



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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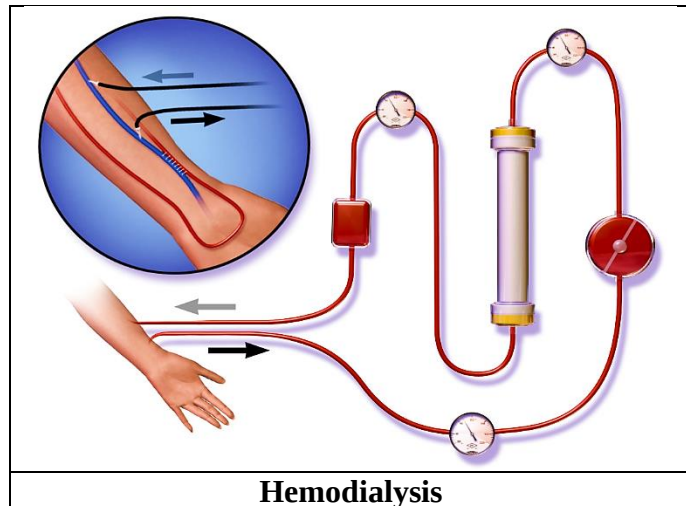
Best Regards,

Medical Team, Micro Labs Ltd



1. Association between the blood endostatin levels and cardiovascular event risk in hemodialysis patients with end-stage renal disease

Introduction: Cardiovascular disease (CVD) is the leading cause of death in end-stage renal disease (ESRD) patients on hemodialysis (HD).¹ Due to the repeated cardiac traumas that HD patients endure, heart dysfunction, structural alterations, and remodeling are brought on by these unfavourable processes, and these are major contributors to the high rates of CV morbidity and mortality.² Numerous studies have proposed biomarkers that may help anticipate the occurrence of CV events in these individuals, and numerous continuing studies have found biomarkers that may facilitate the prediction of the development of CVD. Notably, Endostatin, a carboxyl-terminal fragment of type XVIII collagen is present in the bloodstream, and in several cardiovascular pathologic situations, it has been proposed that circulating serum endostatin levels serve as a measure of extracellular matrix degradation. Patients undergoing HD with ESRD are susceptible to atherosclerosis injury due to ongoing exposure to inflammation, oxidative stress, and endothelial damage. It can be anticipated that endostatin may play a predictive role in the development of vascular calcification and CV events in patients with ESRD on HD, given its function and relationship with vascular calcification. Although few studies have examined the relationship between them, it is evident that confirmation of the therapeutic importance of endostatin in these patients is necessary.¹ This study was conducted to assess circulating endostatin levels and analyze their relationship with CV events in patients with ESRD receiving HD.



Methods: In this prospective study, a total of 372 individuals with ESRD who were older than 18 and receiving HD three times a week for more than three months were included. At the baseline and follow-up visits, prospective data, laboratory results, and blood samples were obtained from patients with end-stage renal disease (ESRD) on HD. Patient outcomes, including cardiovascular events, comorbidities, and mortality, were examined. Based on plasma endostatin levels, the study population was split into three groups: group 1, <146 ng/mL; group 2, 146–196 ng/mL; and group 3, ≥196 ng/mL. Abdominal aortic vascular calcification scores and circulating MBD indicators were examined in relation to baseline plasma endostatin levels. The primary outcome was to analyze the composite of CV and cardiac events.



Results: Multivariate analysis showed plasma levels of patients in endostatin group 3 were substantially correlated with low-density lipoprotein cholesterol levels and pre-dialysis systolic blood pressure. Endostatin levels, however, did not show any relationship to vascular calcification scores or circulating MBD indicators. Patients in endostatin group 3 had a considerably higher cumulative event rate for the composite of CV events (Figure 1). Additionally, an elevated cumulative rate of cardiac events was linked to endostatin group 3 (Figure 2). After controlling for several covariates, endostatin group 3 was linked to a 4.37-fold risk for composite CV events and a 3.88-fold risk for cardiac events in multivariate Cox regression analysis.

