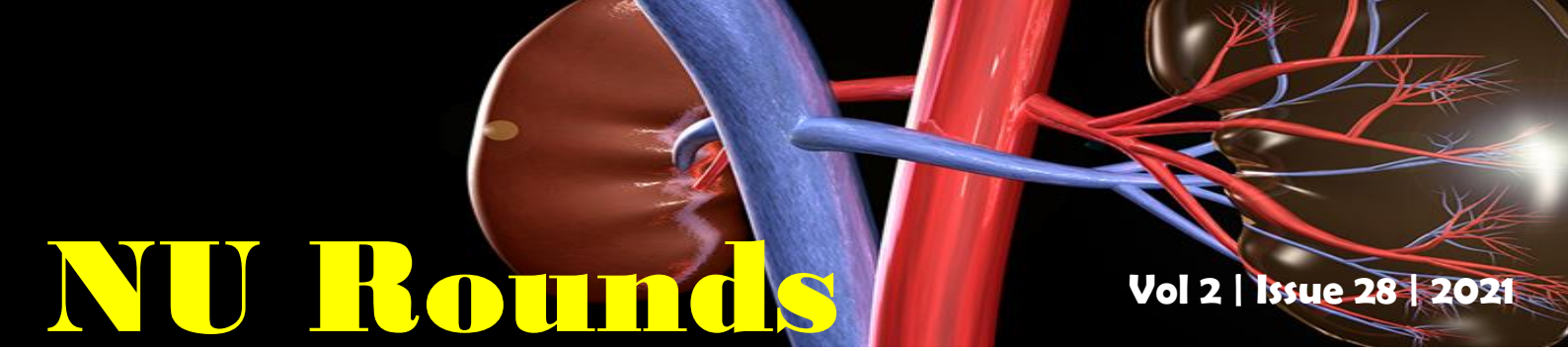

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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Complementary and Alternative Medicine Use in First-time and Recurrent Kidney Stone Formers

Introduction

Adequate evaluation and management is necessary to prevent recurrence of stones. Recognition of risk factors and development of long-term management strategies for dealing with them are the most effective ways to prevent recurrence of kidney stones. For kidney stone prevention dietary and pharmacologic intervention is effective. Adherence is poor because of side effect profiles of prescription medications, cost and difficulty in maintaining dietary changes. National Institutes of Health defines that the subjects with kidney stones may seek to treat their symptoms or reduce recurrence risk with complementary and alternative medicine (CAM). In other chronic conditions, to alleviate the symptoms of chronic diseases or the side effects of conventional treatment, subjects often use CAM as adjunctive therapy to conventional medicine.

Aim: The objective of this study was to evaluate the patterns of complementary and alternative medicine (CAM) among subjects with kidney stones and to analyze the alkali content of commonly used CAM therapies.

Methods: This was a prospective study using structured interviews with subjects with kidney stones to assess knowledge and use of CAM. Patients who presented to a specialty stone clinic for the management of kidney stones were included in this study.

Inclusion criteria: History of kidney stone disease and the age of the patient was ≥ 18 years

Exclusion Criteria: Subjects who were non-verbal or non-English speaking were excluded in this study.

Demographic data was collected. Stone event history was ascertained for spontaneous passage and stone-specific surgeries. Subjects were asked about dietary changes they have made after stone diagnosis. Prescribed and non-prescribed medications, supplements, herbals, and any other consumables with the intent of treating or preventing kidney stones or related symptoms

was recorded. Four general beverage supplements and 4 stone-specific supplements based on interview feedback was used to assess alkali and electrolyte content of commercially available CAM products. The 4 stone-specific therapies tested were Stonebreaker (SB), LithoBalance (LB), KSP Key Lime (KSP-KL), KSP VeryBerry (KSP-VB). Among the liquid formulations, those that had potential for alkali content were selected and the common supplement reported by interviewees were specifically Simply Grapefruit Juice (SGJ), Ocean Spray Cranberry Juice Cocktail (OSCJ), Lakewood Pure Cranberry Juice (LPCJ), and Bragg's Apple Cider Vinegar (BACV). Ion chromatography was used to measure Citrate, malate, and acetate. A standard clinical autoanalyzer was used to measure bicarbonate. Total alkali concentration was calculated using the published pKs of the anions and the measured pH of the supplement. Electrolytes such as sodium, potassium, chloride, calcium, and magnesium was also measured. To elicit information regarding CAM knowledge, formulation/dosing, and patterns of use open-ended questions were used. Several common CAM therapies were then analyzed for their alkali, organic anion, and sugar content.

