NU Rounds

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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 Nephrology and Urology.

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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1. Prostate volume as a potential independent predictor in the selection of low-risk prostate patients for active surveillance

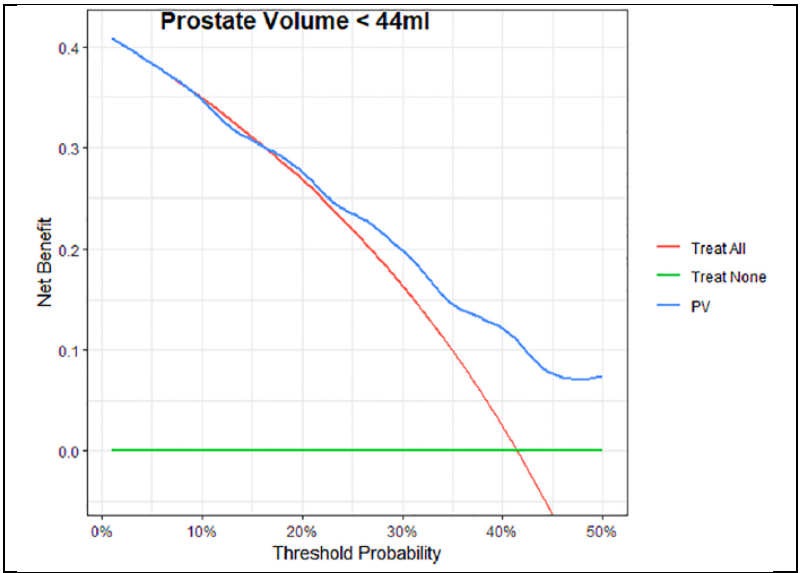
Introduction:

Active Surveillance (AS) for low-risk prostate cancer has been accepted as standard of care. AS for low-risk prostate cancer benefits include the preservation of quality of life and the certainty of effective therapy, if necessary.[1] International guidelines have approved and included the use of multiparametric magnetic resonance imaging (mpMRI) in AS regimens for patients with low-risk PCa. It has not yet been demonstrated that patients with AS must use mpMRI for decision-making. [2]The purpose of this research is to identify diagnostic-period characteristics that can predict disease reclassification, particularly in situations where mpMRI and complex genetic tests are either unavailable or unaffordable.

Prostate volume and Prostate specific antigen density significantly predicted failure from Active Surveillance in patients.

Methods:

According to the following inclusion criteria: PSA ≤10 ng/ml, Gleason score (GS) ≤6 or International Society of Urological Pathology (ISUP) Gleason grade group (GG) 1, maximum cancer core length (MCCI) <50%, and ≤2 positive cores on biopsy, a total of 114 consecutive low-risk PCa patients were enrolled in the AS protocol. Patients were monitored with confirmatory and semi-annual prostate biopsies, yearly PSA tests, and digital rectal examinations (DRE). Upgrading biopsy criteria such as GS ≥ 3 + 4 = 7 or ISUP GG≥ 2, more than two positive cores, MCCI > 50%, or increases in serum PSA > 10 ng/ml were used to identify disease reclassification. To describe AS criteria and find factors that predict illness reclassification, Kaplan-Meier analysis, receiver performance curves (ROC), and uni- and multivariate Cox proportional hazards regression models were used. In order to determine the net benefit of



Decision curves for Prostate volume (PV) to predict 6-years to PCa reclassification in patients. The green line represents the net benefit of treating no patients; the red line is the net benefit of treating all patients similarly; the blue line is the net benefit of treating patients according to the PV model.

employing PV in addition to conventional variables to forecast illness categorization, decision curve analysis (DCA) was finally carried out.