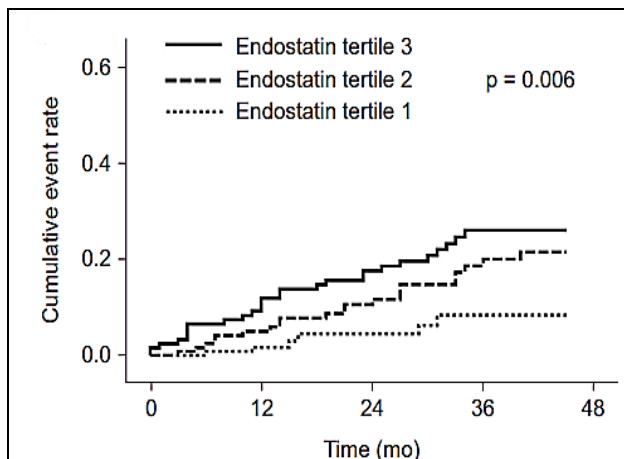


Figure 1. Cumulative rates of cardiovascular events based on endostatin levels.

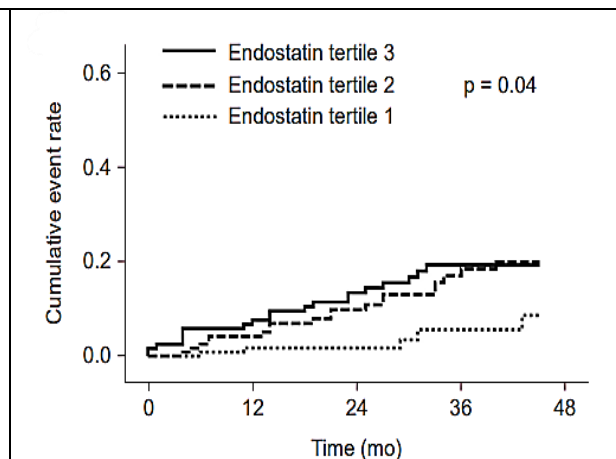


Figure 2. Cumulative rates of cardiac events based on endostatin levels.

Discussion: Higher levels of circulating endostatin were shown to be independently correlated with atherosclerotic risk variables in this investigation, but not with vascular calcification or MBD indicators. In patients undergoing HD, higher levels of circulating endostatin were linked to an increased risk of composite CV events.¹ Ruge T et al. found that in people with stable coronary heart disease, elevated serum endostatin levels may be linked to cardiovascular events. Higher endostatin levels were more strongly correlated with both cardiovascular and overall mortality.³

Conclusion: The current investigation found that circulating endostatin levels were substantially associated with LDL cholesterol levels and pre-dialysis systolic blood pressure, but not with MBD indicators or vascular calcification. In patients with ESRD on HD, higher levels of circulating endostatin were linked to an increased risk of composite CV and cardiac events.

In patients with end-stage renal disease (ESRD) undergoing hemodialysis, endostatin is a biomarker that can be used to predict cardiovascular events.



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2. Evaluation of CKD-associated pruritus and adverse clinical outcomes in maintenance dialysis patients

Introduction: Pruritus, a severe itching sensation, is one of the most debilitating uremic symptoms encountered by patients with advanced chronic kidney disease (CKD), and it is regarded as a significant research priority for patients on or approaching dialysis.¹ Extensive studies have been conducted in the hemodialysis (HD) population on chronic kidney disease-associated pruritus (CKD-aP), or generalized itching due to CKD, and its connections with clinical and patient-reported outcomes (PROs).² CKD-aP is not only uncomfortable but also common. Across all CKD stages, 24% of patients had moderate-to-extreme pruritus, with 10%–13% of cases having severe-to-extreme pruritus.³ Moreover, nephrologists and other medical professionals undervalue its severity and frequency, giving other medical conditions priority over pruritus. Previous observational studies' findings indicated a relationship between pruritus and depressive symptoms, infections, low life expectancy, insomnia, and death. More dynamic evaluations, which include incident cases, would allow for a more accurate quantification of the condition's burden and associated risks.¹ This study aimed to estimate the prevalence of pruritus and its adverse health effects in maintenance dialysis patients.

