

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: We included patients from our tertiary center who underwent robotic radical prostatectomy (RP) and had their serum vitamin D levels assessed no more than three months before the procedure. 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 the 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 RP.

INTRODUCTION

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.^{1,2} Post-prostatectomy incontinence (PPI) is one of the major surgical complications that causes a significant decrease in patients' quality of life.³

It is widely accepted that preoperative pelvic floor muscle exercises significantly contribute to post-prostatectomy continence rates.⁴ It was found that the striated muscles of the pelvic floor have vitamin D receptors, which decrease with aging.⁵ Studies have shown that vitamin D supplementation also positively affects female urinary incontinence and male lower urinary tract symptoms (LUTS).^{6,7}

We hypothesized that serum vitamin D level might affect continence status after robotic radical prostatectomy (RP) and 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 (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 RP due to localized prostate cancer from 2010–2017 were analyzed. Patients who had their serum vitamin D levels assessed

no more than three months before the RP were included in the study.

Patients with preoperative urinary incontinence, neurogenic bladder, and/or overactive bladder (OAB), those with a history of lower urinary tract surgery and/or postoperative radiotherapy, patients with postoperative urethral stricture and/or bladder neck stenosis, and those 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;⁸ 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 was routinely given to all patients.

As per our standard practice, continence status was recorded at one, three, six, and 12 months postoperatively in the uro-oncology outpatient clinic. 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 consisted of continent patients, while group 2 was made up of PPI patients. Examined parameters were patient demographics, prostate volume, preoperative prostate-specific antigen (PSA), Gleason score, pathological stage, and serum 25-hydroxy vitamin D level.

Additionally, patients were classified according to continence status at one, three, and six months postoperatively, and serum vitamin D levels were compared. Normal serum vitamin D level is considered >30 ng/mL.⁹ Further, 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 12 months postoperatively by a specialist nurse and evaluated by a urologist.¹⁰ The UDS results of group 2 patients were re-evaluated and recorded.

Statistical analysis

Continuous variables were expressed as mean \pm 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-squared, 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 (BMI) and prostate volume. SPSS software version 22 (IBM Corp., Armonk, NY, U.S.) was used for statistical analysis.

RESULTS

Three hundred and eighteen patients were enrolled in this study (group 1: 272 [85.5%] and group 2: 46 [14.5%]). Comparative analysis of the groups revealed that mean age, BMI, 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, BMI, 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 at the 12th postoperative month, this difference was insignificant ($p=0.063$ and $p=0.096$, respectively). Mean serum vitamin D levels were <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 one, three, and six 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 one, three, and six months postoperatively ($p=0.039$, $p=0.018$, and $p=0.021$, respectively). Comparison of vitamin D levels at one, three, six, and 12 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 five patients (10.8%) and was the only urodynamic finding in three patients (6.5%). In three patients (6.5%), we observed that the only problem was impaired detrusor contractility (IDC).

DISCUSSION

PPI usually resolves spontaneously within three months after surgery, and 54–66% of patients with PPI become continent during this period.¹¹ Studies with longer followups showed that continence rates were even higher in the 12th postoperative month.^{12,13} On the other hand, the Prostate Cancer Outcomes Study reported that the PPI rates were calculated at 10.4% and 13.9% in

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 (n=318)	Group 1 (n=272)	Group 2 (n=46)	p	All (n=92)	Group 1 (n=46)	Group 2 (n=46)	p
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								0.793 [#]
≤6	225 (70.8)	194 (71.3)	31 (67.4)	0.768 [#]	61 (66.3)	30 (65.2)	31 (67.4)	
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								0.807 [§]
T2	241 (75.8)	205 (75.4)	36 (78.3)	0.202 [#]	70 (76.1)	34 (73.9)	36 (78.3)	
T3a	41 (12.9)	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 n (mean ± SD)	Incontinent n (mean ± SD)		Continent n (mean ± SD)	Incontinent 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.

the 24th and 60th followup months, respectively.¹⁴ In our study, the post-prostatectomy urinary continence rate was 85.5% at 12 months postoperative, which is similar to what is seen in the literature.^{15,16}

Robotic surgery in RP provides advantages, including three-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;¹³ however, the European Association of Urology prostate cancer guidelines reported that there was no significant difference between open, laparoscopic, and robotic RP with respect to this parameter.² Others report that different surgical procedures can have positive or negative effects

on PPI. Longer membranous urethral length, bladder neck preservation, Rocco stitch, anterior fixation of the bladder-urethra anastomosis, and neuromuscular bundle preservation positively affect PPI. Conversely, 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 can have a negative impact.⁷

While the role of surgical techniques in the development of PPI is a popular subject of debate, there are some known predictive factors, including age over 65 years, obesity, comorbidities, transurethral resection of the prostate before RP, and salvage RP after radiotherapy.⁷ Furthermore, preoperatively, the presence of LUTS, sexual dysfunction, and urinary incontinence are associated with PPI.^{15,17} Similar to the current literature, we revealed that the mean age and BMI 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 continence.¹⁸

The literature has not extensively studied the relationship between vitamin D deficiency and PPI, although its association with other types of urinary incontinence was previously described. 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.^{19,20}

Although a comparative analysis of the groups did not reveal a significant difference between the mean serum vitamin D levels at one, three, six, and 12 months postoperatively, age, BMI, 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 one, three, and six 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 vitamin D supplementation has been shown to improve stress urinary incontinence in premenopausal women.²¹ The main pathophysiologic mechanism underlying PPI is sphincter insufficiency.²² 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, the most common finding in UDS was ISD in 82.6%, followed by OAB seen in 10.8%.

Limitations

Our study is not without limitations.

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, we could not evaluate how well the patients understood/performed them.

Also, this was a retrospective, single-center study, which makes it impossible to generalize our findings. In addition, most of the patients included in the study did not have their vitamin D levels measured routinely, which may have introduced bias into the study.

Despite these weaknesses, to our knowledge, ours is the first to investigate the association of serum vitamin D levels with PPI rates.

CONCLUSIONS

It has been determined that serum vitamin D does not positively affect long-term PPI; however, it may be an essential marker in regaining continence in the early postoperative 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.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

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