

ORIGINALNI RAD

PROCENA UTICAJA VITAMINA D NA INTENZITET SIMPTOMA DONJEG URINARNOG TRAKTA I KVALITET ŽIVOTA OSOBA SA BENIGNOM HIPERPLAZIJOM PROSTATE

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SAŽETAK

Uvod/Cilj: Veća je verovatnoća da stariji muškarci sa benignom hiperplazijom prostate (BHP) imaju lošiji kvalitet život. Cilj ovog istraživanja je bio da se ispita uticaj serumskog vitamina D na intenzitet simptoma donjeg urinarnog trakta i kvalitet života osoba sa benignom hiperplazijom prostate.

Metode: Istraživanje je sprovedeno kao studija preseka. U studiju je uključeno 117 osoba sa benignom hiperplazijom prostate (BHP) lečenih u Kliničkom Centru Crne Gore u Podgorici u periodu od 10.05.2022. do 15.08.2022. godine. Podaci su prikupljeni opštim upitnikom, iz elektronskih zdravstvenih evidencija, kao i upitnikom Međunarodni skor simptoma prostate (engl. *International Prostate Symptom Score - IPSS*). U cilju statističke analize podataka korišćen je Spirmanov koeficijent korelacije.

Rezultati: Prosečna starost ispitanika iznosila je 62,97±11,57 godina. Prosečna vrednost intenziteta simptoma kod ispitanika sa BHP prema ISPP upitniku iznosila je 8,54. Od 117 ispitanika sa BHP, 57 (48,7%) je imalo umerene simptome, 56 (47,9%) lake, a 4 (3,4%) teške. Značajna negativna korelacija ($r = -0,316$; $p = 0,010$) je dobijena između vrednosti nivoa vitamina D i prosečno ocenjenih vrednosti simptoma prema ISPP upitniku. Takođe, značajna negativna korelacija je dobijena između vrednosti serumskog vitamina D i svih pojedinačno ocenjenih vrednosti simptoma BHP prema IPSS upitniku (osećaj nepotpunog pražnjenja mokraćne bešike prilikom mokrenja – $p = 0,040$; ponavljanje mokrenja u okviru dva sata od prethodnog mokrenja $p < 0,001$; isprekidano mokrenje – $p = 0,005$; nemogućnost odlaganja potrebe za mokrenjem – $p = 0,036$; tanak i slab mlaz mokraće – $p = 0,001$; naprezanje za početak mokrenja uz osećaj potrebe za mokrenjem – $p = 0,046$ i noćno mokrenje – $p = 0,011$). Na osnovu serumske vrednosti nivoa vitamina D ispitanici su u 52,1% slučajeva imali optimalne vrednosti ovog vitamina, u 29,1% nedovoljne, a u 18,8% deficit. Uočena je inverzna veza između prosečnih vrednosti serumskog vitamina D i kvaliteta života prema ISPP upitniku, ali veza nije bila značajna ($r = -0,365$; $p = 0,160$).

Zaključak: Rezultati istraživanja pokazuju da sa većim vrednostima serumskog vitamina D dolazi do značajne redukcije uroloških simptoma kod osoba sa BHP, što ukazuje na neophodnost prevencije deficita vitamina D. Neophodna su dalja istraživanja u ovoj oblasti u cilju donošenja detaljnijih preporuka.

Ključne reči: benigna hiperplazija prostate, kvalitet života, vitamin D, simptomi

Uvod

Benigna hiperplazija prostate (BHP) je bolest koja ce često dijagnostikuje kod starijih muškaraca (1). Prevalencija BPH se povećava sa 25% među muškarcima od 40 do 49 godina na više od 80% među muškarcima od 70 do 79 godina (2). Veća je verovatnoća da stariji muškarci sa benignom hiperplazijom prostate imaju lošiji kvalitet života (1).

BHP se odnosi na promenu veličine prostate, a ne na potencijalne simptome koje može izazvati,

a koji se obično nazivaju simptomima donjeg urinarnog trakta (engl. *low urinary tract symptoms – LUTS*). Iako mnogi muškarci sa histološkim nalazom BHP, pa čak i anatomske uvećane prostate, nemaju simptome, više od 50% muškaraca u šezdesetim godinama do čak 90% u osamdesetm ima simptome donjeg urinarnog trakta (2,3). BHP je rezultat hiperplazije i epitelnog i stromalnog tkiva i pretežno zahvata prelaznu zonu prostate (4). Kod paci-

THE ASSESSMENT OF THE IMPACT OF VITAMIN D ON THE INTENSITY OF LOWER URINARY TRACT SYMPTOMS AND THE QUALITY OF LIFE OF PERSONS WITH BENIGN PROSTATIC HYPERPLASIA

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SUMMARY

Introduction/Aim: Older men with benign prostatic hyperplasia (BPH) are more likely to have a poor quality of life. The aim of this study was to examine the influence of serum vitamin D on the intensity of lower urinary tract symptoms and the quality of life of persons with benign prostatic hyperplasia.

Methods: The study was conducted as a cross-sectional study. The study included 117 persons with benign prostatic hyperplasia (BPH) treated at the Clinical Center of Montenegro in Podgorica from May 10th, 2022 to August 15th, 2022. Data were collected with the help of the general questionnaire from electronic medical records, as well as with the International Prostate Symptom Score (IPSS) questionnaire. Spearman's correlation coefficient was used for the statistical analysis of data.

Results: The average age of participants was 62.97±11.57. The average value of the intensity of symptoms in patients with BPH according to the IPSS questionnaire was 8.54. Of the 117 participants with BPH, 57 (48.7%) had moderate symptoms, 56 (47.9%) mild, and 4 (3.4%) severe. A significant negative correlation ($r=-0.316$; $p=0.010$) was obtained between vitamin D levels and average values of symptoms according to the IPSS questionnaire. Also, a significant negative correlation was obtained between serum vitamin D values and all individually assessed values of BPH symptoms according to the IPSS questionnaire (sensation of incomplete emptying of the bladder during urination – $p=0.040$; repeated urination within two hours from the previous urination – $p<0.001$; intermittent urination – $p=0.005$; inability to postpone urination – $p=0.036$; a thin and weak urinary stream – $p=0.001$; straining to begin urinating with the sensation of the need to urinate – $p=0.046$ and nocturia – $p=0.011$). Based on the serum level of vitamin D, the participants had optimal levels of vitamin D in 52.1% of cases, insufficient levels in 29.1% of cases and deficit in 18,8%. An inverse relationship between the average values of serum vitamin D and quality of life according to ISPP questionnaire was observed, but this relationship was not significant ($r=-0.365$; $p=0.160$).

Conclusion: The results of the study show that higher levels of vitamin D lead to the significant reduction in urological symptoms in patients with BPH, which points to the need to prevent vitamin D deficiency. Further research in this field is necessary aimed at making more detailed recommendations.

Key words: benign prostatic hyperplasia, quality of life, vitamin D, symptoms

Introduction

Benign prostatic hyperplasia (BPH) is a disease that is often diagnosed in older men (1). The prevalence of BPH increases from 25% in men aged 40 to 49 years to more than 80% in men aged 70 to 79 (2). Older men with benign prostatic hyperplasia are more likely to have a poor quality of life (1).

