table 1. Overall, 216 patients fulfilled inclusion criteria and were evaluated. The median age at RP was 68 years (IQR 63–71 years). The median TRUS-derived prostate volume prior to RP was 24 cm^3 (IQR 18–32 cm^3), and the median time from transurethral desobstruction to RP was 53 months (IQR 11–96 months). The majority of patients had previously undergone TURP (86.6%), while the remaining 13.4% were treated by laser surgery. Overall, 17 patients (7.9%) had evidence of PCa in the histopathological workup of the resected prostate tissue. Seven of those underwent RP within 6 months after transurethral desobstruction because of significant PCa. The remaining 10 patients showed PCa progression during follow-up and were therefore treated with RP. Most patients were treated with open RP (69.9%), and an organ-confined tumor was revealed in the final histopathological workup in 63.4%. Full continence (usage of zero pads or a safety pad) 1 year after surgery was achieved by 74.5% of patients. No evidence of ED (intercourse possible) 1 year after surgery was the case for 38.5% of patients.

Tables 2 and 3 show the results of the univariable logistic regression models (Table 2) and the results of the χ^2 test (Table 3) for the prediction of UIC 12 months after RP. Of the evaluated variables, only the time from transurethral desobstruction to RP was statistically significantly associated with UIC rates. Continuously coded, the odds ratio (OR) was 0.99 (95% CI: 0.985–0.997; $p = 0.003$). Categorized, the UIC rates were as follows: 32.7% (≤12 months) versus 31.3% (13–60 months) versus 17% (≥61 months [$p = 0.04$]).

Table 4. Logistic regression models for the prediction of no erectile dysfunction (sexual intercourse possible) after radical prostatectomy in preoperatively potent men (sexual intercourse possible)

	Odds ratio	95% CI	*p* value
No erectile dysfunction			
Age	0.94	0.86–1.02	0.14
Prostate volume	0.98	0.94–1.02	0.27
Time from transurethral desobstruction to radical prostatectomy	0.997	0.99–1.004	0.42

Tables 4 and 5 show the results of the univariable logistic regression model (Table 4) for the prediction of no ED 1 year after RP and the χ^2 test results (Table 5) for the respective endpoints. None of the tested variables was significantly associated with ED (all p values > 0.05). Comparable findings were observed, when only patients with bilateral nerve-sparing were considered (data not shown).

Table 5. Assessment of categorized variables for the prediction of no erectile dysfunction 1 year after radical prostatectomy (sexual intercourse possible) in preoperatively potent men (sexual intercourse possible)

	No erectile dysfunction, % (*n*/*N*)	*p* value
Age, years		
≤70	42.6 (20/47)	0.42
≥71	31.2 (5/16)	
Prostate volume, cm^3		
≤20	47.6 (10/21)	0.36
≥21	35.7 (15/42)	
Surgical desobstruction		
TURP	36.5 (19/52)	0.27
Laser surgery	54.5 (6/11)	
Time from transurethral desobstruction to radical prostatectomy, months		
≤12	47.1 (8/17)	
13–60	37.5 (6/16)	0.77
≥61	36.7 (11/30)	

Discussion

During the last decades, the surgical procedure of RP has significantly evolved. In consequence, the rates of postoperative ED and UIC have decreased. In spite of these improvements, overall ED and UIC rates after RP are still significant [12–14]. For optimal patient counseling and to decrease the rate of unrealistic expectations regarding the postoperative functional outcomes after surgery, an accurate estimation of the individual patients' risk of postoperative ED and UIC is important.

Previous transurethral surgery of the prostate – usually because of benign prostatic hyperplasia – has repeatedly been reported to be associated with inferior postoperative functional outcomes after RP. For example, Pompe et al. [8] showed that UIC and ED rates were significantly lower 1 year after RP in patients who had undergone previous transurethral desobstruction. More precisely, after propensity score adjustment, the UIC rates 1 year after RP were 25.9 versus 11.6%. In multivariable analyses, previous TURP reached independent predictor status of UIC (OR 2.06; $p = 0.006$). Comparable results were shown for ED analyses, in which previous TURP was significantly associated with a lower rate of erectile function recovery (OR 0.48; $p = 0.02$). Conversely, other studies did not reveal a statistically significant adverse effect of previous TURP on UIC and ED rates after RP. Exemplarily in the study by Zugor et al. [15], the potency and continence rates 1 year after RP were likewise lower in patients treated with previous TURP. However, the observed differences were not statistically significant. Other authors did not find any meaningful difference between groups at all [10].

