Can preoperative vitamin D level be a predictive factor for continence after radical prostatectomy?

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ABSTRACT

Introduction: This study examined whether there is a relationship between vitamin D levels and post-prostatectomy incontinence (PPI).
Methods: Patients who underwent robotic radical prostatectomy in a tertiary center constituted the population of this study. Patients whose serum vitamin D levels were measured three months before robotic radical prostatectomy were included. Continence status was recorded at one, three, six, and 12 months postoperatively. Urinary continence was defined as either no urine leak or using a pad to feel secure against potential minimal leakage. Patients were divided into groups according to continence status at the 12th postoperative month (group 1: continent patients, group 2: PPI patients). Groups were compared in terms of patient characteristics, previously known PPI risk factors, and serum vitamin D levels.
Results: The entire study cohort consisted of 318 patients. The rate of PPI was 14.5%. Since mean age, body mass index, and prostate volume were significantly higher in group 2 than in group 1, propensity score matching was applied. Before and after propensity score matching, serum vitamin D levels were higher in group 1 than in group 2 at the 12th postoperative month but no statistically significant difference was observed; however, after propensity score matching, serum vitamin D levels were significantly higher in continent patients than in incontinent patients at one, three, and six months postoperatively.

Conclusions: Serum vitamin D may be an essential marker in regaining continence in the early period after radical prostatectomy.

INTRODUCTION

Prostate cancer is the second most frequent cancer and constitutes about 15% of all cancer cases. The rate of diagnosis increased due to the increased use of prostate-specific antigen (PSA) tests and the aging population in Europe and the United States [1, 2]. Although early diagnosis and treatment of prostate cancer are associated with relatively high disease-specific survival rates, the risk of overtreatment can lead to adverse effects such as erectile dysfunction and urinary incontinence [3, 4]. Post-prostatectomy incontinence (PPI) is one of the major surgical complications that causes a significant decrease in the quality of life of patients [5].

It is widely accepted that preoperative pelvic floor muscle exercises significantly contribute to post-prostatectomy continence rates [6]. It was found that the striated muscles of the pelvic floor have vitamin D receptors, which decrease with aging [7]. Studies showed that vitamin D supplementation also positively affects female urinary incontinence and lower urinary tract symptoms (LUTS) in males [8, 9]. We hypothesized that serum vitamin D level might affect continence status after robotic radical prostatectomy, a condition that has not been previously studied [10, 11]. In this study, we aimed to examine whether there is a relationship between vitamin D levels and PPI.

METHODS

This retrospective study was approved by the ethics committee of our hospital (Approval Number:2024/181) and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients participating in the study. Data from 1165 patients who performed robotic radical prostatectomy due to localized prostate cancer between 2010 and 2017 were analyzed. Patients whose serum vitamin D levels were measured at any department three months before robotic radical prostatectomy were included in the study. Patients with preoperative urinary incontinence, neurogenic bladder, and/or overactive bladder (OAB), patients who had a history of lower urinary tract surgery and/or postoperative radiotherapy, patients with postoperative urethral stricture and/or bladder neck stenosis, and patients with missing data were excluded.

Additionally, patients whose neurovascular bundles were not preserved during the surgical procedure were not included. All procedures were performed via the Frankfurt technique [12]. All operations were performed by two experienced robotic surgeons. Patients were discharged on the postoperative second day unless the drain output was more than 100 mL/day. The urethral catheter was removed on the postoperative 10th day. Postoperative pelvic floor muscle exercise training is routinely given to all patients.

All patients are routinely followed up in the uro-oncology outpatient clinic after radical prostatectomy. Continence status was recorded at 1st, 3rd, 6th and 12th months postoperatively. Urinary continence was defined as either no urine leak or using a pad to feel secure against potential minimal leakage. Patients were divided into groups according to continence status at the postoperative 12th month (Group 1: continent patients, Group 2: PPI patients). Examined parameters were as follows: patient demographics, prostate volume, preoperative PSA, Gleason score, pathological stage, and serum vitamin D level.

Additionally, patients were classified according to continence status at 1st, 3rd, and 6th months postoperatively, and serum vitamin D levels were compared. Normal serum vitamin D level is considered to be more than 30 ng/mL [13]. Also, a urodynamic study (UDS) using the multichannel urodynamic device (MMS/Laborie, Netherlands) according to the International Continence Society protocol of good urodynamic practice is routinely performed on patients with PPI at 12th months postoperatively by a specialist nurse and evaluated by a urologist [14]. The UDS results of Group 2 patients were re-evaluated and recorded.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as number (percentage). Levene's test was used to determine whether continuous variables were normally distributed. Mean differences between the two groups were compared with student T-test, Pearson Chi-Square, Fisher's exact test, or Mann-Whitney U test. A 1:1 ratio propensity score matching was performed to achieve baseline equivalence in age, body mass index and prostate volume. SPSS software version 22 (IBM Corp., Armonk, NY) was used for statistical analysis.