Results: Out of 103 participants interviewed regarding their use of CAM for kidney stone prevention , 82 (80%) subjects reported knowledge of CAM and 52 (50%) reported using CAM. Subjects with recurrent kidney stones were more likely to report using CAM than patients with first-time episodes (56% vs 26%). Some respondents reported decreased in severity or frequency since starting CAM therapy (17%) and improvements in pain(12%).

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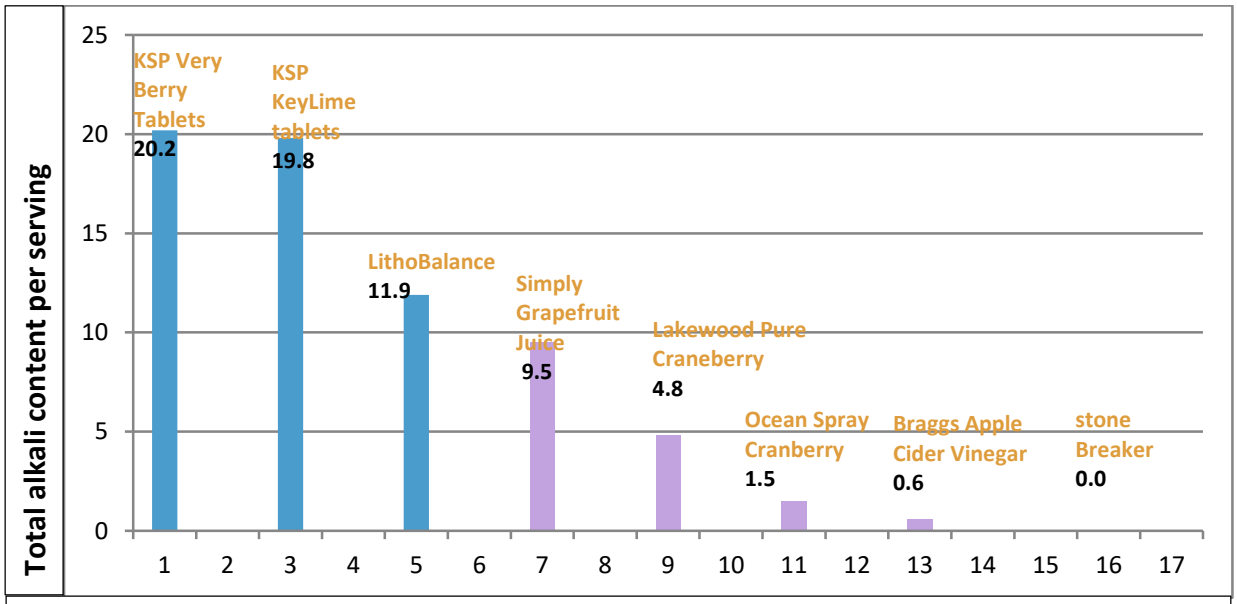
		Full Cohort (n = 103)		First-Time Stone Former (n = 19)		Recurrent Stone Formers (n = 84)		P-value
		n	%	n	%	n	%	
Sources of information on CAM	Friends	45	44	5	26	40	48	0.09
	Family	42	41	9	47	33	39	0.52
	Online research	42	41	5	26	37	44	0.16
	Physician	34	33	3	16	31	37	0.07
	Social media	12	12	3	16	9	11	0.53
	Advertisements	4	4	1	5	3	4	0.56
	Supplement stores	4	4	1	5	3	4	0.56
Where CAM was purchased	Walmart/target	12	12	0	0	12	14	*
	Online	9	9	0	0	9	11	*
	Pharmacy	8	8	2	11	6	7	0.63
	Herbal med store	7	7	1	5	6	7	0.78
	Supplement store	5	5	0	0	5	6	*