Several factors may at least partly be responsible for the conflicting results, such as differences in evaluated sample sizes, age of the evaluated patients, or potential differences regarding the respective surgeon's experience. Moreover, the aforementioned studies usually used previous transurethral surgery as a binary variable (yes vs. no). Naturally, not every prostate after previous transurethral desobstruction is the same. Residual prostate volume or time from transurethral desobstruction to RP may impact on postoperative functional outcomes and should potentially be incorporated in statistical analyses.

In light of the conflicting results, Li et al. [16] recently published a meta-analysis in 2019, in which the effect of a previous TURP before RP on various clinical endpoints was assessed. Regarding functional outcomes, the authors found that previous TURP was associated with statistically significantly lower continence rates 1 year after RP (OR 0.59; $p < 0.001$). Similarly, previous TURP was significantly associated with lower rates of erectile recovery 1 year after surgery (OR 0.62; $p < 0.001$). At present, the study by Li et al. [16] possibly provides the highest level of evidence that previous TURP leads to adverse functional outcomes after RP. However, the possible effect of residual prostate volume or time from TURP to RP was not evaluated in their study.

This said, in the current report we tested the hypothesis that such factors could indeed further impact on urinary continence and erectile function rates. We aimed to evaluate a preferably homogenous patient collective. Therefore, we restricted our analysis to patients who underwent RP between 2010 and 2019. Moreover, patients receiving adjuvant or salvage radiation therapy within 1 year after RP or with known metastatic disease were likewise excluded. The following was observed: overall, we corroborated the previously described relatively high UIC rates 1 year after surgery. Using a strict definition for incontinence (usage of any pad expect a safety pad was considered as incontinent), the UIC rate was as high as almost 26%. This number is much higher in comparison to those from patients without previous prostatic surgery, in whom rates of approximately 10% have been reported [14]. Regarding potency, we likewise found and corroborated a substantial rate of ED after RP. Even though we restricted this analysis to previously potent patients (defined as sexual intercourse possible) with at least unilateral nerve-sparing surgery, only 38.5% of patients could maintain performing sexual intercourse 1 year after surgery.

The main aim of our analysis was the identification of risk factors, which are associated with higher odds of postoperative UIC or ED. Regarding UIC, the only tested variable which reached statistical significance was the time from transurethral desobstruction to RP. UIC rates were relatively high, when 60 months or less had passed from transurethral desobstruction to RP but significantly declined if >5 years had gone by. This could possibly mean that the adverse effect of previous surgery of the prostate exerts on urinary continence after RP diminishes with time.

When we assessed ED rates after RP, none of the tested variables showed a statistically significant association with the probability of postoperative ED. However, this finding should be interpreted with caution, as only 63 patients were preoperatively potent and had sufficient follow-up data. It is possible that a larger sample size might reveal different findings.

Our report has some shortcomings, which need to be considered for interpretation of the data. The retrospective design with its inherent limitations is a clear shortcoming. Moreover, with an overall sample size of 216 patients we cannot fully rule out that this number is too small for detection of statistically significant differences between groups. Additionally, our definition of ED is debatable, as we did not use validated questionnaires such as the International Index of Erectile Function (IIEF), but relied on a more pragmatic approach (sexual intercourse possible yes vs. no). This said, especially our findings regarding ED should be interpreted with caution. Finally, our dataset does not allow us to differentiate between stress UIC and urgency incontinence. It is possible that a certain proportion of our evaluated patients rather suffer from urgency incontinence, which cannot fully be attributed to the RP.

Taken together, we found that the time from transurethral desobstruction to RP influenced postoperative UIC rates. Since prospective randomized controlled trials are not possible in this field, large (preferably multicenter) studies with robust follow-up data are desirable to better identify and counsel patients at risk of adverse functional outcomes when RP after transurethral prostate surgery is intended.

Statement of Ethics

This study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. All patients provided written informed consent. This study was approved by the local ethics committee of Hamburg (Reference No. 0MC-375/16).

Conflict of Interest Statement

Nothing to disclose.