Methods: In this observational study, 3281 maintenance dialysis patients were included. Two complimentary analyses are included in this study. Clinically recognizable pruritus was the study outcome in the first analysis, which also evaluated its prevalence, incidence, and key baseline factors. In the second investigation, a variety of unfavourable health outcomes were examined in relation to pruritus, which was regarded as a time-varying exposure. All-cause death, severe infection-related hospitalizations (comprising endocarditis, peritoneal dialysis-related peritonitis, catheter-related sepsis from *Staphylococcus* spp., or skin infection), and incident diagnoses of anxiety/depression and sleep disorders were among the unfavourable health outcomes. Factors linked to new-onset and prevalent pruritus are analyzed using cause-specific hazards models and multivariable logistic regression, respectively.

Results: In this study, 456 (14%) patients experienced pruritus at the time of enrollment. Pruritus was reported by 539 more patients (19%) with a median follow-up of 3.3 years. Pruritus was inversely correlated with older age, female sex, serum albumin level, C-reactive protein, serum calcium, and serum phosphorus levels. Adjusted hazard ratios, or aHRs, for sleep disorders (1.96), anxiety/depression (1.56), and hospitalization for severe infections (1.36) were higher in pruritus-associated patients than in non-prickly patients for the latter, which was associated with an increased risk of sepsis and peritonitis related to peritoneal



dialysis (Table 1). The development of pruritus did not significantly correlate with death from all causes.

Table 1. Pruritus and adverse health outcomes	
Outcomes	adjusted hazard ratios (95%CI)
All-cause mortality	0.94 (0.84-1.05)
Hospitalized for severe infections	1.36 (1.18-1.57)
Anxiety/depression	1.56 (1.23-1.98)
Sleep disorders	1.96 (1.60-2.39)

Discussion: Patients experiencing pruritus in this study had greater rates of anxiety/depression, sleep disturbances, and hospitalization for serious infections (the latter due to an increased risk of sepsis and peritoneal dialysis-related peritonitis).¹ According to Sukul N et al., the prevalence of depression, restless sleep, and feeling exhausted rose over the study period among patients with incident pruritus while decreasing among patients with resolved pruritus. The persistent and absent groups showed very little variation in PROs over time. The adjusted HRs for all-cause mortality, all-cause hospitalization, and cardiovascular events were 1.29, 1.17, and 1.48 for patients with persistent CKD-aP, respectively, compared to individuals without CKD-aP.²

Conclusion: This study concluded that patients undergoing dialysis experience clinically recognized pruritus, identifies populations at risk of pruritus development, and demonstrated that patients with pruritus are at a significant risk of adverse health outcomes. Management strategies for pruritus include dialysis optimization, CKD-associated mineral and bone disease treatment, extemporaneous compounded topical preparations, systemic pharmacological treatments, ultraviolet therapy, and the use of difelikefalin, a recently developed selective agonist of kappa opioid receptors, in hemodialysis.

Individualized clinical therapy could greatly enhance patients' quality of life and possibly even improve their health outcomes by preventing and treating this undesirable uremic symptom.

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3. Clinical comparison of single-use and reusable digital flexible ureteroscopy for the treatment of lower pole stones

Introduction: The European Association of Urology Urolithiasis Guidelines state that flexible ureteroscopy is the preferred treatment for renal stones smaller than 20 mm and may be used as a second-line therapy for renal stones larger than 20 mm. Both renal and ureter stones can be treated with the flexible ureteroscopy (FURS), which has a broad range of suitable stone sizes.¹ The FURS offered benefits that required additional research since it provided access to the renal cavities. The main reason fiber-optic FURS were created was to address worries that the urothelium would be harmed during upper ureter access by rigid URS (rURS). Flexible ureteroscopes, however, have a high rate of lens damage during FURS operations, and it has been noted that these instruments require replacement after 6–21 procedures, which restricts their clinical use and raises maintenance expenses. It has been demonstrated that the deflection performance of single-use FURS was better than that of reusable digital or fiber FURS, and the deflection can reach 297° even with the insertion of a 275 µm fiber. Furthermore, the use of single-use FURS eliminates the possibility of equipment damage, which outweighs the unethical practice of repeatedly treating lower pole stones with reusable FURS.² The purpose of this study was to assess the safety and therapeutic effectiveness of reusable and single-use digital flexible ureteroscopy (FURS) in the treatment of lower pole stones.