	Full cohort (n = 52)		First-time stone former (n = 5)		Recurrent stone Formers (n = 47)		P-value*
	n	%	n	%	n	%	
Participants who perceived that stone burden or frequency decreased following CAM use	9	17	1	20	8	17	0.55
Participants who perceived that symptoms improved following CAM use	6	12	0	0	6	13	*
Participants who perceived that they have had adverse side effects from CAM use	4	8	0	0	4	9	*

Sources of information, purchase, and attitudes on CAM therapies for kidney stone prevention

CAM Therapy	KSP Very Berry Tablets	KSP Key Lime Tablets	Simply Grapefruit Juice	Litho Balance	Braggs Apple Cider Vinegar	Lakewood Pure Cranberry Juice	Ocean Spray Cranberry Juice Cocktail	Stone Breaker
Na	9.5	9.7	< 10	< 10	< 10	< 10	< 10	< 10
K	4.5	4.1	8.9	9.7	< 3	4.4	1.3	< 3
Cl	< 10	< 10	< 10	< 10	< 10	< 10	< 10	< 10
Ca	< 0.1	< 0.1	0.4	< 0.1	< 0.1	0.2	< 0.1	< 0.1
Mg	3.6	3.6	0.8	1.4	< 0.2	0.5	< 0.2	< 0.2
Bicarb	4.6	4.6	< 2	< 2	< 2	< 2	< 2	< 2
pH	4.98	4.81	3.39	4.06	3.10	2.45	2.59	5.01
Citrate	9.5	9.9	12.9	11.3	0.0	16.1	3.0	0.0
Malate	0.0	0.0	0.8	0.0	0.2	19.0	4.9	0.0
Acetate	0.0	0.0	1.8	0.0	26	2.2	2.0	0.0
Total alkali content (mEq/L)	42	41	40	25	21	20	6	0
Carbohydrate content (g)	3	4	25	3	0	19	28	0
Serving size	1 Tab	1 Tab	240 mL	10 g	30 mL	240 mL	240 mL	0.7 mL
Recommended servings per day	2-3	2-3	ND	2-3	ND	ND	ND	3
Estimated daily cost	$1.66	$1.66	$0.49	$1.10	$0.18	$3.17	$0.59	$0.77

Chemical analysis of selected CAM therapies



Total alkali content per serving of tested supplements. Green bars represent beverage supplements, Purple bars represent stone-specific supplements.

Conclusion: To alleviate symptoms or prevent recurrence subjects with kidney stones may use complementary and alternative medicine (CAM). CAM therapies have significant alkali content that may reach those achievable with commonly prescribed pharmacologic agents for stone prevention. Subjects receive information from a variety of data sources, and providers should be aware of complementary and alternative medicine use to ensure these interventions are safe and do not mitigate other interventions.

Reference: Joshi A, Tallman JE, Calvert JK, Brewer T, Miller NL, Yang L, Asplin JR, Hsi RS. Complementary and Alternative Medicine Use in First-time and Recurrent Kidney Stone Formers. Urology. Oct 2021;156:58-64

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Three-channel ion chromatograph for improved metabolic evaluation of urolithiasis

Introduction: Urolithiasis is a multi-etiological disease which results from a combination of environmental and genetic factors. High recurrence rate is one of the most challenging aspects of this disease. Recurrence rate of urolithiasis for the formation of calcium oxalate stones may be up to ≥13% for over 5 years. An in-depth metabolic evaluation may reveal the presence of urinary stones for most of the subjects. This includes the analysis of the output of stone formation factors such as oxalate, calcium, uric acid and stone inhibition factors (magnesium and citrate) in urine collected over the course of 24 h. In order to complete a metabolic evaluation ion chromatography (IC) is used to measure small organic molecules in urine, including oxalate and citrate and other indicators may be measured by chemical methods or colorimetry.

Aim: To verify the measurement precision of novel Ion Chromatography (IC) instrument, 3 single-channel CIC100-type IC (CIC100) manufactured by Qingdao Shenghan Chromatographic Technology Co., Ltd. as the control instrument.