BPH refers to the change in the size of the prostate, but not to the potential symptoms that can be caused by it, which are usually called lower urinary tract symptoms (LUTS). Although many men with the histological findings of BPH, and even anatomically enlarged prostate, have no symptoms, more than 50% of men in their

jenta sa BPH može da se javi često mokrenje, pritisak u stomaku tokom mokrenja, poremećaj sna, prisustvo rezidualnog urina i drugo. Ovo dovodi do problema mentalnog zdravlja i izaziva neprijatnosti u svakodnevnom životu, što dovodi do pogoršanja zdravlja i narušavanja kvaliteta života. Kvalitet života vezan za zdravlje predstavlja subjektivnu procenu i zadovoljstvo pojedinca ukupnim situacijama, životom i životnim iskustvom, to je koncept koji uključuje elemente potrebne za razumevanje zadovoljstva u životu pojedinca (5). BHP može se povezati sa raznim drugim zdravstvenim problemima koji mogu imati značajne negativne reperkusije na kvalitet života (6). Kod pacijenata sa benignom hiperplazijom prostate, medicinski troškovi rastu sa povećanjem starosti i dužine lečenja. Shodno tome, da bi se smanjili troškovi, važno je imati strateški pristup BHP (5).

Sve je više dokaza da nedostatak vitamina D može biti važan faktor rizika za nastanak različitih poremećaja zdravlja. *In vitro* studije i studije na životinjama pokazuju da vitamin D smanjuje ćeljsku proliferaciju i diferencijaciju prostate delujući preko receptora za vitamin D (VDR) (7). Takođe, niske vrednosti vitamina D, posebno aktivni 25-hidroksivitamin D (25-OH D), prisutne su kod pacijenata sa BPH što može biti osnov za razvoj bolesti. Nedavno randomizovano kontrolisano istraživanje je pokazalo da je suplementacija vitaminom D efikasna u smanjenju zapremine prostate i nivoa PSA, kao i poboljšanju simptoma BHP (8). Osim dobro poznate funkcije u metabolizmu kalcijuma, vitamin D takođe pomaže u sprečavanju pojave i razvoja mnogih hroničnih bolesti, uključujući kardiovaskularne bolesti, dijabetes i maligne tumore (8).

Zdravstveno stanje pojedinca može uticati na njegov svakodnevni život, što utiče i na njegovo zadovoljstvo životom. Pored toga, kako su aktivnosti svakodnevnog života povezane sa kvalitetom života, a fizičke aktivnosti mogu poboljšati mentalno i psihofizičko zdravlje, izgleda da ograničenja svakodnevnih aktivnosti kod pacijenata sa BHP utiču na kvalitet života (5).

Cilj ovog istraživanja je ispitati uticaj nivoa vitamina D na intenzitet simptoma donjeg urinarnog trakta i kvalitet života pacijenata sa benignom hiperplazijom prostate.

Metode

Istraživanjem je obuhvaćeno 117 ispitanika sa potvrđenom dijagnozom benigne hiperplazi-

je prostate koji su lečeni u Kliničkom Centru Crne Gore (KCCG) u Podgorici u periodu od 10.05.2022. do 15.08.2022. godine. Etički komitet KCCG je dao saglasnost za sprovođenje istraživanja (br. 03/01-1070/1).

U okviru ove studije preseka od svih ispitanika prikupljeni su podaci opštim upitnikom, iz dostupnih elektronskih zdravstvenih evidencija i upitnikom Međunarodni skor simptoma prostate - MSSP (engl. *International Prostate Symptom Score* - IPSS). Iz zdravstvenog kartona pacijenata sa BHP preuzeti su podaci o vrednostima serumskog PSA izražene u ng/ml (referentne vrednosti za opštu populaciju su 0-4 ng/ml), serumskom vitaminu D (optimalnim vrednost > 50 nmol/l), urei (referentne vrednosti 2,5 do 7,1 mmol/l) i kreatininu (referentne vrednosti 62 do 106 μmol/l), bakterijskom nalazu urina, postojanju retencije urina i kalkuloze mokraćne bešike.

Ispitanici su na osnovu referentnih vrednosti PSA podeljeni u dve grupe: ispitanici sa vrednostima PSA ≤ 4 ng/ml (referentne vrednosti) i ispitanici sa vrednostima PSA > 4 ng/ml (patološke vrednosti). U odnosu na referentne vrednosti serumskog vitamina D ispitanici su podeljeni u tri grupe: osobe sa deficitom vitamina D (< 30 nmol/l), osobe sa nedovoljnim vrednostima vitamina D (od 30 do 50 nmol/l) i osobe sa optimalnim vrednostima vitamina D (> 50 nmol/l). Za procenu intenziteta simptoma donjeg urinarnog trakta pacijenata sa BHP korišćen je Međunarodni skor simptoma prostate (MSSP) upitnik. Ovaj upitnik se sastoji od osam pitanja. Sedam pitanja iz upitnika odnose se na tegobe vezane za mokrenje poslednjih meseci, od kojih se četiri pitanja odnose na simptome mokrenja (osećaj nepotpunog pražnjenja mokraćne bešike, isprekidanost mlaza pri mokrenju, slab mlaz pri mokrenju, naprezanje pri mokrenju), a tri na simptome retencije urina (učestalost mokrenja, urgencija - nemogućnost odgađanja mokrenja, nokturija). Sedam pitanja iz upitnika boduje se na skali od 0 do 5, gde 0 označava nedostatak simptoma, a 5 najveći intenzitet simptoma. Ukupan MSSP rezultat se računa kao zbir svih odgovora na sedam pitanja vezanih za tegobe sa mokrenjem. Maksimalni skor ovog upitnika je 35 i njegove vrednosti se koriste za procenu intenziteta simptoma. Ispitanici sa BHP su prema ukupnom skoru MSSP upitnika podeljeni u tri grupe: osobe sa blagim (do 7 bodova), srednjim (od 8 do 19 bodova) i teškim (20 i više bodova) simptomima. U okviru istog upitni-

sixties and even 90% in their eighties have lower urinary tract symptoms (2,3). BPH is the result of hyperplasia of both epithelial and stromal tissue and it mainly affects the transition zone of the prostate (4). In patients with BPH, frequent urination, abdominal pressure during urination, sleep disturbance, presence of residual urine may appear. This leads to mental health problems and causes inconvenience in daily life, thus leading to the worsening of health and quality of life, as well. The quality of life related to health represents the subjective assessment and satisfaction with overall situations, life and life experience. It is a concept that includes the elements necessary to understand the satisfaction in the life of an individual (5). BPH may be associated with other health problems which can have significant negative repercussions on the quality of life (6). In patients with benign prostatic hyperplasia, medical costs increase with the increase in age and length of treatment. Therefore, in order to reduce the costs, it is important to have a strategic approach to BPH (5).

There is more and more evidence that vitamin D deficiency may be an important risk factor for the occurrence of various health disorders. In vitro studies, as well as studies carried out on animals have shown that vitamin D reduces cell proliferation and differentiation of the prostate through the vitamin D receptor (VDR) (7). Also, low levels of vitamin D, especially active 25-hydroxyvitamin D (25-OH D), are present in patients with BPH, which can be the basis for the development of the disease. A recent randomized controlled study has shown that vitamin D supplementation is efficient in reducing the volume of the prostate and PSA level, and improving the symptoms of BPH (8). In addition to the well-known function in calcium metabolism, vitamin D also helps to prevent the occurrence and development of many chronic diseases, including cardiovascular diseases, diabetes and malign tumors (8).

An individual's health condition can affect his daily life, which also influences his satisfaction with life. In addition, since activities of daily life are connected with the quality of life, and physical activity can improve mental and psychophysical health, it seems that limitations in daily activities in patients with BPH affect the quality of life (5).

The aim of this study is to examine the influence of vitamin D levels on the intensity of symptoms of

the lower urinary tract and the quality of life of patients with benign prostatic hyperplasia.

Methods

The study included 117 participants with the confirmed diagnosis of benign prostatic hyperplasia, who were treated at the Clinical Center of Montenegro in Podgorica from May 10th, 2022 until August 15th, 2022. The study was approved by the Ethics Committee of the Clinical Center of Montenegro (no. 03/01-1070/1).