RESULTS

Three hundred and eighteen patients were enrolled in this study [Group 1: 272 (85.5% patients and Group 2: 46 (14.5%) patients]. Comparative analysis of the groups revealed that mean age, body mass index, and prostate volume were significantly higher in Group 2 ($p=0.005$, $p<0.001$, and $p=0.037$, respectively). Therefore, propensity score matching was performed at a 1:1 ratio. After propensity score matching, no significant difference was found between the two groups in terms of age, body mass index, prostate volume, PSA, Gleason score and pathological stage. Before and after propensity score matching, although the mean serum vitamin D level was higher in Group 1 than in Group 2, this difference was insignificant ($p=0.063$ and $p=0.096$, respectively). Mean serum vitamin D levels were lower than 30 ng/ml in both groups. Comparative analysis of clinical data and demographics of both groups are summarized in **Table 1**.

Before propensity score matching, the mean serum vitamin D level was higher in continent patients than in incontinent patients at 1st, 3rd, and 6th months postoperatively; this difference was insignificant ($p=0.198$, $p=0.086$, and $p=0.057$, respectively). However, after propensity score matching, serum vitamin D levels were significantly higher in continent patients than in incontinent patients at 1st, 3rd, and 6th months postoperatively ($p=0.039$, $p=0.018$, and $p=0.021$, respectively). Comparison of vitamin D levels at 1st, 3rd, 6th and 12th months postoperatively of continent vs incontinent patients was shown in **Table 2**.

The most common urodynamic finding was intrinsic sphincter deficiency (ISD) in 38 patients (82.6%). OAB was detected in 5 patients (10.8%) and was the only urodynamic finding in only 3 patients (6.5%). In 3 patients (6.5%), we observed that the main and the sole problem was impaired detrusor contractility (IDC).

DISCUSSION

PPI usually resolves spontaneously within three months after surgery, and 54-66% of the patients with PPI become urinary continent during this period [15]. Studies with longer follow-ups showed that continence rates were even higher in the postoperative 12th month [16, 17]. On the other hand, the Prostate Cancer Outcomes Study reported that the PPI rates were calculated as 10.4% and 13.9% in the 24th and 60th month follow-up, respectively [18]. In our study, we assessed our patients concerning PPI in the postoperative 12th month. The post-prostatectomy urinary continence rate was 85.5% in our series, which is an acceptable range in the literature [19, 20].

Robotic surgery in radical prostatectomy provides advantages, including 3-dimensional imaging, magnification of the surgical field, and flexible instrumentation, all of which help the surgeon preserve the anatomically crucial structures for maintenance of urinary continence [17]. However, the European Association of Urology Prostate Cancer guidelines reported that there was no significant difference between open, laparoscopic, and robotic radical prostatectomy with respect to this parameter [4]. However, several surgical manipulations have positive or negative effects on PPI by different authorities. Longer membranous urethral length, bladder neck preservation, Rocco stitch, anterior fixation of the bladder-urethra anastomosis, and neuromuscular bundle preservation positively affect PPI. Extensive dissection of the prostatic apex to create a more defined urethral stump, laxity of the posterior supporting structures, neurovascular bundle damage, and devascularization of the urinary bladder are factors that have a negative impact on PPI [9].

While the role of surgical techniques in the development of PPI is a popular subject of debate, it is known that there are some other predictive factors. Patients older than 65, obesity, comorbidities, transurethral resection of the prostate before radical prostatectomy, and salvage radical prostatectomy after radiotherapy are well-known risk factors of PPI [9]. Also, preoperatively, the presence of LUTS, sexual dysfunction, and urinary incontinence are associated with PPI [19, 21]. Similar to the current literature, we revealed that the mean age and body mass index were higher in the patient group with PPI. Although we did not examine the preoperative LUTS, we found that mean prostate volume was significantly higher in Group 2, which was also reported by Galfano et al. The high prostate volume was a disadvantage for achieving immediate PPI [22].

The literature did not extensively study the relationship between Vitamin D deficiency and PPI, although its association with other types of urinary incontinence was previously appreciated. In this study, we investigated the relationship between serum vitamin D levels and PPI based on the fact that preoperatively performed pelvic floor exercises are known to reduce the risk of PPI, and vitamin D deficiency had a significant negative impact on the contractile capacity of pelvic floor muscles [23, 24]. Although a comparative analysis of the groups did not reveal a significant difference between the mean serum vitamin D levels at 1st, 3rd, 6th, and 12th months postoperatively, age, body mass index, and prostate volume were significantly different between the groups. Propensity score matching was performed at a 1:1

ratio to reduce selection bias. After propensity score matching, serum vitamin D levels were observed to be significantly higher in continent patients than in incontinent patients at 1st, 3rd, and 6th months postoperatively. This might be a sign of serum vitamin D level may influence the PPI, especially in the early postoperative period.

