

## NU Rounds

Vol 3 | Issue 34 | 2022

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

## 1. Atypical hemolytic uremic syndrome and malignant hypertension patients' clinical features and outcomes

### Introduction:

The uncommon thrombotic microangiopathy (TMA) condition known as atypical hemolytic uremic syndrome (aHUS) is frequently brought on by alternative complement dysregulation.<sup>1</sup> Hemolytic anemia, thrombocytopenia, and renal failure brought on by platelet thrombi in the microcirculation of the kidney and other organs are the characteristics of hemolytic-uremic syndrome (HUS).<sup>2</sup> Malignant hypertension (MHT), which can also result in TMA, is a complication that can affect patients with aHUS.<sup>1</sup> This study evaluated the clinical characteristics and outcomes of a patient population with malignant hypertension and an uncommon hemolytic uremic syndrome.

The results of this study support the high severity and poor prognosis of untreated atypical hemolytic uremic syndrome (aHUS), and they also imply that eculizumab is useful for treating aHUS ± malignant hypertension.

### Methods:

In order to better understand the potential connection between aHUS and malignant hypertension, this analysis of the Global aHUS Registry (NCT01522183) examined demographics and clinical traits in eculizumab-treated and untreated patients with aHUS, with (n = 71) and without (n = 1026) malignant hypertension.

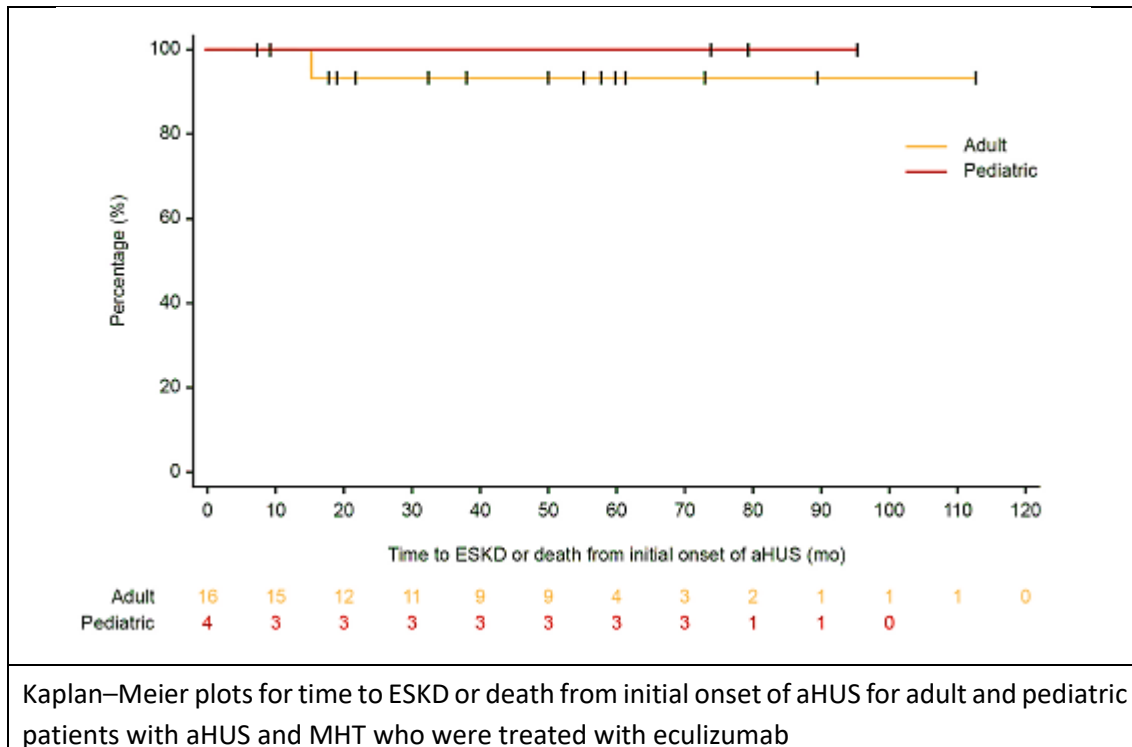
### Results:

Despite similar demographics, patients with aHUS and malignant hypertension required greater renal replacement therapy, including kidney transplantation (47% vs. 32%), and had more pathogenic variations and anti-complement factor H antibodies (56% vs. 37%) than patients without malignant hypertension. Patients with malignant hypertension who were not being treated had a higher prevalence of variants and antibodies (65%) and required more kidney transplants (65% vs. none). A multivariate analysis revealed that treated individuals with aHUS + malignant hypertension had a significantly lower risk of end-stage renal disease or mortality compared to untreated patients, regardless of the presence of malignant hypertension (adjusted HR (95% CI), 0.11 [0.01-0.87], P = 0.036).