Within this cross-sectional study, data were collected from all participants using the general questionnaire, from available electronic health records, and the International Prostate Symptom Score (IPSS). Data about serum PSA values expressed in ng/ml (reference values for the general population are 0-4 ng/ml), serum vitamin D (optimal value > 50 nmol/l), urea (reference values 2.5-7.1 mmol/l), creatinine (reference values 62-106 μ mol/l), bacterial findings in urine, the presence of urine retention and bladder calculus were taken from health records of patients with BPH.

The participants were divided into two groups according to PSA reference values: participants with PSA values < 4 ng/ml (reference values) and participants with PSA values > 4 ng/ml (pathological values). The participants were divided into three groups according to the values of serum vitamin D: persons with vitamin D deficiency (< 30 nmol/l), persons with insufficient values of vitamin D (from 30 to 50 nmol/l) and persons with optimal vitamin D values (> 50 nmol/l). The International Prostate Symptom Score (IPSS) was used to assess the intensity of lower urinary tract symptoms in patients with BPH. This questionnaire consists of eight questions. Seven questions refer to the symptoms related to urination in the past months, of which four questions refer to the symptoms of urination (sensation of incomplete emptying of the bladder, intermittency of urinary stream, weak urinary stream, strain during urination), while three questions refer to the symptoms of urine retention (frequency of urination, urgency – inability to postpone urination, nocturia). Seven questions from the questionnaire are scored on the scale from 0 to 5, where 0 signifies the absence of symptoms, and 5 the greatest intensity of symptoms. The total IPSS score is calculated as the sum of all responses to seven questions related to urinary symptoms. The maximum score

ka, dodatno, osmo pitanje odnosilo se na ličnu procenu ispitanika o kvalitetu života prema stepenu subjektivnog doživljaja tegoba. Na osnovu ovog pitanja, ispitanici su procenjivali kvalitet života birajući jedan od šest odgovora, pri čemu se ocena kvaliteta kretala od 0 (što podrazumeva jako dobar kvalitet života) do 6 (što podrazumeva ogorčenje). Ispitanici su klasifikovani u tri grupe prema kvalitetu života: dobar (oni koji su naveli da imaju jako dobro ili dobro zadovoljstvo životom), indiferentan (podjednako zadovoljni i nezadovoljni) i loš (oni koji su naveli da su nezadovoljni ili nesrećni životom). Na osnovu dobijene vrednosti Kronbahovog alfa koeficijenta koji iznosi 0,798, vidljivo je da ovaj upitnik ima visok stepen pouzdanosti i unutrašnje konzistentnosti u okviru ovog istraživanja, te kao takav može poslužiti kao vredan alat za procenu inteziteta simptoma i kvaliteta života.

Statistička analiza podataka sprovedena je korišćenjem SPSS 16 programa. Podaci su prikazani kroz frekvencije i procenete. U statističkoj analizi korišćeni su Spirmanov koeficijent korelacije za merenje jačine i smera odnosa između dve varijable, odnosno za utvrđivanje povezanosti i jačine povezanosti varijabli. Kao mera statističke značajnosti korišćena je p vrednost manja od 0,05. Vrednost Spirmanovog koeficijenta korelacije (r) blizu +1 ili -1, ukazuje na jak linearni odnos između varijabli, dok ako je blizu 0, to ukazuje na nedostatak bilo kakve veze.

Rezultati

U istraživanju koje je sprovedeno u Kliničkom Centru Crne Gore u Podgorici učestvovalo je ukupno 117 ispitanika sa potvrđenom dijagnozom BHP. Prosečna starost ispitanika iznosila je $62,97 \pm 11,57$ godina. Najmlađi pacijent imao je 30 godina, a najstari 86 godina. Najveći broj ispitanika 38 (32,5%) je bio uzrasta 60-70 godina, 36 (30,8%) uzrasta 70 i više godina, 27 (23,1%) 50-60 godina i 16 (13,6%) mlađe od 50 godina.

Prosečna vrednost PSA kod ispitanika iznosila je $3,36 \pm 2,27$ ng/ml. Najmanja zabeležena vrednost je bila 0,1 ng/ml, a najviša 100,0 ng/ml. Od 117 ispitanika sa BHP, 85,5% je imalo vrednost PSA ≤ 4 , a 14,5% veće od 4 ng/ml. Kod većine ispitanika nalaz uree (111 tj. 94,9%) i kreatinina (112 tj. 95,7%) su bili uredni. Patološki nalaz bakteriološkog pregleda urina je imalo 17 (14,5%) ispitanika, a kalkulozu bešike dva (1,7%) ispitanika. Retencija urina je bila prisutna kod 12 (10,3%) ispitanika.

Prosečna vrednost vitamina D je iznosila $51,47 \pm 22,21$ nmol/l i kretala se u rasponu od 8,60 nmol/l do 117,00 nmol/l. Ispitanika sa deficitarnim vrednostima vitamina D (< 30 nmol/l) je bilo 22 (18,8%), sa nedovoljnim vrednostima vitamina D (od 30 do 50 nmol/l) 34 (29,1%) i sa optimalnim (> 50 nmol/l) 61 (52,1%).

Prosečna vrednost intenziteta simptoma kod ispitanika sa BHP prema MSSP upitniku iznosila

Tabela 1. Distribucija ispitanika sa benignom hiperplazijom prostate prema učestalosti simptoma mokrenja i otežanog pražnjenja mokraćne bešike (prema IPSS upitniku) poslednjih meseci

Simptomi mokrenja i otežanog pražnjenja mokraćne	Nisam imao osećaj		Manje od 1 u 5 mokrenja		Manje od polovine broja mokrenja		Približno polovini mokrenja		Više od polovine broja mokrenja		Gotovo uvek		Ukupno	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Osećaj nepotpunog pražnjena mokraćne bešike prilikom mokrenja	8	6,8	47	40,2	37	31,6	22	18,8	3	2,6	0	0	117	100
Ponavljjanje mokrenja u okviru dva sata od prethodnog	22	18,8	41	35,0	38	32,5	13	11,1	2	1,7	1	0,9	117	100
Isprekidano mokrenje (mlaz krene pa stane)	47	40,1	38	32,5	20	17,1	7	6	1	0,9	4	3,4	117	100
Nemogućnost odlaganja potrebe za mokrenjem	102	87,2	13	11,1	2	1,7	0	0	0	0	0	0	117	100
Tanak i oslabljen mlaz mokraćne	43	36,8	40	34,2	16	13,6	9	7,7	7	6	2	1,7	117	100
Naprezanje za početak mokrenja uz osjećaj potrebe za mokrenjem	34	29,1	55	47	21	17,8	5	4,3	1	0,9	1	0,9	117	100

of this questionnaire is 35, and its values are used for the assessment of the intensity of symptoms. According to the total score of IPSS, the participants with BPH were divided into three groups: persons with mild (up to 7 points), moderate (from 8 to 19 points), and severe (20 or more than 20 points) symptoms. Within the same questionnaire, the additional eighth question referred to the participant's personal assessment of the quality of life according to the subjective experience of symptoms. Within this question, the participants assessed the quality of life, by choosing one of six answers, where the assessment of quality ranged from 0 (which signifies a very good quality of life) to 6 (which indicates bitterness). The participants were classified into three groups according to the quality of life: good (those who stated that they had very good or good satisfaction with life), indifferent (equally satisfied and dissatisfied), and poor quality of life (those who stated they were dissatisfied or unhappy). Based on the obtained value of the Cronbach's alpha coefficient, which was 0.798, it is evident that this questionnaire has a high degree of reliability and internal consistency within this study, and therefore, it can be a valuable tool for the assessment of the intensity of symptoms and quality of life.

The statistical analysis was carried out with the help of the SPSS 16 program. Data were presented through frequencies and percentages. Spearman's correlation was used in the statistical analysis to

measure the intensity and direction of relationship between two variables, that is, to establish the connectedness and intensity of connectedness between the variables. P value of less than 0.05 was used as a measure of statistical significance. The value of Spearman's correlation coefficient (r) near +1 or -1 indicates a strong linear relationship between the variables, and if it is close to 0, it indicates the lack of any relationship.

