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Age Is Predictive of Immediate Postoperative Urinary Continence after Radical Retropubic Prostatectomy

Fabio Campodonico[a] Egi Edward Manuputty[d] Sara Campora[b]
Matteo Puntoni[c] Massimo Maffezzini[a]

[a]Urology Unit, [b]Medical Oncology Unit and [c]Scientific Direction, Galliera Hospital, Genova, Italy;
[d]Department of Surgery, Cikini CCI Hospital, Jakarta, Indonesia

Key Words
Radical prostatectomy · Immediate urinary continence · Age

Abstract
Introduction: Immediate continence is a goal to take into consideration for better patient satisfaction after radical prostatectomy. Factors predicting urinary continence at catheter removal were investigated. ***Materials and Methods:*** We evaluated preoperative, operative, clinical, hormonal and pathological variables in a homogeneous series of radical retropubic prostatectomies (RRPs) following the principles of urinary sphincter restoration technique. ***Results:*** The study included 201 patients who underwent RRP. The overall immediate continence rate at catheter removal was 67.7% (136 patients); 28.8% (58 patients) were using one protective pad daily and 3.5% (7 patients) were incontinent. At 6-month follow-up incontinence had reached the lowest level of 2.5% (5 patients) and at 12 months the patients using one pad daily had decreased to 11.9% (24 patients). Multivariate logistic analysis showed that the only two factors independently associated with immediate continence were age <65 years (OR = 2.63, 95% CI 1.13–5.88, p = 0.02) and potency (OR = 3.6, 95% CI 1.2–10.7, p = 0.01) adjusting for D'Amico risk group, surgical margins, extracapsular extension, clinical stage, PSA, testosterone, LH and FSH. No significant association was noted for PSA, hormonal levels, hospital stay, prostate size, clinical stage, risk group, TNM stage, pathological Gleason score or extracapsular extension. ***Conclusions:*** In our series age <65 years was associated with immediate continence after RRP. Moreover, patients who were immediately continent had a 3.6-fold probability to be potent within 12 months.

Introduction

Radical retropubic prostatectomy (RRP) represents the standard therapy for clinically intracapsular prostate cancer (PCa) in surgically fit candidates. Recently the PIVOT trial showed that RRP did not significantly reduce PCa-related mortality, as compared with observation, at least in low-risk localized PCa [1]. RRP is associated with side effects, thus patients have to be carefully selected and informed before surgery. This issue has been focused on in the SPCG-4 study reporting the functional outcomes and quality of life at 10-year follow-up after surgery. The prevalence of anxiety, erectile dysfunction and urine leakage was found to be higher in patients who had undergone RRP compared with the watchful waiting group and

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E-Mail karger@karger.com
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Fabio Campodonico, MD
Urology Unit, Galliera Hospital
Via Volta 8
IT–16128 Genova (Italy)
E-Mail fabio.campodonico@galliera.it

the control group [2]. The anatomic approach has dramatically reduced the risk of permanent dissatisfying sequelae such as postoperative urinary incontinence and impotence [3]. Since other forms of therapy are available for intracapsular disease, namely external beam irradiation, brachytherapy, focal therapy etc., increased attention has been paid to the quality of life attained by each treatment modality. Minimally invasive approaches have been developed in the form of laparoscopic and robotic radical prostatectomy, gaining widespread consensus even in the absence of a direct objective comparison demonstrating superiority over the open anatomic approach [4]. Once oncological goals are reliably achieved, advances in the knowledge of the anatomy and functions of the prostate and periprostatic structures as well as continuous surgical refinements represent the main way towards high-quality functional outcomes whatever surgical approach chosen, either open, laparoscopic or robotic. Accurate identification and dissection of the external urinary sphincter and distribution of the anatomic nerve bundles represent two key points to ensure quality of life after surgery [5]. Most reports on the recovery of postoperative urinary continence focus on data acquired weeks or months after surgery, since it seems to be accepted that some degree of urine leakage can be present at discharge from hospital and over the first period at home. On the contrary, immediate postoperative continence constitutes a goal to take into consideration for better patient satisfaction after surgery and to allow comparison with different forms of less invasive treatments.

In this report we address immediate urinary continence, at the moment of catheter removal, after open RRP with the anatomic approach, in patients with clinically intracapsular PCa.

Patients and Methods

Between July 2002 and November 2009, a total of 373 patients were treated at our institution for clinically localized PCa. Of these, 130 underwent brachytherapy while the other 243 were addressed to RRP. The follow-up of this group was strictly limited to 201 patients who fulfilled all requested criteria and who resided in the region.