Results:

PCa was identified with regular transrectal prostate biopsy guided by ultrasonography (TRUS-Bx). The average (interquartile range) follow-up was 32.7 (12–26) months. In 46 cases (about 40%), the disease was reclassified. Prostate specific antigen (PSA) (p = 0.05), prostate volume (PV) (p = 0.022), PSA density (PSAD) (p 0.001), and the quantity of positive cores (p = 0.021) were all statistically significant criteria for reclassifying the disease. The only statistically significant independent variables that predict disease reclassification in the multivariate analysis were PSAD (p 0.001) and PV (p = 0.003). Maximal areas under the curve were 0.69 and 0.63, respectively, with a PSAD cut-off of 0.16 ng/ml2 and a PV cut-off of 44 ml. Patients with PSAD <0.16 ng/ml2 or PV > 44 ml had almost twice as long a median life free from disease reclassification during AS, according to a Kaplan-Meier study. The model, which included PV, was clinically beneficial in predicting disease reclassification between threshold probabilities of 20–50%, according to DCA.

Discussion:

In addition to PSAD, this investigation found PV as a potent independent predictor for disease categorization in low-risk PC patients. Most crucially, these measurements are readily available and easily calculable at the time the AS protocol is started.2 Currently, it is recognized that PSAD plays a part in identifying patients with low-risk illnesses for AS.[1] According to Nordström et al.'s analysis of 5291 men's biopsy data from the population-based STHLM3 trial, incorporating PSA density into the diagnostic algorithm may help evaluate men with low-grade PCa (25). In a long-term outcomes study of PCa patients on AS, Maggi et al. discovered that males with GG1 and GG2 diagnoses and PSAD levels of 0.15 ng/ml2 or higher had worse upgrade-free survival and lower treatment-free survival

Conclusion:

PV and PSAD were highly predictive of AS failure. Patients with a baseline PV of less than 44 ml are more likely to have disease reclassification and are therefore not suited for regimens that are considered acceptable for AS. Consequently, researchers think PV may aid in the selection of PCa patients for AS, particularly in populations where the use of mpMRI is restricted.

Reference:

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3. Nordström T, Akre O. Prostate-specific antigen (PSA) density in the diagnostic algorithm of prostate cancer informing prostate biopsy decisions is easily accessible. Prostate Cancer Prostatic Dis 2018.21:57–63.
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2.A Study assessing young men's testosterone levels. Reconsidering the 300 ng/dl Cutoff for Testosterone Deficiency in Men 20 to 44 Years Old

Introduction:

Low serum testosterone levels combined with hypogonadism's signs and symptoms are referred to as TESTOSTERONE DEFICIENCY.[1] Younger men are increasingly expressing worries about testosterone deficiency, despite the condition often being associated with older men. The past 20 years have also seen a fall in young men's testosterone levels, sperm counts, and fertility.[2] The synthesis of male testosterone decreases with age. So it is unexpected that young men are assessed for testosterone shortage using the same 300 ng/dL cutoff that was created from older men's samples.[1] The aim of this study is to identify age-specific cutoffs for low testosterone levels in males between the ages of 20 and 44, as well as to describe the normative total testosterone levels.

The reference ranges for testosterone in young men differ from those in older males

Methods:

Researchers examined the National Health and Nutrition Examination Surveys, which examine national representative samples. Men with testosterone levels between the ages of 20 and 44 were included. Men on hormonal drugs, those with a history of orchiectomy or testicular cancer, and those with afternoon or evening laboratory levels were eliminated. In order to assess the testosterone levels of all men aged 20 to 44, researchers divided the male population into 5-year intervals. Age-specific thresholds for low testosterone levels were determined using the American Urological Association's definition of a "normal testosterone level" (the "middle tertile").

Results:

There were 1,486 guys in the final analytic cohort. The middle tertile values varied according to age, being 409-558 ng/dL (20-24 years old), 413-575 ng/dL (25-29 years old), 359- 498 ng/dL (30-34 years old), 352-478 ng/dL (35-39 years old), and 350-473 ng/dL. (40-44 years old). 409, 413, 359, 352, and 350 ng/dL were the age-specific cutoffs for low testosterone levels, respectively.

Discussion:

In the urological literature, testosterone reference ranges for elderly men have long been established.[1] 22 Few studies, nevertheless, have looked at young men's testosterone levels. The Endocrine Society commissioned a research in 2017 to investigate testosterone reference ranges for young males in an effort to close this disparity.[3] The average testosterone levels for men aged 19 to 39 were found to range between 228 and 895 ng/dL in this study, which pooled morning testosterone samples from the Framingham Heart Study and Sibling Study of Osteoporosis.