Methods: A three-channel ion chromatograph (IC) was developed to improve the efficiency which automatically measures the concentration of common metabolic indicators of urolithiasis in urine (i.e., oxalate, citrate, uric acid, calcium, and magnesium). Standard curve was prepared using working solution of these indicators to validate its precision and specificity. 3 CIC100 were used as the control instrument to verify the measurement precision and efficiency of the new ion chromatography. 24-h urine sample was collected from human subjects. 100 subjects without history of urinary system diseases such as infections, hematuria, or stones, provided their 24-h urine. 135 Subjects with stones were also selected and analyzed their 24-h urine samples. Urine sample obtained was ten times and sent to the chromatographs belonging to the newly developed and control ICs. To detect the concentrations of the five target urinary stone-related compounds (USRCs), Urine samples of 135 patients with stones were injected into the chromatographs of the two groups and t-test was used to perform statistical analysis.

Results: Good linear relationships in concentration ranges of 0–10 mg/L was observed in all analytes. The measurement errors of the newly developed IC were all less than 5%. The recovery rate in urine ranged from 99.6 to 100.4%, coefficient of variation ranged from 1.39 to 2.99% and these results matched between newly developed ion chromatograph (IC) and the control ICs. Efficiency test revealed that Analysis was finished at the average number of 14 people per day with the new IC and the average number in the control group is 3.85/day.

	3-Channel IC Concentration (mg/L)	**Control group Concentration (mg/L)**	**t**	**P**
Oxalate	0.998±0.0084	0.998±0.0081	−0.024	0.981
Citrate	2.498±0.0104	2.501±0.0098	−1.743	0.084
Calcium	2.498±0.0075	2.500±0.0099	−1.145	0.255
Magnesium	1.500±0.0060	1.499±0.0086	1.400	0.165
Uric acid	4.992±0.0415	4.960±0.301	1.045	0.299

Results from the precision experiments conducted with standard solutions

	New ion chromatograph Concentration (mg/L)	**Control Group Concentration (mg/L)**	**t value**	**P value**
Oxalate	25.81±19.76	25.88±19.73	−1.036	0.302
Citrate	220.63±164.17	220.82±164.62	−0.268	0.789

Calcium	129.28±131.49	122.34±106.58	1.004	0.317
Magnesium	52.86±67.89	52.87±68.06	−0.029	0.977
Uric acid	254.68±220.66	253.38±220.156	1.589	0.114
Results obtained from patients with stones				

Conclusion: The results described herein show that new three-channel IC is comparable to those obtained with conventional ICs. The new IC showed significantly higher measurement efficiency. Overall, this multi-channel system significantly improves the efficiency of metabolic evaluation while retaining accuracy and precision.

Reference: Li Q, Liu G, Cheng Y, Tang W. Three-channel ion chromatograph for improved metabolic evaluation of urolithiasis. BMC urology. 2021 Nov;21(1):1-7.

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Usefulness of MRI targeted prostate biopsy for detecting clinically significant prostate cancer in men with low prostate-specific antigen

Introduction: Prostate-specific antigen (PSA) testing has facilitated early detection of prostate cancer (PCa) in recent decades, leading to a downward migration in the stage of newly diagnosed PCa. There are several reports that showed half of the PCa diagnosed in men with PSA levels lower than 4.0 ng/mL had clinically aggressive characteristics, which suggest that the conventional Prostate-specific antigen cutoff value should be lowered. There are also results that shows lower PSA cutoff value which result in overdiagnosis and overtreatment of PCa.