Results

The study, which was carried out at the Clinical Center of Montenegro in Podgorica, included 117 participants with the confirmed diagnosis of BPH. The average age of participants was 62.97 ± 11.57 . The youngest patient was 30 years old, while the oldest was 86. The largest number of participants, that is, 38 of them (32.5%) were in the age group 60-70 years, 36 (30.8%) were in the age group 70 and older, 27 (23.1%) were in the age group 50-60 years and 16 (13.6%) were younger than 50.

The average value of PSA in participants was 3.36 ± 2.27 ng/ml. The smallest registered value was 0.1 ng/ml, while the highest was 100.0 ng/ml. Of the 117 participants with BPH, 85.5% had a PSA value < 4 , while 14.5% > 4 ng/ml. In the majority of participants, the findings of urea (111, that is, 94.9%) and creatinine (1112, that is, 95.7%) were within normal ranges. 17 (14.5%) participants had the pathological findings of the bacteriological examination of urine, and two of them (1.7%)

Table 1. Distribution of participants with benign prostatic hyperplasia according to the frequency of symptoms and difficulties related to urination (based on IPSS questionnaire) in the past months

Urinary symptoms and difficulties related to urination	I did not have the sensation		Less than once in 5 times		Less than half the time		About half the time		More than half the time		Almost always		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sensation of incomplete emptying of the bladder	8	6.8	47	40.2	37	31.6	22	18.8	3	2.6	0	0	117	100
Had to urinate again less than two hours after you finished urinating	22	18.8	41	35.0	38	32.5	13	11.1	2	1.7	1	0.9	117	100
Intermittency (stop and start again)	47	40.1	38	32.5	20	17.1	7	6	1	0.9	4	3.4	117	100
Inability to postpone urination	102	87.2	13	11.1	2	1.7	0	0	0	0	0	0	117	100
A thin and weak urinary stream	43	36.8	40	34.2	16	13.6	9	7.7	7	6	2	1.7	117	100
Strain to begin urination with the feeling of need to urinate	34	29.1	55	47	21	17.8	5	4.3	1	0.9	1	0.9	117	100

Tabela 2. Distribucija ispitanika sa benignom hiperplazijom prostate prema broju uriniranja tokom noći tokom poslednjih nekoliko meseci

Broj uriniranja tokom noći tokom poslednjih nekoliko meseci	Br. (%)
0	5 (4,3)
1	44 (37,6)
2	35 (29,8)
3	23 (19,7)
4	5 (4,3)
5+	5 (4,3)
Ukupno	117 (100,0)

je 8,54 i kretala se od 0,00 do 27,00. Od 117 ispitanika sa BHP, 57 (48,7%) je imalo umerene, 56 (47,9%) lake, a 4 (3,4%) teške simptome donjeg urinarnog trakta.

Prema podacima MSSP upitnika, najveći broj ispitanika 47 (40,2%) odgovorilo je da je tokom poslednjih meseci manje od jednom u pet mokrenja

imalo osećaj da nije potpuno ispražnjena mokraćna bešika, 37 (31,6%) u manje od polovine broja mokrenja, 22 (18,8%) kod svakog drugog mokrenja, 3 (2,6%) kod više od polovine broja mokrenja, dok 8 (6,8%) ispitanika nije imalo ovaj problem (Tabela 1). Tokom poslednjih meseci najveći broj ispitanika (41 tj. 35,0%) navodi da su manje od jednom u pet mokrenja morali ponovo mokriti unutar dva sata od prethodnog mokrenja, 38 (32,5%) kod manje od polovine broja mokrenja, 22 (18,8%) nije imalo taj osećaj, 13 (11,1%) kod svakog drugog mokrenja, 2 (1,7%) u više od polovine broja mokrenja, dok 1 (0,9%) nije imao ovaj problem. Najveći broj ispitanika (72,5%), tokom poslednjih meseci, nije imao isprekidano mokrenje ili se ono javljalo manje od jednom u pet mokrenja, a 3,4% je skoro uvek imalo ove tegobe. Nemogućnost odlaganja potrebe za mokrenjem nije imalo čak 102 (87,2%) ispitanika, a 13 (11,1%) navodi ovaj problem ređe od jednom na pet mokrenja i 2 (1,7%) kod svakog drugog mokrenja. Tanak i oslabljen mlaz nije imalo 36,8% ispitanika tokom poslednjih meseci, a 1,7% gotovo uvek pri mokrenju. Naprezanje da

Tabela 3. Analiza korelacije između vrednosti serumskog vitamina D i prosečne ocene simptoma mokrenja i otežanog pražnjenja mokraćne bešike u poslednjih meseci kod ispitanika sa benignom hiperplazijom prostate

Simptomi mokrenja i otežanog pražnjenja mokraćne bešike	Korelacija sa nivoom serumskog vitamina D	
Osećaj nepotpunog pražnjenja mokraćne bešike prilikom mokrenja	Spearmanov koeficijent korelacije (r)	-0,190*
	Koeficijent značajnosti (p)	0,040
	N	117
Ponavljanje mokrenja u okviru dva sata od prethodnog	Spearmanov koeficijent korelacije (r)	-0,349**
	Koeficijent značajnosti (p)	0,000
	N	117
Isprekidano mokrenje (mlaz krene pa stane)	Spearmanov koeficijent korelacije (r)	-0,260**
	Koeficijent značajnosti (p)	0,005
	N	117
Nemogućnost odlaganja potrebe za mokrenjem	Spearmanov koeficijent korelacije (r)	0,019*
	Koeficijent značajnosti (p)	0,036
	N	117
Tanki i oslabljeni mlaz mokraće	Spearmanov koeficijent korelacije (r)	-0,303**
	Koeficijent značajnosti (p)	0,001
	N	117
Naprezanje za početak mokrenja uz osjećaj potrebe za mokrenjem	Spearmanov koeficijent korelacije (r)	-0,177*
	Koeficijent značajnosti (p)	0,046
	N	117
Učestalost noćnog ustajanja zbog mokrenja	Spearmanov koeficijent korelacije (r)	-0,235*
	Koeficijent značajnosti (p)	0,011
	N	117

Table 2. Distribution of participants with benign prostatic hyperplasia according to the number of urinations during night in the past months

Number of urinations during night in the past month	N (%)
0	5 (4.3)
1	44 (37.6)
2	35 (29.8)
3	23 (19.7)
4	5 (4.3)
5+	5 (4.3)
Total	117 (100.0)

had calculosis of the bladder. Urine retention was present in 12 (10.3%) participants.

The average value of vitamin D was 51.47 ± 22.21 nmol/l and it ranged from 8.60 nmol/l to 117.0 nmol/l. There were 22 (18.8%) participants with vitamin D deficiency (< 30 nmol/l), 34 (29.1%) with

the insufficient values of vitamin D (from 30 to 50 nmol/l) and 61 (52.1%) with optimal vitamin D levels (> 50 nmol/l).

The average value of the intensity of symptoms in patients with BPH according to the ISPP questionnaire was 8.54 and it ranged from 0.00 to 27.00. Of the 117 participants with BPH, 57 (48.7%) had moderate symptoms, 56 (47.9%) mild, and 4 (3.4%) had severe symptoms.