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Author Contributions

Julia Tolle: design of the study, drafting of the manuscript, data acquisition, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Sophie Knipper: data acquisition, data analysis and interpretation, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Randi Pose: data acquisition, drafting of the manuscript, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Pierre Tennstedt: statistical analyses, data acquisition, drafting of the manuscript, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Derya Tilki: drafting of the manuscript, concept of the study, interpretation of the data, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Markus Graefen: data interpretation, critical revision of the manuscript for intellectual content, final approval of the manuscript, and agreement to be accountable for all aspects of the work. Hendrik Isbarn: design of the study, statistical analyses, drafting of the manuscript, data acquisition, final approval of the manuscript, and agreement to be accountable for all aspects of the work.

References

1 Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. J Urol. 1982 Sep;128(3):492–7.
2 Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. Prostate. 1983;4(5):473–85.
3 Schlomm T, Heinzer H, Steuber T, Salomon G, Engel O, Michl U, et al. Full functional-length urethral sphincter preservation during radical prostatectomy. Eur Urol. 2011;60(2):320–9.
4 Antonelli A, Palumbo C, Noale M, Porreca A, Maggi S, Simeone C, et al. Impact of surgical approach on patient-reported outcomes after radical prostatectomy: a propensity score-weighted analysis from a multicenter, prospective, observational study (The Pros-IT CNR Study). Urol Int. 2019;103(1):8–18.
5 Wei Y, Wu YP, Lin MY, Chen SH, Lin YZ, Li XD, et al. Impact of obesity on long-term urinary incontinence after radical prostatectomy: a meta-analysis. Biomed Res Int. 2018 Apr;2018:8279523.
6 Ficarra V, Novara G, Rosen RC, Artibani W, Carroll PR, Costello A, et al. Systematic review and meta-analysis of studies reporting urinary continence recovery after robot-assisted radical prostatectomy. Eur Urol. 2012 Sep;62(3):405–17.
7 Ficarra V, Novara G, Ahlering TE, Costello A, Eastham JA, Graefen M, et al. Systematic review and meta-analysis of studies reporting potency rates after robot-assisted radical prostatectomy. Eur Urol. 2012 Sep;62(3):418–30.
8 Pompe RS, Leyh-Bannurah SR, Preisser F, Salomon G, Graefen M, Huland H, et al. Radical prostatectomy after previous TUR-P: oncological, surgical, and functional outcomes. Urol Oncol. 2018 Dec;36(12):527.e21–527.e28.
9 Colombo R, Naspro R, Salonia A, Montorsi F, Raber M, Suardi N, et al. Radical prostatectomy after previous prostate surgery: clinical and functional outcomes. J Urol. 2006 Dec;176(6 Pt 1):2459–63; discussion 63.
10 Palisaar JR, Wenske S, Sommerer F, Hinkel A, Noldus J. Open radical retropubic prostatectomy gives favourable surgical and functional outcomes after transurethral resection of the prostate. BJU Int. 2009 Sep;104(5):611–5.
11 Adam M, Tennstedt P, Lanwehr D, Tilki D, Steuber T, Beyer B, et al. Functional outcomes and quality of life after radical prostatectomy only versus a combination of prostatectomy with radiation and hormonal therapy. Eur Urol. 2017 Mar;71(3):330–6.
12 Haglind E, Carlsson S, Stranne J, Wallerstedt A, Wilderäng U, Thorsteinsdottir T, et al. Urinary incontinence and erectile dysfunction after robotic versus open radical prostatectomy: a prospective, controlled, nonrandomised trial. Eur Urol. 2015 Aug;68(2):216–25.
13 Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol. 2017 Apr;71(4):618–29.
14 Haese A, Knipper S, Isbarn H, Heinzer H, Tilki D, Salomon G, et al. A comparative study of robot-assisted and open radical prostatectomy in 10 790 men treated by highly trained surgeons for both procedures. BJU Int. 2019 Jun;123(6):1031–40.
15 Zugor V, Labanaris AP, Porres D, Witt JH. Surgical, oncologic, and short-term functional outcomes in patients undergoing robot-assisted prostatectomy after previous transurethral resection of the prostate. J Endourol. 2012 May;26(5):515–9.
16 Li H, Zhao C, Liu P, Hu J, Yi Z, Chen J, et al. Radical prostatectomy after previous transurethral resection of the prostate: a systematic review and meta-analysis. Transl Androl Urol. 2019 Dec;8(6):712–27.