Methods: In this retrospective case-control study, 135 patients underwent reusable flexible ureteroscopy (FURS), and 78 patients underwent single-use digital FURS. Patients' medical records were examined to collect information; an unenhanced CT scan was performed to confirm the presence of a unilateral, single lower pole stone with a maximum diameter of ≤ 2.0 cm; there was no history of ureteral stricture or surgery; the heart, lung, liver, and kidney were all functioning normally; and there was no urinary tract infection or infection under preoperative control. Preoperative laboratory testing included liver and kidney function, coagulation function, urine and blood analysis, urine bacterial culture, and other standard procedures for all patients. The density and diameter of the calculi as well as IPA, IL, and IW were determined from the imaging results of an unenhanced urinary CT scan and an intravenous pyelography (IVP) test. Demographic, clinical characteristics, anatomical parameters of the lower calyx, and perioperative signs were compared between the two groups.

Results: Mini-percutaneous nephrolithotomy (mini-PCNL) was performed on thirty-six patients in the subgroup with an infundibuloureter angle (IPA) less than 45°. Of them, 25 patients underwent reusable FURS, and 11 patients underwent single-use FURS. The two FURS groups' clinical and demographic characteristics were similar. However, in the IPA <45° subgroup, single-use FURS was superior. The working fiber lengths in the single-use FURS group measured 1.75 ± 0.47 mm and the reusable FURS group 3.20 ± 0.68 mm, respectively. In comparison to the single-use FURS (8/78, 10.3%), the reusable FURS (31/135, 23.0%) used a stone basket far more frequently. The single-use FURS group outperformed the reusable FURS group in terms of stone-free rate (SFR) and shorter operation times ($P < 0.05$) (Table 1). Between the two groups, there was no statistically significant difference in the intraoperative transfer of miniPCNL or postoperative problems ($P > 0.05$).



Table 1. Comparison of the perioperative indicators for the groups using reusable and single-use FURS

Variables	SU-FURS (n=78)	R-FRUS (n= 135)
Transfer of Mini-PCNL	14.1%	18.5%
Use of stone basket	10.3%	23.0%
Operation time (min)	51.27±13.80	69.50±16.76
Postoperative hospital stays (days)	2.86±1.50	3.14±1.37
The length of working fibre (mm)	1.75±0.47	3.20±0.68
Stone-free rate	88.5%	77.0%
R-FURS Reusable flexible ureteroscopy, SU-FURS Single-use flexible ureteroscopy,		

Discussion: This study demonstrated that the two FURS groups' clinical and demographic characteristics were similar. The single-use FURS group outperformed the reusable FURS group in terms of stone-free rate (SFR) and operating time.² In the Kam J et al., the URF-V2 group outperformed the single-use scopes in terms of visibility and maneuverability when they were compared to reusable digital flexible ureteroscopy. However, no variations were noted in scope failure, complication rates, relook flexible ureteroscope rates, or operating time.³ According to Li Y et al., the visibility and mobility profiles of single-use digital flexible ureteroscopes were comparable to those of reusable digital flexible ureteroscopes. Additionally, there was evidence that single-use flexible ureteroscopes outperform reusable FURS in terms of clinical results, even attaining a greater SFR.⁴

Conclusion: The current study concluded that reusable and single-use FURS serve as alternate techniques for removing lower pole stones (2 cm or less). Single-use FURS offers a high stone-free rate, a reduced operating time, and a high success rate in lithotripsy.

Single-use flexible ureteroscopy (FURS) not only offers a high success rate for lithotripsy, a fast operation time, and a high stone clearance rate, but it should also be preferred when the anatomy of the lower calyx is challenging.

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4. Case report of a patient who had successful percutaneous nephrolithotomy after receiving an ipsilateral dual kidney transplant

Introduction: Complex kidney stones can be managed using a less invasive surgery called percutaneous nephrolithotomy (PCNL). There are particular issues and obstacles when applying it to renal calculi, particularly in the context of donor renal allografts. End-stage renal disease (ESRD) can now be effectively treated with dual kidney transplantation (DKT), which entails the transplantation of two allograft kidneys into a single recipient. Long-term investigation showed that DKT has better graft viability than single kidney transplantation, in addition to increasing nephron mass.¹ Moreover, DKT can shorten the waiting period for kidney transplant recipients. DKT was prone to the same difficulties and complications as single kidney transplantation, such as transplant lithiasis. Renal allografts can usually be treated with the same procedures used for stone burden in native kidneys, such as pyelolithotomy, ureteroscopy, extracorporeal shockwave lithotripsy (ESWL), and percutaneous nephrolithotomy (PCNL).² PCNL has demonstrated a statistically significant stone-free rate (SFR) at three months when compared to alternative methods. PCNL is a minimally invasive method that can handle a high stone burden in kidney transplant recipients and navigate their unique anatomical features.¹ This case highlighted the use of PCNL to treat urolithiasis in dual transplant kidneys, a unique problem not widely documented in the literature.