Surgical Technique

RRP was performed by a single surgeon (M.M.) following the Walsh procedure with essentially two additional technical steps focusing on optimizing urinary continence preservation [6, 7]. First, the dorsal vascular complex was divided proximal to the prostate. This aimed at preserving as many striated fibers of the external sphincter as possible. Second, the length of the urethra was preserved as much as possible. The urethra was exposed after preparation of the gland's apex. The urethral length is proportional to the amount of smooth muscle sphincter preservation since the two organs are adjacent to and opposing each other. Appreciating the different shapes of the gland is critical in order to achieve adequate urethra exposure. Bladder neck preservation was accurately performed as one of the main tools to achieve early continence. The urethral anastomosis was created with six sutures over an 18 F Foley catheter, and 180 ml of saline was injected through the catheter to test the anastomosis' water tightness. A standard limited lymphadenectomy was performed in each patient. The urinary catheter was removed on postoperative day 5 and the patient discharged on the same day.

Continence Evaluation

Continence was considered as preserved if patients were dry at catheter removal. Immediate continence was evaluated according to the following test: The bladder was filled with 100 ml of saline at room temperature, and patients were invited to urinate standing into a reservoir when the micturition stimuli were prompted. The voided volume was measured in order to evaluate the residual volume. Patients were considered continent if they needed no protection to keep their outer garments dry. Patients were strictly considered as having stress continence if they occasionally leaked a few drops with abdominal straining and if they needed to use only one protective pad a day. Patients who needed to use two or more pads a day were considered incontinent. The continence state was assessed at follow-up visits and by telephone interviews at 1, 3, 6 and 12 months. Before surgery there was no urinary questionnaire addressed to any patient.

Biochemical Analysis

One week before surgery all patients were evaluated for biochemical and hormonal parameters. Testosterone was measured for potential impact on muscle tropism and tonus of the external urinary sphincter; LH and FSH were measured as complementary tests in the regulation of sexual hormonal states; free thyronine was measured for its impact on muscle cell turnover.

Sexual Function Evaluation

A patient was considered potent if able to have intercourse without the use of type 5 phosphodiesterase (PDE5) inhibitors. The interviews were conducted 6 and 12 months after surgery.

Statistical Analysis

Data were summarized as number (percentage) of subjects. The univariate relationships between the study outcome (immediate urinary continence) and clinical, demographical and biochemical factors were examined using the Pearson χ^2 or the Fisher exact test when factors were categorical variables; we used the independent sample t test or the Mann-Whitney U test in case of continuous variables. A logistic regression multivariate model was used to test the association between the outcome and all factors considered, and the Wald test was used to assess the statistical significance. All analyses were conducted using the SPSS software (version 15, SPSS Inc.). Two-tailored probabilities were reported and a p value of 0.05 was used to define nominal statistical significance.

Ethical Approval

Institutional ethics committee approval is not required in Italy for nonexperimental and observational studies, which also applied to our study since patients did not receive any questionnaires but only telephone interviews.

Results

Table 1 shows the preoperative and histopathological data of the 201 evaluable patients. The mean patient age at surgery was 63.8 years (range 49–75). Median PSA was 8.8 ng/ml. Clinical stage was T1 in 165 (82.1%) patients, T2 in 26 (12.9%) and T3 in 10 (5%). The pathological TNM revealed organ-confined cancer as T2 in 122 patients (60.7%), T3 in 67 (33.3%) and N-positive in 12 cases (6%). According to the D'Amico classification, 102 patients (50.7%) were in the low-risk group, 77 (38.3%) in the intermediate-risk group and 22 (10.9%) in the high-risk group. All patients were continent before surgery. Nerve-sparing surgery was done in 171 (85.1%) of 201 patients, bilateral in 71 and unilateral in 110 patients. The potency rate was collected by telephone interview. Two patients had had previous prostatic surgery; one patient who had previously undergone transurethral prostatectomy was immediately continent, while a patient with previous open prostatectomy had stress incontinence and one pad at 12 months.

Figure 1 shows that the overall immediate continence rate at catheter removal was 67.7% (136 patients); patients wearing one protective pad were 28.8% (58 patients) and incontinence was seen in 3.5% (7 patients). At 6-month follow-up incontinence had reached the lowest level of 2.5% (5 patients) and at 12 months the patients using one pad daily had decreased to 11.9% (24 patients). Multivariate logistic analysis showed that the only two factors independently associated with immediate continence were age <65 years (OR = 2.63, 95% CI 1.13–5.88, p = 0.02) and potency (OR = 3.6, 95% CI 1.2–10.7, p = 0.01) adjusting for D'Amico risk group, surgical margins, extracapsular extension, clinical stage, PSA, LH and FSH. No significant association was noted for PSA, hormonal levels, hospital stay, prostate size, clinical stage, risk group according to D'Amico, TNM stage, postoperative Gleason score and extracapsular disease extension. The retrospectively evaluated potency significantly affected immediate continence. Mean hospital stay was 5.6 days.