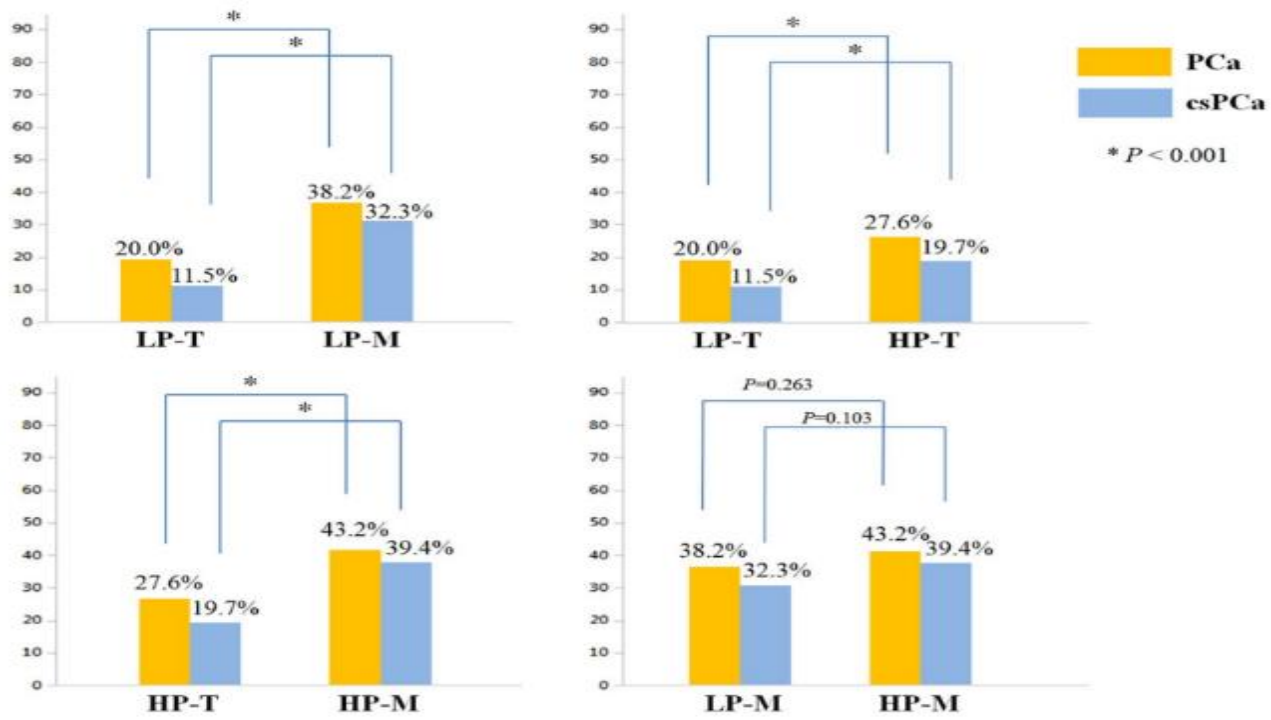
Aim: The objective of this study was to evaluate the detection rates of prostate cancer (PCa) and clinically significant PCa (csPCa) using magnetic resonance imaging-targeted biopsy in men with low prostate-specific antigen (PSA) levels.

Methods: Medical records of 5,932 men with PSA levels of 2.5–10.0 ng/mL who underwent prostate needle biopsy were reviewed. The subjects excluded in this study were Men with with a history of previous prostate biopsy , history of prostate surgery (e.g., transurethral resection of the prostate) and use of 5-alpha-reductase inhibitors before biopsy. Ultimately, 5502 subjects who underwent prostate biopsy were analyzed in this study. According to prebiopsy PSA level and biopsy modality this study cohort was divided into 4 groups, LP-T [men with low PSA (2.5–4.0 ng/mL) who underwent TRUS-Bx], LP-M [men with low PSA (2.5–4.0 ng/mL) who underwent MRI-TBx], HP-T [men with high PSA (4.0–10.0 ng/mL) who underwent TRUS-Bx], and HP-M [men with high PSA (4.0–10.0 ng/mL) who underwent MRI-TBx]. Detection rates of PCa and csPCa between groups were compared. Association of biopsy modality with detection of PCa and csPCa in men with low PSA levels were analyzed. All subjects received antibiotic medication prior to the biopsy procedure. Using an 18-gauge biopsy needle mounted on an automatic biopsy gun in a biplanar ultrasound probe TRUS-Bx was systematically performed on 12 cores, including both the standard and lateral sextant schemes.

Results: The detection rates of PCa (20.0% vs. 38.2%) and csPCa (11.5% vs. 32.3%) was higher in the LP-M group than in the LP-T group. Between the LP-M and HP-M groups there were no significant differences in the detection rates of PCa (38.2% vs. 43.2%) and csPCa. There were no significant differences in age and PSA level between the biopsy modalities in low PSA groups. MRI-TBx could predict the detection of csPCa in men with low PSA levels.