Total Morning Testosterone Levels by Age Group: The 33rd percentile was used to determine age-specific cutoffs for low testosterone levels for men in each 5-year age grouping as well as in all men 20 to 44 years old

Age group, y	Mean morning testosterone (ng/dL)	33rd Percentile
20-24	501	409
25-29	514	413
30-34	456	359
35-39	438	352
40-44	430	350
All men	466	374

Conclusion:

Traditionally, testosterone deficiency has been diagnosed without regard to a patient's age. However, the reference ranges for testosterone in young men differ from those in older males. Therefore, when evaluating young men who come with low testosterone levels, age-specific normative values and cutoffs should be taken into account.

Reference:

1. Zhu A, Andino J, Daignault-Newton S, Chopra Z, Sarma A, Dupree JM. What Is a Normal Testosterone Level for Young Men? Rethinking the 300 ng/dL Cutoff for Testosterone Deficiency in Men 20-44 Years Old. J Urol. 2022 Dec;208(6):1295-1302.
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3.A Study on Comparing the effectiveness of the urine dipstick and urine protein-to-creatinine ratio for predicting microalbuminuria in patients with non-diabetic lifestyle-related diseases and diabetes

Introduction:

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The current definition of microalbuminuria (MA) is a level of urine albumin that is both higher than the normal value and lower than what can be detected by a standard dipstick. In microalbuminuria, urine albumin excretion (UAE) ranges from 30 to 300 mg/d.[1] In disorders caused by an unhealthy lifestyle, microalbuminuria increases the risk of renal dysfunction, cardiovascular disease, mortality, and dementia. Type 2 diabetes, obesity, metabolic syndrome, non-familial dyslipidemia, hypertension, hyperuricemia, myocardial infarction, stroke, liver disease, cancer, etc. are all disorders linked to lifestyle. The effectiveness of dipstick proteinuria for predicting microalbuminuria in non-diabetic lifestyle-related disorders and the impact of dipstick proteinuria on the cut-off value (CO) and accuracy of uPCR remain unknown. Researchers thus examined the effectiveness of dipstick measures and the uPCR for detecting microalbuminuria in the current investigation.

The urine protein-to-creatinine ratio can help in the early detection of microalbuminuria, even in cases where proteinuria on a dipstick is negative and with non-diabetic lifestyle-related disorders.

Methods:

Patients with lifestyle-related disorders ≥18 years were enrolled as participants. At the start of the study, their estimated glomerular filtration rate was ≥15 ml/min/1.73 m2 and their uPCR was <0.5 g/gCr. Each case received three measurements of the urine dipstick, urine PCR, and urine albumin-to-creatinine ratio (uACR). Microalbuminuria was defined as uACR of 30-299 mg/gCr for at least 2 out of 3 measurements. The optimal CO was determined by Youden's Index. A logistic regression model was used to evaluate the factors related to microalbuminuria.

Results:

Three dipstick proteinuria assessments were independently beneficial in 313 non-diabetic cases for detecting microalbuminuria, and the CO was set when a trace finding was observed at least once in three instances (sensitivity 0.56, specificity 0.80, positive predictive value [PPV] 0.73, negative predictive value [NPV] 0.65). Even in cases with three consecutive negative proteinuria findings, a single uPCR measurement was more accurate than three dipstick measurements at detecting microalbuminuria. The CO of the second uPCR with G1-3a (n = 136) was 0.06 g/gCr (sensitivity 0.76, specificity 0.84, PPV 0.68, NPV 0.89), while that with G3-b4 (n = 59) was 0.10 g/gCr (sensitivity 0.56, specificity 0.91. PPV 0.83, NPV 0.71). In patients with G1-3a (sensitivity 0.67, specificity 0.94, PPV 0.82, NPV 0.86) and G3b-4 (sensitivity 0.78, specificity 0.94, PPV 0.91, NPV 0.83) with both COs being 0.23 g/gCr, the sum of three uPCRs was helpful for diagnosing microalbuminuria. Even though the sensitivity increased, these COs of microalbuminuria remained same when trace or more proteinuria was present. In instances with negative proteinuria, a high uPCR and a low urine specific gravity or creatinine level were independent predictors for an uACR ≥30 mg/gCr, even if the uPCR was a significant predictor of an uACR≥ 30 mg/gCr.