According to the ISPP questionnaire, the largest number of participants, that is, 47 of them (40.2%) answered that less than once in five urinations they had the feeling that the bladder was not completely emptied, 37 (31.6%) in less than half of the number of urinations, 22 (18.8%) in every second urination, 3 (2.6%) in more than half of the number of urinations, while 8 (6.8%) participants did not have this problem (Table 1). During the past months, the largest number of participants (41, that is, 35.0%) stated that less than once in five times they had to urinate once again less than two hours after they finished urinating, 38

Table 3. Analysis of correlation between serum vitamin D levels and average assessment of urinary symptoms and difficulties related to urination in the past months in participants with benign prostatic hyperplasia

Urinary symptoms and difficulties in urinating	Correlation with serum vitamin D level	
Sensation of incomplete emptying of the bladder during urination	Spearman's correlation coefficient (r)	-0.190*
	Coefficient of significance (p)	0.040
	N	117
Repeated urination less than two hours after you finished urinating	Spearman's correlation coefficient (r)	-0.349**
	Coefficient of significance (p)	0.000
	N	117
Intermittency (strain stops and starts again)	Spearman's correlation coefficient (r)	-0.260**
	Coefficient of significance (p)	0.005
	N	117
Inability to postpone the urination	Spearman's correlation coefficient (r)	0.019*
	Coefficient of significance (p)	0.036
	N	117
A thin and weak urinary stream	Spearman's correlation coefficient (r)	-0.303**
	Coefficient of significance (p)	0.001
	N	117
Straining to begin urination with the sensation of the need	Spearman's correlation coefficient (r)	-0.177*
	Coefficient of significance (p)	0.046
	N	117
Frequent nocturia	Spearman's correlation coefficient (r)	-0.235*
	Coefficient of significance (p)	0.011
	N	117

Tabela 4. Distribucija ispitanika sa benignom hiperplazijom prostate (BHP) prema kategoriji simptoma bolesti (prema MSSP upitniku) i vrednosatima serumskog vitamina D u poslednjih nekoliko meseci

Kategorije simptoma BHP (prema IPSS upitniku)	Vrednosti serumskog vitamina D			Ukupno (N=117) Br (%)
	Deficit (N=22) Br (%)	Nedovoljno (N=34) Br (%)	Optimalno (N=61) Br (%)	
Laki	5 (22,7)	14 (41,2)	37 (60,7)	56 (47,9)
Srednji	15 (68,2)	18 (52,9)	24 (39,3)	57 (48,7)
Teški	2 (9,1)	2 (5,9)	0 (0,0)	4 (3,4)

$r = -0,316$; $p = 0,010$

bi započeli mokrenje tokom poslednjih meseci nije imalo 29,1% ispitanika, a 0,9% skoro uvek.

Osmo pitanje iz MSSP upitnika odnosilo se na učestalost noćnog mokrenja tokom poslednjih meseci (Tabela 2). Samo 4,3% ispitanika nije mokriло noću, a 37,6% je mokriло tokom noći bar jednom, 29,8% dva puta, 19,7% tri puta, a 8,6% četiri i više puta.

Značajna negativna korelacija, dobijena prema Spirmanovom koeficijentu korelacije, je uočena između serumskih vrednosti vitamina D i svih pojedinačno ocenjenih vrednosti simptoma donjeg urinarnog trakta (osećaj nepotpunog pražnjenja mokraćne bešike prilikom mokrenja, ponavljanje mokrenja u okviru dva sata od prethodnog mokrenja, isprekidano mokrenje, nemogućnost odlaganja potrebe za mokrenjem, tank i slab mlaz mokraće, naprezanje za početak mokrenja uz osećaj potrebe za mokrenjem i noćno mokrenje) procenjenih prema MSSP upitniku (Tabela 3).

Prema urološkim simptomima donjeg urinarnog trakta od 117 ispitanika sa BHP, teške simptome imalo je 4 (3,4%) ispitanika, srednje teške 57 (48,7%), a lake 56 (47,9%) (Tabela 4). Od 22 ispitanika sa deficitom vitamina D, srednje i teške

simptome BHP je imalo 77,3% ispitanika, a od 34 ispitanika sa nedovoljnim vrednostima vitamina D, 58,8% ispitanika. Među ispitanicima sa optimalnim vrednostima vitamina D, 60,7% je imalo lake, 39,3% srednje, a ni jedan ispitanik teške simptome BHP. Značajna negativna korelacija, dobijena prema Spirmanovom koeficijentu korelacije, je uočena kod osoba sa BHP između serumskih vrednosti vitamina D i ukupno ocenjene vrednosti simptoma donjeg urinarnog trakta prema IPSS upitniku.

Na osnovu simptoma donjeg urinarnog trakta 72 (61,5%) ispitanika je bilo zadovoljno kvalitetom života, 28 (23,9%) je bilo indiferentno, a 17 (14,5%) je ukazalo da ima loš kvalitet života (Tabela 5). Među 22 osobe sa deficitom vitamina D čak 59,1% je iskazalo da ima loš ili indiferentan kvalitet života, a od 34 ispitanika sa nedovoljnom količinom vitamina D 41,2%. Dobar kvalitet života je bio kod najvećeg broja ispitanika sa optimalnim vrednostima vitamina D i to kod njih 70,5%. Na osnovu Spirmanovog koeficijenta korelacije postoji inverzna veza između prosečnih vrednosti vitamina D i kvaliteta života prema MSSP upitniku, ali korelacija nije bila značajna.

Tabela 5. Distribucija ispitanika prema vrednostima serumskog vitamina D i kvalitetu života

Kvalitet života*	Vrednosti serumskog vitamina D			Ukupno (N=117) Br (%)
	Deficit (N=22) Br (%)	Nedovoljno (N=34) Br (%)	Optimalno (N=61) Br (%)	
Dobar	9 (40,9)	20 (58,8)	43 (70,5)	72 (61,5)
Indiferentan	5 (22,7)	10 (29,4)	13 (21,3)	28 (23,9)
Loš	8 (36,4)	4 (11,8)	5 (8,2)	17 (14,5)

*Kvalitet života procenjen na osnovu MSSP upitnika; $r = -0,365$; $p = 0,160$

Table 4. Distribution of participants with benign prostatic hyperplasia (BPH) according to the category of symptoms (according to the IPSS questionnaire) and values of serum vitamin D in the past months

Categories of BPH symptoms (according to IPSS questionnaire)	Values of serum vitamin D			Total (N=117) Br (%)
	Deficit (N=22) Br (%)	Insufficient (N=34) Br (%)	Optimal (N=61) Br (%)	
Mild	5 (22.7)	14 (41.2)	37 (60.7)	56 (47.9)
Moderate	15 (68.2)	18 (52.9)	24 (39.3)	57 (48.7)
Severe	2 (9.1)	2 (5.9)	0 (0.0)	4 (3.4)

$r = -0,316$; $p = 0,010$

(32.5%) less than half the time, 22 (18.8%) did not have that sensation at all, 13 (11.1%) about half the time, 2 (1.7%) more than half the time, while 1 (0.9%) did not have this problem. The largest number of participants (72.5%), during the last months, did not have the intermittency or it occurred less than once in five times, while 3.4% almost always had these symptoms. The inability to postpone urination was not felt by 102 (87.2%) participants, while 13 (11.1%) stated this problem less than once in five times and 2 (1.7%) in every other urination. A thin and weak urinary stream was not present in 36.8% of participants in the last months, while 1.7% almost always had it during urination. 29.1% of respondents did not strain to begin urination, while 0.9% strained almost often.

The eighth question from the IPSS questionnaire referred to the frequency of nocturia during the past months (Table 2). Only 4.3% of participants did not urinate at night, while 37.6% urinated during the night at least once, 29.8% twice, 19.7% three times and 8.6% four or more times.

A significant negative correlation, which was obtained according to the Spearman's correlation coefficient, was observed between serum levels

of vitamin D and all individually assessed values of symptoms of lower urinary tract (sensation of incomplete emptying of the bladder during urination, repeated urination less than two hours after they finished urinating, intermittency, inability to postpone urination, a thin and weak urinary stream, straining to urinate with the sensation of the need to urinate and nocturia), which were assessed according to the IPSS questionnaire (Table 3).