Table 1. Main demographics and clinical characteristics of treated patients by median age

	Age <65 years (n = 100)	Age ≥65 years (n = 101)	Total	p value
Hospital stay, days	5.3±3.7	5.8±3.9		0.3
PSA, ng/ml	8.7±5.7	9.2±5.3		0.5
Prostate weight, g	45.5±19.1	53.7±27.0		0.02
Testosterone, ng/ml	4.7±2.1	4.6±2.0		0.9
LH, mlU/ml	5.0±2.5	6.7±4.6		0.005
FSH, mlU/ml	7.1±4.6	9.5±9.8		0.05
Free thyronine, pg/ml	3.4±0.5	3.3±0.5		0.06
Nerve sparing				0.006
No	18 (19)	35 (34)	53	
Unilateral	39 (40)	46 (44)	85	
Bilateral	40 (41)	23 (22)	63	
cT				0.7
1	79 (81)	86 (83)	165	
2	12 (12)	14 (14)	26	
3	6 (6)	4 (4)	10	
D'Amico risk group				0.4
Low	53 (55)	49 (47)	102	
Intermediate	33 (34)	44 (42)	77	
High	10 (10)	11 (11)	21	
Postoperative Gleason score				0.3
5 (3+2, 2+3)	8 (9)	5 (5)	13	
6 (3+3, 4+2)	21 (22)	29 (28)	50	
7 (4+3, 3+4)	54 (57)	49 (47)	103	
8 (4+4)	8 (9)	15 (14)	23	
9 (4+5, 5+4)	3 (3)	6 (6)	9	
pT				0.5
2a	18 (19)	18 (17)	36	
2b	14 (14)	9 (9)	23	
2c	25 (26)	38 (37)	63	
3a	29 (30)	30 (29)	59	
3b	5 (5)	3 (3)	8	
N1	6 (6)	6 (6)	12	
Extracapsular extension				0.9
No	60 (63)	64 (62)	124	
Yes	36 (38)	40 (39)	76	
Potency (at 12 months)				0.3
No	60 (74)	73 (81)	133	
Yes	21 (26)	17 (19)	38	

Values are means ± SD or n (%).

Discussion

Radical prostatectomy offers the benefit of excellent oncological outcomes, but it can be associated with a significant impairment of sexual function and, less frequently, urinary incontinence. Both of these complications improve with time, but the residual dysfunctions compromise the patient's quality of life. Urinary incontinence is widely considered as a major impairment for the patient and for the surgeon as well. Today, with the increasing demand of early patient recovery and discharge, immediate urinary continence has become one of the main goal of surgical technique. Multiple (preop-

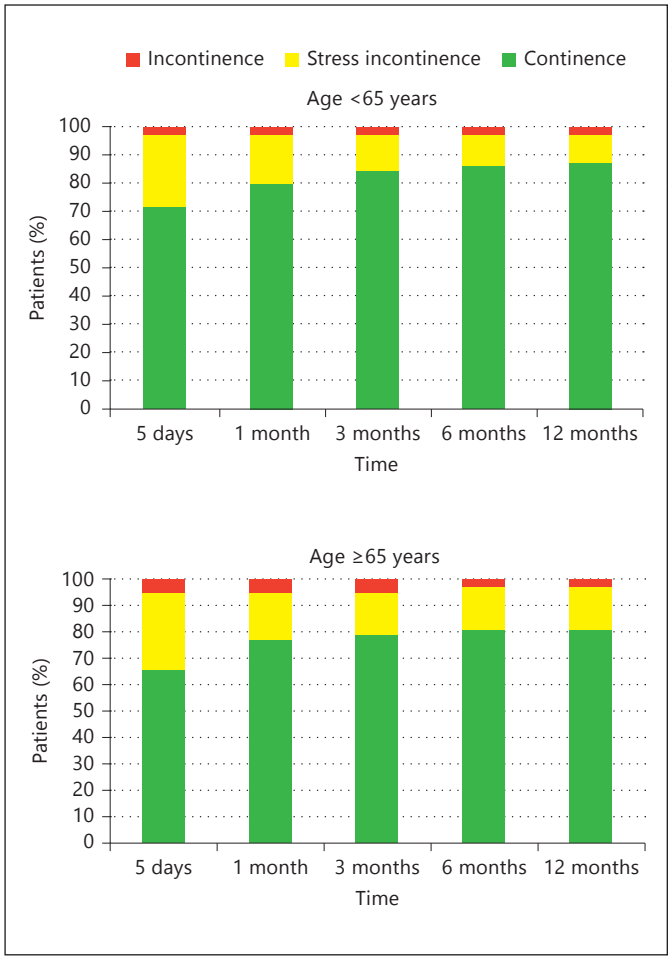

Fig. 1. Continence at catheter removal (day 5) and during follow-up, comparing two age groups.