In the continence mechanisms, general anatomical structure and pelvic floor strength are much more prominent in women than men. Since Vitamin D increases pelvic floor muscle strength, the relationship between stress urinary incontinence and vitamin D levels has been investigated, and it stated that vitamin D level deficient people are prone to stress urinary incontinence [7]. The main pathophysiological mechanism underlying PPI is due to sphincter insufficiency [25]. Severe devascularization of the bladder can affect detrusor functions, causing OAB or IDC, while advanced dissection of the prostatic apex can cause ISD. In our study, in accordance with the literature data, the most common finding in UDS was ISD (82.6%), followed by OAB seen in 10.8%.

We also have some limitations. As it is known, sunlight and season can affect vitamin D levels. Due to the study's retrospective design, we did not evaluate vitamin D measurement only during the summer months. Although we offered pelvic floor muscle exercises to all patients, some might need help understanding how to do well. Also, it is a retrospective single-center study, which makes it impossible to generalize its findings. In addition, most of the patients included in the study did not have their vitamin D levels measured routinely, and this may have been done for an unknown reason, which may have introduced bias into the study. This is another limitation of the retrospective methodology. Despite these weaknesses, to our knowledge, our study is the first to investigate the association of serum vitamin D levels with PPI rates. This study will provide ideas for prospective multicenter studies with larger patient numbers.

CONCLUSIONS

It has been determined that serum vitamin D has no favorable effect on long-term PPI. However, it may be an essential marker in regaining continence in the early period. Prospective randomized controlled studies conducted with larger patient numbers are needed to investigate the serum vitamin D levels and the effect of vitamin D replacement in patients with PPI.

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FIGURES AND TABLES

Table 1. The comparison of demographics and clinical data of the groups

Variables (mean ± SD)/n (%)	**Before propensity score matching**				**After propensity score matching**			
	All	**Group 1**	**Group 2**	**p**	**All**	**Group 1**	**Group 2**	***p***
	(n=318)	(n=272)	(n=46)		(n=92)	(n=46)	(n=46)	
Age, years	65.6±7.3	65.3±7.6	67.8±5	**0.005***	67.8±6.1	67.9±7	67.8±5	0.496**
BMI, kg/m^2	26.4±2.6	26.3±2.6	27.4±2.6	**<0.001****	27.4±2.8	27.3±3	27.4±2.6	0.398**
PV, mL	48.3±21.3	47.3±21.6	55.1±18.8	**0.037****	53.4±21.6	53.1±24	55.1±18.8	0.546**
PSA, ng/mL	8.6±6.2	8.8±6.4	7.6±4.9	0.232*	7.9±4.5	8.3±4.1	7.6±4.9	0.119**
Vitamin D level, ng/mL	27.6±13.2	28.2±13.5	24.3±10.9	0.063*	26.4±12.6	28.6±13.9	24.3±10.9	0.096*
Gleason score								
≤6	225 (70.7)	194 (71.3)	31 (67.4)	0.768#	61 (66.3)	30 (65.2)	31 (67.4)	0.793#
7	70 (22.0)	58 (21.3)	11 (23.9)		21 (22.8)	10 (21.7)	11 (23.9)	
8–10	23 (7.2)	20 (7.3)	4 (8.7)		10 (10.9)	6 (13)	4 (8.7)	
Pathologic stage								
T2	241 (75.7)	205 (75.3)	36 (78.3)	0.202#	70 (76.1)	34 (73.9)	36 (78.3)	0.807&
T3a	41 (12.8)	33 (12.1)	8 (17.4)		17 (18.5)	9 (19.6)	8 (17.4)	
T3b	36 (11.3)	34 (12.5)	2 (4.3)		5 (5.4)	3 (6.5)	2 (4.3)	

*Student t-test, **Mann-Whitney U test; #Pearson Chi-squared test; &Fisher's exact test. Statistically different values are marked in bold. BMI: body mass index; PSA: prostate-specific antigen; PV: prostate volume; SD: standard deviation.

Table 2. Comparison of vitamin D levels of post-prostatectomy incontinent vs. continent patients

	Before propensity score matching			**After propensity score matching**		
	Vit D level, ng/mL		**p***	**Vit D level, ng/mL**		**p***
	Continent	**Incontinent**		**Continent**	**Incontinent**	
	n (mean ± SD)	n (mean ± SD)		n (mean ± SD)	n (mean ± SD)	
Month 1	120 (28.8±12.6)	198 (26.9±13.5)	0.198	22 (31.3±12.7)	70 (24.9±12.3)	**0.039**
Month 3	200 (28.6±13.4)	118 (25.9±12.7)	0.086	35 (30.4±13.6)	57 (24±11.4)	**0.018**
Month 6	248 (28.3±13.5)	70 (24.9±11.7)	0.057	42 (29.7±13.6)	50 (23.7±11.1)	**0.021**
Month 12	272 (28.2 ± 13.5)	46 (24.3 ± 10.9)	0.063	46 (28.6±13.9)	46 (24.3±10.9)	0.096

*Student t-test test. Statistically different values are marked in bold. SD: standard deviation; Vit: vitamin.