According to the urinary symptoms of lower urinary tract, of the 117 participants with BPH, 4 (3.4%) participants had severe symptoms, 57 (48.7%) had moderately severe symptoms, and 56 (47.9%) had mild symptoms (Table 4). Of the 22 participants with vitamin D deficiency, 77.3% had moderate and severe symptoms of BPH, and of the 34 participants with insufficient levels of vitamin D, 58.8% participants. Among the participants with optimal levels of vitamin D, 60.7% had mild, 39.3% moderate, and none of the participants had severe symptoms of BPH. A significant negative correlation, obtained according to Spearman's correlation coefficient, was observed in people with BPH between serum vitamin D values and

Table 5. Distribution of participants according to the values of serum vitamin D and the quality of life

Quality of life*	Values of serum vitamin D			Total (N=117) Br (%)
	Deficit (N=22) Br (%)	Insufficient (N=34) Br (%)	Optimal (N=61) Br (%)	
Good	9 (40.9)	20 (58.8)	43 (70.5)	72 (61.5)
Indifferent	5 (22.7)	10 (29.4)	13 (21.3)	28 (23.9)
Poor	8 (36.4)	4 (11.8)	5 (8.2)	17 (14.5)

*Quality of life assessed according to the IPSS questionnaire; $r = -0,365$; $p = 0,160$

Diskusija

U našem istraživanju učestvovalo je 117 ispitanika sa postavljenom dijagnozom BHP. Uзраст ispitanika se kretao od 30 do 86 godina. Najviše ispitanika sa BHP je bilo u starasnoj dobi od 60 do 70 godina (32,5%), a zatim od 70 i više godina (30,8%). Poznato je da prevalencija BHP raste sa starenjem. Autopsijske studije su pokazale histološku prevalenciju BPH od 8%, 50% i 80% u 30-im, 50-im i 80-im godinama života (9). Zanimljivi su rezultati multinacionalne studije prevalencije (MSAM-7) u kojoj je anketirano 12.815 muškaraca dobi od 50 do 80 godina u Ujedinjenom Kraljevstvu, SAD-u, Francuskoj, Nemačkoj, Holandiji, Italiji i Španiji. U svim zemljama prevalencija je rasla sa 22% kod muškaraca starih 50 do 59 godina na 45% kod muškaraca starih 70 do 80 godina (10). U studiji koja je sprovedena u Hrvatskoj 78,4% bolesnika sa BHP je bilo starije od 60 godina, a prosečna dob bolesnika je iznosila 67 godina (11).

Prosečna vrednost PSA kod naših ispitanika iznosila je 3,36 ng/ml. Najveći procenat ispitanika 85,5% imao je vrednost PSA \leq 4 ng/ml dok je kod 14,5% ispitanika vrednost PSA iznosila $>$ 4 ng/ml. U retrospektivnom istraživanju u kojem su korišćeni klinički biohemijski podaci 169 pacijenata lečenih na odelenju za urologiju KBC Kosovska Mitrovica, prosečna vrednost serumskog PSA kod pacijenata sa BHP iznosila je 17,0 ng/ml (12).

Studija *Tóth* i saradnika, je otkrila da se nivo PSA povećavao sa godinama, dok nije pronađena razlika u nivoima PSA u različitim podgrupama vitamina D (13). Studija *Grammatikopoulou* i saradnika, koji su ispitivali populaciju muškaraca sa BHP davajući im suplemente vitamina D, pokazala je da je efikasnost vitamina D i većine prehrambenih faktora neadekvatna da bi se preporučila njihova upotreba (14).

Velika studija *Kristal* i saradnika je ispitivala ishranu kao faktor rizika za pojavu BHP, kod 4770 učesnika u periodu 1994-2003. godine koji su bili u placebo grupi i nisu imali BHP na početku (15). Uočeno je da ishrana sa malo masti i crvenog mesa, umerenim sadržajem alkohola, kao i sa dosta povrća i proteina doprinosi sprečavanju nastanka simptoma BHP. Međutim, nije utvrđeno da antioksidansi iz hrane/suplemenata smanjuju rizik za BHP. Takođe, rizik nije manji većom potrošnjom cinka, kalcijuma i omega-3 masnih kiselina. Neophodno je dalje ispitivati značaj ishrane u prevenciji razvoja BHP i za regulisanje simptomima ove bolesti.

U našoj studiji, prosečna vrednost vitamina D iznosila je 51,47 nmol/l. Kod 52,1% ispitanika sa BPH zabeležena je optimalna vrednost vitamina D, a nedovoljna kod 29,1% i deficit kod 18,8% ispitanika. Prema našim podacima, prosečna vrednost skora uroloških simptoma prema MSSP upitniku kod osoba sa BHP je iznosila 8,54. Pored toga, većina ispitanika 57 (48,7%) je imala srednji stepen tegoba (umereni simptomi), nešto manje 56 (47,9%) laki stepen tegoba, a 4 (3,4%) teške simptome. Ispitanici s većim nivoom vitamina D su imali značajno manje izražene simptome BHP, dok su ispitanici s manjim nivoom vitamina D imali više izražene simptome BHP. Utvrđena je i negativna korelacija između nivoa vitamina D i svih simptoma povezanih s mokrenjem kod muškaraca sa BHP, što ukazuje na važnost adekvatnog nivoa vitamina D u prevenciji i lečenju ovih simptoma.

U našoj studiji, postojala je inverzna veza između nivoa vitamina D i kvaliteta života, ali veza nije bila značajna. U Hrvatskoj je 2012. godine sprovedeno istraživanje o kvalitetu života bolesnika sa BHP u kojoj je bilo uključeno 1364 bolesnika iz cele države (11). Većina bolesnika je, prema MSSP upitniku, opisala kvalitet života kao zadovoljavajući (20%), čudan osećaj (20%) i kao nezadovoljavajući (21,8%). Bolesnici koji su bili aktivno praćeni imali su napredak u kvalitetu života u odnosu na ostatak bolesnika. Bolesnici koji su aktivno praćeni ocenili su kvalitet života kao jako dobar (15%), dobar (25,2%) i kao zadovoljavajući (17,8%) (11). U studiji koja je sprovedena u Hrvatskoj, simptomi koje su bolesnici naveli kao one koji izazivaju najveće nezadovoljstvo, odnosno one koje im najviše narušavaju kvalitet života, bili su simptomi povećane učestalosti mokrenja, nokturija, urgencija i urgentna inkontinencija (11). U istraživanju po tipu studije preseka u kojem su bile uključene 4 države Evrope (Francuska, Španija, Portugalija i Nemačka) bilo je uključeno 480 muškaraca starijih od 50 godina sa simptomima BHP te su rezultati pokazali veliki uticaj simptomima donjeg urinarnog trakta na kvalitet života bolesnika (16). Kvalitet života najmanje je bio narušen kod bolesnika iz Nemačke (3,52 boda) u odnosu na ostale zemlje gde je prosečan broj bodova bio 4,27 – 4,55. Samo 10% bolesnika navelo je da bi bili zadovoljni ako bi proveli ostatak života sa trenutnim simptomima (16).

Osnovna prednost ovog istraživanja može se posmatrati kroz relativno ujednačen uzorak po pojedinim medicinskim /zdravstvenim parametrima,

the total value of lower urinary tract symptoms, according to the IPSS questionnaire.

Based on the symptoms of lower urinary tract, 72 (61.5%) participants were satisfied with the quality of life, 28 (23.9%) were indifferent, and 17 (14.5%) stated that they had the poor quality of life (Table 5). Among the 22 persons with vitamin D deficiency, 59.1% of them stated that they had poor or indifferent quality of life, and of the 34 participants with the insufficient amount of vitamin D 41.2%. A good quality of life was found in the largest number of participants with optimal levels of vitamin D, 70.5%. Based on the Spearman's correlation coefficient, there is an inverse relationship between average vitamin D values and quality of life according to the ISPP questionnaire, but this correlation was not significant.