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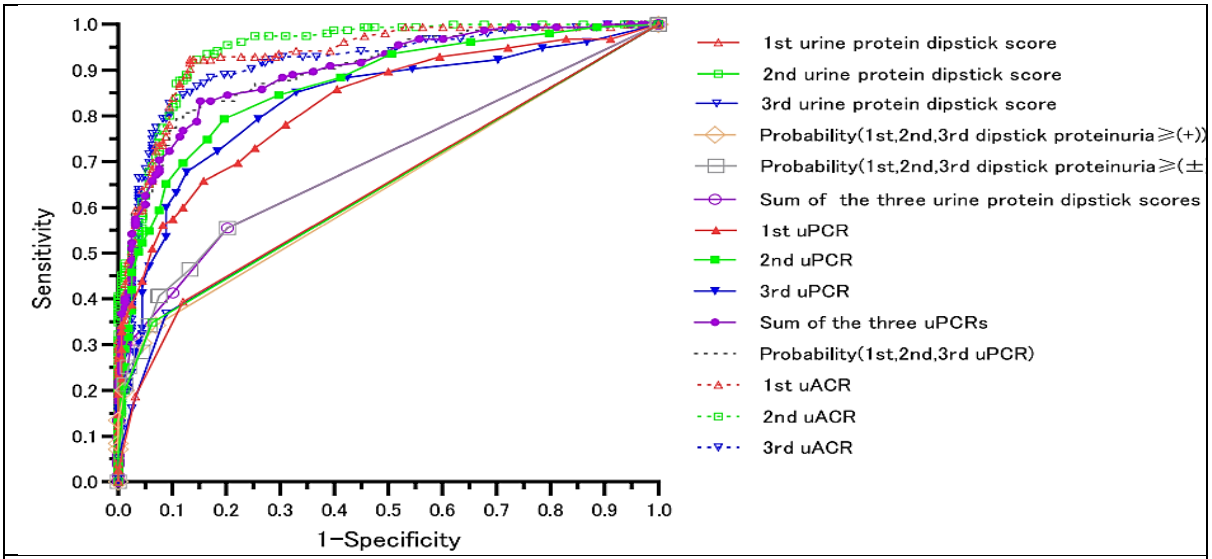

The ROC curve for the differentiation of normoalbuminuria and micro- and macroalbuminuria using the urine protein dipstick score, urine protein-to-creatinine ratio, and urine albumin-to-creatinine ratio in non-diabetic patients. Probability (1st, 2nd, 3rd dipstick proteinuria ≥ (+)): Probability of micro- and macroalbuminuria based on the logistic model using dummy variable dipstick proteinuria ≥ (+): 1, dipstick proteinuria(±) (-): 0. Probability (1st, 2nd, 3rd dipstick proteinuria ≥ (±)): Probability of micro- and macroalbuminuria based on the logistic model using dummy variable dipstick proteinuria ≥ (±):1, dipstick proteinuria(-):0. Probability (1st, 2nd, 3rd uPCR): Probability of micro- and macroalbuminuria based on the logistic model using 1st, 2nd, and 3rd uPCR.

Discussion:

In this investigation, even patients who tested negative on a dipstick test for microalbuminuria had microalbuminuria detected by uPCR. The CO of uPCR for microalbuminuria in cases with three consecutive negative proteinuria findings for both groups was 0.06 g/gCr.[2] Only when there is a suspicion of developing diabetic nephropathy in Japan is the measurement of albuminuria covered by insurance.[3] Diabetes is at risk due to obesity and the metabolic syndrome.[3] In this study, patients who were obese and had high blood pressure had high levels of uACR and uPCR.[2]

Conclusion:

Although a urine dipstick evaluation is helpful for detecting microalbuminuria in cases of non-diabetic lifestyle-related diseases, measuring the uPCR, especially using the early-morning urine three times, as well as in dipstick-negative proteinuria cases, may lead to the early detection of microalbuminuria and prompt intervention for CKD due to the non-lifestyle-related diseases.