erative, surgical and postoperative) factors have been associated with an early return to continence. Preoperative factors include advanced age [8], high body mass index [9], prostate size [10], decreased urethral length [11], previous endoscopic or open prostatic surgery [12] and preoperative urinary symptoms [13]. Surgical factors are surgeon experience [14], bladder neck preservation [15], nerve-sparing procedure [16] and modified reconstructive techniques around the anastomosis. Postoperative factors impairing continence are the presence of pelvic hematoma, vesicourethral leakage and anastomotic stenosis [3].

However, all these factors have been investigated in studies considering as early continence the 3-month outcome, and none of these correlated the influence of hormonal profile. Recently there is a growing interest in postoperative functional outcomes of new robotic series. Nevertheless, in general, very few data concerning continence are available in studies comparing robotics to RRP, and conclusions on whether any particular technique is better in achieving continence are unfeasible [17]. Moreover, several studies have focused on the early recovery of continence after robotic radical prostatectomy, but only one has reported the postoperative continence rate on day 1 [18]. In these series the 1-week continence rate ranged from 13.1 to 38.37% [19]. Thus, up to nowadays the post-prostatectomy immediate continence rate is considered an understudied factor. We evaluated as preoperative parameters patient age, PSA, clinical stage, D'Amico risk group and hormonal status. Only age at surgery <65 years was significantly associated with immediate continence recovery. This result is in accordance with the well-known association between age and 3-month continence recovery. Stanford et al. [20], in a population-based longitudinal cohort study including more than 1,200 men treated with RRP (data from Prostate Cancer Outcomes Study) reported that age <60 years was associated with a higher continence rate. Only Wille et al. [21] found no significant relation between older age and incontinence.

With regards to hormonal profile, we evaluated a set of hormones, including testosterone and thyroid hormones, which have physiological impacts on the metabolism and trophism of the muscular tissue composing the pelvic floor. It has been reported that the hypogonadism in the elderly or during androgen deprivation therapy impairs urinary function [22]. Gacci et al. [23] evaluated how serum testosterone affected urinary continence in 257 patients who underwent RRP. They found a strong association between urinary continence and sexual potency in eugonadal patients and the lack of this correlation in hypogonadal men. They concluded that the bladder has PDE5 receptors and that therapy with PDE5 inhibitors affects continence, providing relaxation of the smooth muscle and improving perfusion of the bladder wall exclusively in patients with an adequate testosterone level. Our study showed no statistical association or any trend with immediate continence, and it could not be compared to the previous study because at catheter removal none of our patients was under PDE5 inhibitor therapy.

With regards to operative technique we evaluated the impact of nerve-sparing surgery on early continence recovery. Potency was an independent factor of association to immediate urinary continence. Patients who were continent immediately after catheter removal had a 3.6-

fold probability to be potent at 12 months, thus indicating a direct association between nerve-sparing surgery, immediate continence and potency at a mid-term follow-up. Burkhard et al. [24] reported a strong association between continence and nerve-sparing RRP. They suggested that the preservation of efferent and afferent innervation results in a significant increase in urethral pressure and in the maintenance of conscious and unconscious sensation of urine entering the membranous urethra, thus inducing a spinal reflex or voluntary sphincter contraction.

With regards to prostatic parameters, no variable concerning gland volume and PCa was correlated with immediate continence. This results is in accordance with other studies evaluating long-term continence outcomes [25, 26]. Only Moul et al. [27] reported pathological stage as a factor significantly predicting urinary incontinence.

Finally, we observed a steady 12-month incontinence of 2.5% without starting a systematic postoperative physiotherapy program. Pelvic floor rehabilitation was given to patients who did not spontaneously show improved continence at 2-month follow-up.

The major strength of our study are the homogenous patient characteristics and treatment (a single surgeon with a consistent surgical technique). The major limitations are the small number of evaluated patients and the lack of a validated questionnaire on urinary continence and sexual activity at baseline and postoperatively.

Conclusions

The overall continence rate at catheter removal was 67.7%. The age-related analysis showed an association between immediate continence and patient age <65 years. No significant association was found for clinical, hormonal or cancer-related factors. Patients who were immediately continent showed a higher probability of being potent within 12 months.

In our practice, apart from the most relevant objective of oncological cure, we would emphasize the surgical technique's goal of achieving immediate continence after RRP. Thus, the preoperative discussion with the patient may include the expectance to be continent at catheter removal, based on age.

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