Discussion

The study included 117 participants with BPH diagnosis. The results of the study indicated that the average age of participants was 62.97 and it ranged from 30 to 86. The majority of participants with BPH were in the age group 60-70 years (32.5%), and then in the age group 70 and older (30.8%). It is known that the prevalence of BPH increases with age. Autopsy studies have shown the histological prevalence of BPH of 8%, 50% and 80% in the thirties, fifties and eighties, respectively (9). The results of the multinational study of prevalence (MSAM-7), which included 12,815 men aged 50 to 80 in the United Kingdom, the USA, France, Germany, the Netherlands, Italy and Spain, are interesting. In all countries, the prevalence increased from 22% in men aged 50-59 years to 45% in men aged 70-80 (10). In a study, which was carried out in Croatia, 78.4% of patients with BPH were older than 60, while the average age of patients was 67 years (11).

The average value of PSA in our participants was 3.36 ng/ml. The largest percentage of participants, 85.5% had a PSA value \leq 4 ng/ml, while in 14.5% of participants, the value of PSA was $>$ 4 ng/ml. In a retrospective study, in which clinical biochemical data of 169 patients treated at the Department of Urology of the Clinical Center "Kosovska Mitrovica" were used, the average value of serum PSA in patients with BPH was 17.0 ng/ml. In one study, which was conducted in Iran, researchers found that the average value of PSA in patients with BPH was 5.64 ng/ml (12).

A study by Tóth et al. found that PSA levels increased with age, while no difference was found in PSA levels in different vitamin D subgroups (13). A study by Grammatikopoulou et al., who examined a population of men with benign prostatic hyperplasia by supplementing them with vitamin D, showed that the effectiveness of vitamin D and most dietary factors was inadequate to recommend their use (14).

A large study by Crystal et al. examined dietary risk factors for BPH in 4770 participants in the Prostate Cancer Prevention Trial (1994-2003) who were in the placebo group and did not have BPH at baseline (15). It has been observed that a diet with little fat and red meat, moderate alcohol content, as well as plenty of vegetables and protein contributes to the prevention of BPH symptoms. However, antioxidants from foods/supplements have not been found to reduce the risk of BPH. Also, the risk is not lower with higher consumption of zinc, calcium and omega-3 fatty acids. It is necessary to further examine the importance of nutrition in preventing the development of BPH and managing the symptoms of this disease.

In our study, the average value of vitamin D was 51.47 nmol/l. In 52.1% of the subjects with BPH, the optimal value of vitamin D was recorded, and in 29.1%, it was insufficient and 18.8% of the subjects had a deficit. According to our data, the average score of urological symptoms according to the IPSS questionnaire in people with BPH was 8.54. In addition, the majority of respondents 57 (48.7%) had a medium level of symptoms (moderate symptoms), a little less 56 (47.9%) had a mild level of symptoms, and 4 (3.4%) had severe symptoms. Subjects with higher levels of vitamin D had significantly less pronounced BPH symptoms, while subjects with lower levels of vitamin D had more pronounced BPH symptoms.

Our research also found a negative correlation between the level of vitamin D and all symptoms related to urination in men with BPH, which indicates the importance of an adequate level of vitamin D in the prevention and treatment of these symptoms. In our study, there was an inverse relationship between vitamin D levels and quality of life, but the relationship was not significant. In 2012, a study on the quality of life of patients with BPH was conducted in Croatia, and it included 1364 patients from the whole country (11). The majority of patients, according to the IPSS questionnaire,

te standardizovan merni instrument i dovoljan broj ispitanika za sprovođenje istraživanja. Glavnim nedostatkom istraživanja možemo smatrati to što je istraživanje sprovedeno na malom broju ispitanika i što kod studije preseka ne možemo definisati šta je uzrok, a šta posledica poremećaja zdravlja. Ispitivanje je sprovedeno od maja do avgusta meseca, dakle u mesecima kada je najveća izloženost suncu te to može uticati na nivo vitamina D. Sledeći nedostatak studije bi bio vezan takođe za termin ispitivanja jer u tim mesecima zbog visoke dnevne temperature su obično najmanje izražene iritativne tegobe donjeg urinarnog trakta.

Preporuke za dalja istraživanja bi išle u smeru uključivanja više varijabli različitog karaktera, koje bi produbile ispitivane odnose i dovele do relevantnijih zaključaka višestrukih razmera. Njavažnja preporuka bi bila da se ovakvo istraživanje sprovede u dizajnu prospektivne studije gde bi se i nivo vitamina D i učestalost javljanja urinarnih simptoma pratili kod ispitanika u funkciji vremena.

Zaključak

Značajna negativna korelacija je dobijena između vrednosti nivoa vitamina D i svih pojedinačno ocenjenih vrednosti uroloških simptoma procenjenih prema IPSS upitniku, kao i sa ukupno ocenjenim vrednostima simptoma. Međutim, postoji inverzna veza između prosečnih vrednosti vitamina D i kvaliteta života prema ISPP upitniku, ali veza nije značajna. Neophodna su dalja istraživanja u ovoj oblasti u cilju davanja preporuka za korišćenje vitamina D.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

Reference

- Lee SU, Lee SH, So AH, Park JI, Lee S, Oh IH, et al. Association between benign prostatic hyperplasia and suicide in South Korea: A nationwide retrospective cohort study. *PLoS One*. 2022;17(3):e0265060. doi: 10.1371/journal.pone.0265060. eCollection 2022.
- Sarma AV, Wei JT. Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms. *N Engl J Med*. 2012;367(3):248-57. doi: 10.1056/NEJMcp1106637.
- Langan RC. Benign Prostatic Hyperplasia. *Prim Care Clin Off Pract*. 2019;46(2):223-32. doi: 10.1016/j.pop.2019.02.003.
- Kim EH, Larson JA, Andriole GL. Management of Benign Prostatic Hyperplasia. *Annu Rev Med*. 2016;67(1):137-51. doi: 10.1146/annurev-med-063014-123902.
- Park S, Lee KS, Choi M, Lee M. Factors associated with quality of life in patients with benign prostatic hyperplasia, 2009–2016. *Medicine (Baltimore)*. 2022;101(36):e30091. doi: 10.1097/MD.00000000000030091.
- Egan KB. The Epidemiology of Benign Prostatic Hyperplasia Associated with Lower Urinary Tract Symptoms. *Urol Clin North Am*. 2016;43(3):289–97. doi: 10.1016/j.ucl.2016.04.001
- Liu ZM, Wong C, Chan D, Woo J, Chen YM, Chen B, et al. Association of Circulating 25(OH)D and Lower Urinary Tract Symptoms: A Four-Year Prospective Study among Elderly Chinese Men. *Nutrients*. 2016;8(5):273. doi: 10.3390/nu8050273.
- Chen Y, Xu H, Liu C, Gu M, Chen Q, Zhan M, et al. Therapeutic Effects of 25-Hydroxyvitamin D on the Pathological Process of Benign Prostatic Hyperplasia: An In Vitro Evidence. *Dis Markers*. 2021;2021:4029470. doi: 10.1155/2021/4029470
- Barry MJ, Fowler FJ Jr, Bin L, Pitts JC 3rd, Harris CJ, Mulley AG Jr. The natural history of patients with benign prostatic hyperplasia as diagnosed by North American urologists. *J Urol*. 1997;157(1):10-4; discussion 14-5.
- Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). *Eur Urol*. 2003;44(6):637-49. doi: 10.1016/j.eururo.2003.08.015.
- Kuliš T, Gašparić M, Prižmić M, Kovačić D, Kolumbić Lakoš A, Kaštelan Ž. Simptomi i kvaliteta života u bolesnika s BPH. *Medicus*. 2015;25(1):87-92.
- Ilić A, Denović D. Kliničko morfološke karakteristike patoloških promjena u prostati. *Praxis Medika*. 2019;48(1):1-8. doi: 10.5937/pramed19010011
- Tóth Z, Szalay B, Gyarmati B, Jalal DA, Vásárhelyi B, Szabó T. Vitamin D Deficiency has no Impact on PSA Reference Ranges in a General University Hospital - A Retrospective Analysis. *EJIFCC*. 2020;31(3):225-230.
- Grammatikopoulou MG, Gkiouras K, Papageorgiou ST, Myrogiannis I, Mykoniatis I, Papamitsou T, et al. Dietary Factors and Supplements Influencing Prostate Specific-Antigen (PSA) Concentrations in Men with Prostate Cancer and Increased Cancer Risk: An Evidence Analysis Review Based on Randomized Controlled Trials. *Nutrients*. 2020;12(10):2985. doi: 10.3390/nu12102985.
- Kristal AR, Arnold KB, Schenk JM, Neuhaus ML, Goodman P, Penson DF, Thompson IM. Dietary patterns, supplement use, and the risk of symptomatic benign prostatic hyperplasia: results from the prostate cancer prevention trial. *Am J Epidemiol*. 2008;167(8):925-34. doi: 10.1093/aje/kwm389.
- Speakman M, Kirby R, Doyle S, Ioannou C. Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) - focus on the UK. *BJU Int*. 2015;115(4):508-19. doi: 10.1111/bju.12745.