Case Presentation: A 43-year-old male patient admitted to the hospital with a history of end-stage renal disease underwent a twin-dead donor kidney transplant, wherein both kidneys were inserted into the right iliac fossa. An intraoperative peritoneal incision was made by the kidney transplant surgeon to provide sufficient room for the implantation of both kidneys. After the procedure, the patient's superomedially placed transplant kidney in the right iliac fossa was discovered to have a sizable staghorn stone (Figure 1). Due to a significant stone burden, plans were made for percutaneous nephrolithotomy. Initially, a peritoneal incision was made at the time of kidney transplantation, and bowel overlaid it. This made the attempt to obtain access by placing a needle under direct ultrasound view unsuccessful. In order to facilitate the kidney transplant procedure, interventional radiology was consulted. The procedure was completed effectively and did not result in any complications or damage to the surrounding colon. Interventional radiology then successfully implanted a nephroureteral stent (Figure 2).



Figure 1. Computed tomography (CT) scan of the transplanted kidney revealed 2.6 cm of staghorn calculi.



The patient was brought to the PCNL room and laid down in a supine posture on the table after access had been achieved in a safe and sufficient manner. In order to manage his significant stone burden, the nephroureteral stent was changed out for a wire, and the tract was widened to allow access to the transplant kidney's top pole. The nephroscope was then inserted after the PCNL sheath was advanced over the balloon dilatation to obtain access. A massive staghorn stone, measuring about 2.6 cm in diameter, was found within the renal pelvis during pyeloscopy (Figure 3). Once the entire stone burden was eliminated, a percutaneous nephrolithotomy was carried out using a Lithoclast device. Following routine closure of the patient's epidermis and subcutaneous tissues, a 5 French by 12 cm double-J ureteral stent was implanted at the end of the surgical procedure to facilitate the decompression of the collecting system. At the two-month follow-up, renal ultrasonography revealed no residual stone burden, indicating that the patient had recovered satisfactorily from the surgery. Renal function remained stable, with creatinine at 1.0.

Discussion: Large stones can be treated with a single surgical procedure using percutaneous nephrolithotomy (PCNL), which is still a safe and efficient treatment option for de novo allograft urolithiasis. A satisfactory stone-free rate (SFR) was achieved while minimizing the risk of minor complications.³ To treat graft lithiasis, PCNL was an useful and effective option that has few perioperative problems and has good stone clearance.⁴



Figure 2. Interventional Radiology inserts the nephroureteral stent.

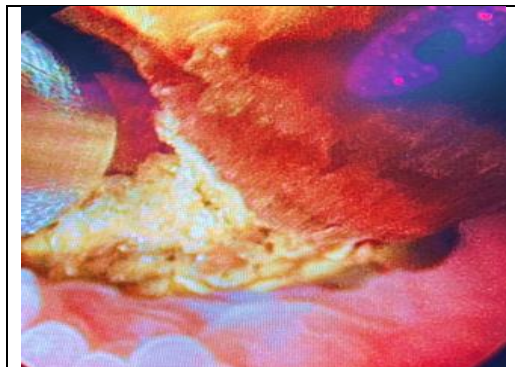


Figure 3: A big staghorn stone inside the renal pelvis revealed by pyeloscopy.

Conclusion: Percutaneous nephrolithotomy (PCNL) was a safe approach for treating significant stone loads in individuals undergoing single or dual kidney transplants. When standard modalities for access fail, interventional radiology can help provide safe and appropriate access to transplant kidneys in difficult patients.

For individuals who have had one or more kidney transplants, percutaneous nephrolithotomy is a safe choice for treating significant stone loads.



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