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1. Prasad RM, Tikaria R. Microalbuminuria. [Updated 2022 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022.
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4. A rare case of bilateral renal infarction, vertebral artery dissection and mesenteric ischemia associated with catastrophic fibromuscular dysplasia

Introduction:

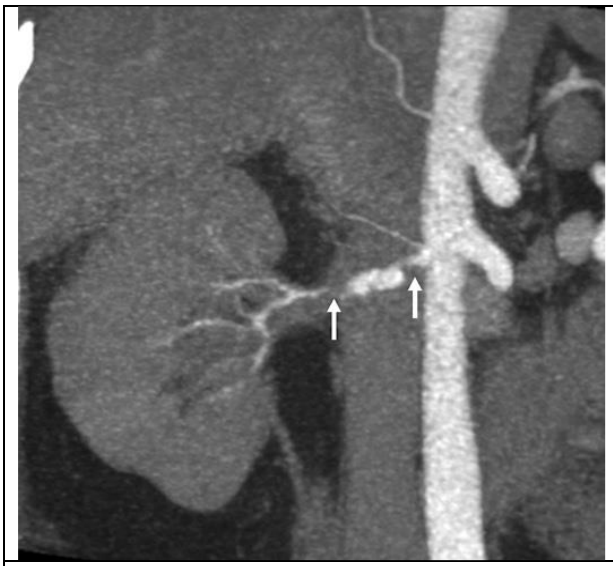
Fibromuscular dysplasia (FMD) is a rare systemic vascular disease that causes 10% to 20% of cases of renal artery stenosis. Although it can affect any artery bed, FMD is an idiopathic, non-inflammatory, and non-atherosclerotic illness that frequently affects the renal and carotid arteries. Young adults who have FMD may also experience stroke, which is how it typically manifests as renovascular hypertension.[1] Depending on the artery areas involved, FMD's clinical manifestations vary, which frequently makes diagnosis difficult. In this case report, a previously healthy and fit 37-year-old female presents with an extremely unique FMD presentation that has never been documented.[2] Patient had bilateral renal infarction, sequential vertebral artery dissections, mesenteric ischaemia, and required ongoing renal replacement therapy.

The case emphasises the significance of early FMD consideration, particularly when characteristics (such as hypertension) are incongruent with more prevalent diagnosis causing flank pain (such as pyelonephritis).

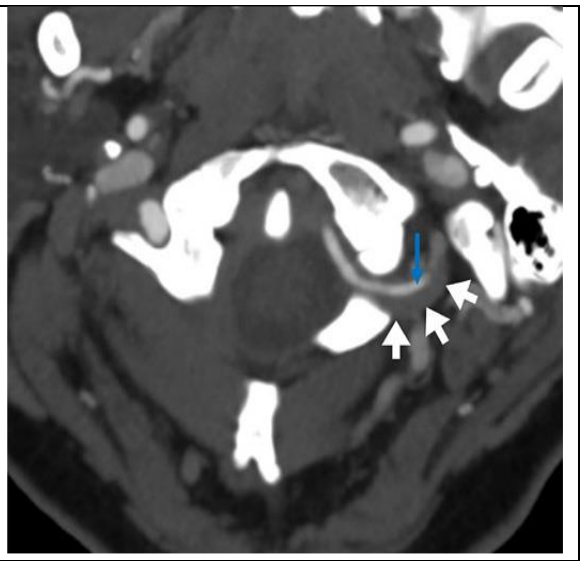
Case Presentation:

A 37-year-old female with a prescription of combined oral contraceptive pill arrived with sudden onset severe left sided flank pain after experiencing a similar, self-limiting right sided episode one week earlier. She had high blood pressure (180/90 mm Hg) and was apyrexic. Capillary refill time and pulse quality were both satisfactory. Both renal angles of the abdomen could be palpated as being painful. ECG was normal. Only the presence of protein was detected in the urine, which was confirmed by subsequent testing. Serum creatinine was 155 mmol/L, indicating acute renal damage. White cell count was 9.9 109/L and C-reactive protein (CRP) was 21 mg/L. At 850 iu/L, lactate dehydrogenase levels were higher.A computed tomography (CT) scan revealed renal asymmetry with an enlarged left kidney but no calculi. To treat infection, and more specifically pyelonephritis, intravenous pivmecillin/tazobactam was started. Oral amlodipine was also given to treat hypertension. The patient experienced fevers during the following days, and the CRP increased to 326 mg/L. When her serum creatinine increased to 491 mol/L, she developed oligoanuria. Doppler ultrasonography of the kidneys showed adequate cortical perfusion on both sides. After experiencing left-sided neck pain consistent with carotidynia on day 4, the patient started having tonic-clonic seizures. Left

vertebral artery dissection, right vertebral artery abnormal appearances, internal carotid artery, and a minor acute cortical infarct in the right occipital lobe were all detected by cerebral CT angiography. Five days following the non-contrast CT, a renal CT angiography revealed two 90% stenoses of the right renal artery and several stenoses on the left that were up to 70%. Extensive branched vessel stenoses were visible in both kidneys. In comparison to the left kidney's length of 12.9 cm, the right kidney's length was 9.8 cm (9.5 cm on the initial CT) (12.3 cm on first CT). Both kidneys' minor interval enlargement is probably the result of oedematous change. Acute infarcts were thought to be indicated by wedge-shaped opacities in the left kidney. A femoral venous catheter was used to start acute hemodilysis. The extent of the parenchymal infarction led to the conclusion that the risks of doing an angioplasty on the left renal artery outweighed any possible benefits. Prednisolone was given orally following 500 mg of methylprednisolone had been given intravenously for five days. Following a CT aortogram and fluorodeoxyglucose positron emission tomography, this was tapered and stopped even though the former showed signs of ischaemia in the ascending colon but neither indicated evidence of medium- or large-vessel vasculitis. Low molecular weight heparin anticoagulation was started. A right vertebral artery dissection was discovered on CT angiography three weeks after the patient's first admission, along with further carotidynia. Warfarin was then used as a anticoagulant, and then clopidogrel. Excellent blood pressure management was established on 5 mg of ramipril daily after the start of peritoneal dialysis. One year after initial presentation, the patient is still doing well on peritoneal dialysis and is under consideration for a kidney transplant.



Renal angiogram of the right renal artery showing multiple short stenosis (white arrows) in addition to the right kidney which shows globally poor enhancement.



Thick-walled dissected left vertebral artery. The contrast-filled stenosed lumen can be seen (blue arrow) with the outer wall of the thickened artery marked with short white arrows.

Discussion:

Researchers describe a remarkably uncommon case of FMD in which the patient simultaneously experienced cerebral involvement and bilateral renal infarction, necessitating renal replacement treatment. Even though 75–80% of FMD patients have renal disease, infarction is uncommon, occurring in just 0.9% of cases. Only a few case reports have mentioned bilateral renal infarction.[2] 469 FMD patients were imaged as part of the ARCADIA investigation, and 66.3% of those patients had multi-vessel FMD. Patients with bilateral renal involvement but without infarction had higher rates of cerebrovascular illness.[3]

Conclusion:

Researchers describe a remarkably uncommon instance of FMD in which the patient simultaneously experienced cerebral involvement and bilateral renal infarction, necessitating renal replacement treatment. The instance emphasises the significance of early FMD consideration, particularly when characteristics (such as hypertension) are incongruent with more prevalent diagnosis causing flank pain (such as pyelonephritis). Head-to-toe cross-sectional imaging should be a primary concern early on, and inflammatory disorders should be thoroughly ruled out due to the potential involvement of many arterial beds and the inherent limitations of certain imaging techniques.

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