described the quality of life as satisfactory (20%), a strange feeling (20%) and as unsatisfactory (21.8%). The quality of life of patients who were actively monitored improved in comparison to other patients. The patients who were actively monitored assessed the quality of life as very good (15%), good (25.2%) and satisfactory (17.8%) (11). In a study conducted in Croatia, the symptoms that the patients stated as those that cause the greatest dissatisfaction, that is, those that most impair their quality of life, were the symptoms of increased frequency of urination, nocturia, urgency and urge incontinence (11). A cross-sectional study, which involved four European countries (France, Spain, Portugal and Germany) included 480 men older than 50 with BPH symptoms of lower urinary tract, and the results showed a great influence of symptoms of lower urinary tract, on the patients' quality of life (16). The quality of life was the least impaired in patients from Germany (3.52 points) compared to other countries where the average number of points was 4.27 - 4.55. Only 10% of patients stated that they would be satisfied if they spent the rest of their lives with current symptoms (16).

The main advantage of this study can be a relatively uniform sample in terms of certain medical/health parameters, as well as a standardized measuring instrument and a sufficient number of participants necessary to conduct the study. The main limitation of the study may be the small number of participants, as well as the fact that in a cross-sectional study, one cannot define the cause and the consequence of health disorder. The study was conducted from May to August, when exposure to the sun is the greatest, so it can affect the level of vitamin D. The other limitation of the study is also related to the time of examination, because in these months the irritating symptoms of lower urinary tract are usually least pronounced, due to high daily temperatures.

Recommendations for future research would go in the direction of including more variables that are different in character and that would deepen the examined relationships and lead to more relevant conclusions. The most important recommendation would be that this kind of research should be designed as a prospective study, where both the level of vitamin D and frequency of urinary symptoms would be monitored in subjects in the function of time.

Conclusion

A significant negative correlation was obtained between vitamin D levels and all individually assessed values of urological symptoms, which were evaluated according to the IPSS questionnaire, as well as with the overall assessment of symptoms. However, there is an inverse relationship between average vitamin D values and quality of life according to IPSS questionnaire, but the relationship is not significant. Further research in this field is necessary, aimed at giving recommendations for the use of vitamin D.

Competing interests

The authors declared no competing interests.

References

1. Lee SU, Lee SH, So AH, Park JI, Lee S, Oh IH, et al. Association between benign prostatic hyperplasia and suicide in South Korea: A nationwide retrospective cohort study. *PLoS One*. 2022;17(3):e0265060. doi: 10.1371/journal.pone.0265060. eCollection 2022.
2. Sarma AV, Wei JT. Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms. *N Engl J Med*. 2012;367(3):248-57. doi: 10.1056/NEJMc1106637.
3. Langan RC. Benign Prostatic Hyperplasia. *Prim Care Clin Off Pract*. 2019;46(2):223-32. doi: 10.1016/j.pop.2019.02.003.
4. Kim EH, Larson JA, Andriole GL. Management of Benign Prostatic Hyperplasia. *Annu Rev Med*. 2016;67(1):137-51. doi: 10.1146/annurev-med-063014-123902.
5. Park S, Lee KS, Choi M, Lee M. Factors associated with quality of life in patients with benign prostatic hyperplasia, 2009–2016. *Medicine (Baltimore)*. 2022;101(36):e30091. doi: 10.1097/MD.00000000000030091.
6. Egan KB. The Epidemiology of Benign Prostatic Hyperplasia Associated with Lower Urinary Tract Symptoms. *Urol Clin North Am*. 2016;43(3):289–97. doi: 10.1016/j.ucl.2016.04.001
7. Liu ZM, Wong C, Chan D, Woo J, Chen YM, Chen B, et al. Association of Circulating 25(OH)D and Lower Urinary Tract Symptoms: A Four-Year Prospective Study among Elderly Chinese Men. *Nutrients*. 2016;8(5):273. doi: 10.3390/nu8050273.
8. Chen Y, Xu H, Liu C, Gu M, Chen Q, Zhan M, et al. Therapeutic Effects of 25-Hydroxyvitamin D on the Pathological Process of Benign Prostatic Hyperplasia: An In Vitro Evidence. *Dis Markers*. 2021;2021:4029470. doi: 10.1155/2021/4029470
9. Barry MJ, Fowler FJ Jr, Bin L, Pitts JC 3rd, Harris CJ, Mulley AG Jr. The natural history of patients with benign prostatic hyperplasia as diagnosed by North American urologists. *J Urol*. 1997;157(1):10-4; discussion 14-5.
10. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual



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- dysfunction: the multinational survey of the aging male (MSAM-7). *Eur Urol.* 2003;44(6):637-49. doi: 10.1016/j.eururo.2003.08.015.
11. Kuliš T, Gašparić M, Prižmić M, Kovačić D, Kolumbić Lakoš A, Kaštelan Ž. Simptomi i kvaliteta života u bolesnika s BPH. *Medicus.* 2015;25(1):87-92.
 12. Ilić A, Denović D. Kliničko morfološke karakteristike patoloških promjena u prostati. *Praxis Medika.* 2019;48(1):1-8. doi: 10.5937/pramed19010011
 13. Tóth Z, Szalay B, Gyarmati B, Jalal DA, Vásárhelyi B, Szabó T. Vitamin D Deficiency has no Impact on PSA Reference Ranges in a General University Hospital - A Retrospective Analysis. *EJIFCC.* 2020;31(3):225-230.
 14. Grammatikopoulou MG, Gkiouras K, Papageorgiou ST, Myrogiannis I, Mykoniatis I, Papamitsou T, et al. Dietary Factors and Supplements Influencing Prostate Specific-Antigen (PSA) Concentrations in Men with Prostate Cancer and Increased Cancer Risk: An Evidence Analysis Review Based on Randomized Controlled Trials. *Nutrients.* 2020;12(10):2985. doi: 10.3390/nu12102985.
 15. Kristal AR, Arnold KB, Schenk JM, Neuhaus ML, Goodman P, Penson DF, Thompson IM. Dietary patterns, supplement use, and the risk of symptomatic benign prostatic hyperplasia: results from the prostate cancer prevention trial. *Am J Epidemiol.* 2008;167(8):925-34. doi: 10.1093/aje/kwm389.
 16. Speakman M, Kirby R, Doyle S, Ioannou C. Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) - focus on the UK. *BJU Int.* 2015;115(4):508-19. doi: 10.1111/bju.12745.



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