Variables	Low PSA groups			High PSA groups			LP-T versus HP-T	LP-M versus HP-M
	LP-T	LP-M	*P* value	HP-T	HP-M	*P* value	*P* value	*P* value
No. of patients, *n* (%)	2018 (36.7)	186 (3.4)		2953 (53.7)	345 (6.3)			
Age, years			0.100			0.689	<0.001	0.152
Mean ± SD	61.9 ± 8.5	62.9 ± 8.4		63.9 ± 9.3	64.1 ± 8.6			
Median (range)	62.0 (33.0–87.0)	63.0 (37.0–81.0)		64.8 (31.0–89.0)	64.4 (31.0–86.0)			
PSA, ng/mL			0.207			0.907	<0.001	<0.001
Mean ± SD	3.3 ± 0.4	3.3 ± 0.4		6.0 ± 1.6	6.0 ± 1.6			
Median (range)	3.3 (2.5–3.9)	3.4 (2.5–3.9)		5.6 (4.0–9.9)	5.5 (4.0–9.9)			
Prostate volume, mL			<0.001			<0.001	<0.001	<0.001
Mean ± SD	37.3 ± 15.4	32.1 ± 11.5		43.8 ± 21.7	37.2 ± 17.9			
Median (range)	33.9 (12.0–231.0)	29.7 (12.0–83.0)		38.8 (12.0–298.0)	32.6 (5.0–103.0)			
PSA density, ng/mL²			<0.001			<0.001	<0.001	<0.001
Mean ± SD	0.10 ± 0.04	0.12 ± 0.04		0.17 ± 0.09	0.20 ± 0.11			
Median (range)	0.09 (0.01–0.30)	0.11 (0.03–0.32)		0.15 (0.03–0.58)	0.17 (0.05–0.78)			
PI-RADSv2 score†								0.105
3, *n* (%)		8 (7.3)			18 (9.1)			
4, *n* (%)		72 (65.5)			105 (53.0)			
5, *n* (%)		30 (27.3)			75 (37.9)			

Clinical characteristic of men who underwent prostate biopsy.



Detection rates of prostate cancer and clinically significant prostate cancer in each group.

	Population	Median PSA	Definition of csPCa	Reference standard	MRI-TBx technique	Detection rate of csPCa by MRI-TBx	Detection rate c csPCa by TRUS
PRECISION[10]	252 in MRI-TBx 248 in Standard biopsy	6.75 ng/mL in MRI-TBx 6.50 ng/mL in Standard biopsy	GS≥3+4	10–12 core TRUS-Bx	Cognitive or fusion targeted biopsy of mpMRI lesion without systematic biopsy	38% (95/252)	26% (64/248)
4M[11]	626 (cohort)	6.4 ng/mL	GS≥3+4	10–12 core TRUS-Bx	In-bore MR-guided biopsy with 12-core systematic biopsy	25% (159/626)	23% (146/626)
MRI-FIRST[12]	251 (cohort)	6.5 ng/mL	GS≥3+4	10–12 core TRUS-Bx	Cognitive or fusion targeted biopsy of mpMRI lesions with 12-core systematic biopsy	32% (81/251)	30% (75/251)

Data from three major manuscripts of MRI-TBx. csPCa Clinically significant prostate cancer, PSA

Prostate-specifc antigen, TRUS-Bx Transrectal ultrasound-guided biopsy, MRI-TBx Magnetic resonance imaging-targeted biopsy.

Conclusion: This study concluded that performing magnetic resonance imaging-targeted biopsy (MRI-TBx) in men with low prostate specifc antigen (PSA) levels significantly improved the detection rates of PCa and csPCa as much as that in men with high PSA levels. Hence, it may be necessary to recommend MRI-TBx in men with low prostate specific antigen levels.

Reference: Bang S, Yu J, Chung JH, Song W, Kang M, Sung HH, Jeon HG, Jeong BC, Seo SI, Lee HM, Jeon SS. Usefulness of MRI targeted prostate biopsy for detecting clinically significant prostate cancer in men with low prostate-specific antigen levels. Scientific Reports. 2021 Nov 9;11(1):1-8.