### Discussion:

In this study, data from the biggest aHUS patient comparison of those with and without concomitant MHT to date are presented. Regardless of treatment status, approximately two thirds of study participants who presented with comorbid aHUS and MHT symptoms reported that MHT symptoms also occurred at the same time as aHUS symptoms. Additionally, patients with aHUS and MHT were more likely to have pathogenic genetic variants or anti-CFH antibodies than patients with aHUS alone. Even though the use of eculizumab as a treatment is not directly correlated with the frequency of pathogenic genetic variants or anti-CFH antibodies, the results indicate that many of the patients listed as untreated may have developed

ESKD prior to the introduction of eculizumab or may not have been initially recognised as having aHUS before developing ESKD.<sup>1</sup> In fact, aHUS diagnosis frequently happens late in the disease's progression, after a TMA recurrence, the need for long-term dialysis, or a kidney transplant.<sup>3</sup>



## Conclusion:

These findings support the high severity and poor prognosis of untreated aHUS and imply that eculizumab is helpful for those who have the malignant hypertension associated with aHUS. Additionally, this findings suggest the consideration of aHUS in patients with malignant hypertension and TMA and emphasise the significance of accurate, prompt diagnosis and therapy in these populations.

## References:

1. Halimi et al. Clinical characteristics and outcomes of a patient population with atypical hemolytic uremic syndrome and malignant hypertension: analysis from the Global aHUS registry. J Nephrol. 2022 Sep 24.
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## 2. Deep hypothermic circulatory arrest (DHCA) for the treatment of post-operative kidney dysfunction after aortic arch surgery.

### Introduction:

For brain protection during aortic arch surgeries, deep hypothermic circulatory arrest (DHCA) was developed.<sup>1</sup> Patients with aortic arch aneurysm and acute or chronic type A aortic dissection can have their proximal and whole aortic arch corrected with hypothermic circulatory arrest.<sup>2</sup> The impact of deep hypothermic circulatory arrest (DHCA) on simultaneous renal ischemia is still debatable.<sup>1</sup> Few research have used the criteria to evaluate the associations between DHCA and AKI, and the majority of earlier investigations have not used urine volume as a marker. To demonstrate the effects of DHCA on kidney function, this study used the Kidney Disease: Improving Global Outcomes (KDIGO) criteria and examined both serum Cr and urine volume levels.

The deep hypothermic circulatory arrest is closely related to AKI up to 48 hrs post-operative and death during the 3 months following surgery.

### Methods:

This was a retrospective observational study. This study included 63 thoracic aortic surgery patients who received DHCA, and 24 heart surgery patients who did not receive DHCA. Each patient's mean age, preoperative serum creatinine (Cr) level, preoperative estimated glomerular filtration rate (eGFR), peak serum Cr level up to 48 hours post-operatively, rate of Cr elevation compared to preoperative serum Cr, rate of urine volume up to 48 hours post-operatively, and AKI staging using the KDIGO criteria were all estimated. The clinical post-operative outcomes for 3 months and the 3-month post-operative death rate were evaluated. Between patients with and without DHCA, mean values showing renal function or the distribution of the AKI stages were compared. To compare the values for each group's kidney function, the distribution of AKI stages, and mortality, patients with DHCA were further split up based on how long they had been in ischemia.

### Results:

In comparison to patients without DHCA, the measures indicating AKI in the former group were much worse. Patients who had experienced an ischemia state for longer than 40 minutes showed significantly greater peak serum Cr, elevated rate of serum Cr, and decreased urine output up to 48 hours after surgery as compared to those who had not received DHCA. The amount of ischemia and the distribution of AKI stages were correlated. The patients who had DHCA had a considerably greater 3-month post-operative mortality rate than those who did not have DHCA.

### Discussion:

It has been proposed that the long-term effects of DHCA are more closely related to mortality than to late renal function. The majority of patients who survive recover from AKI. Patients who have suffered from severe AKI often progress to CKD. Patients who had heart surgery reported experiencing similar outcomes.<sup>3</sup> Patients in this group who have experienced post-operative AKI are more likely to experience a late myocardial infarction as a post-operative risk. <sup>1</sup>The statistical result is found to be influenced by the post-operative serum Cr level (s). As a result, death and post-operative cardiac events are correlated with AKI severity. A significant CKD risk factor has been found to be AKI. <sup>4</sup>The findings of the current study indicate that while DHCA does not increase the chance of developing CKD, it may increase mortality rates in perioperative patients with severe AKI.

| AKI Stage (KDIGO) | 0          | 1         | 2         | 3         |
|-------------------|------------|-----------|-----------|-----------|
| DHCA(+) (n=22)    | 7 (31.8%)  | 8 (36.4%) | 3 (13.6%) | 4 (18.2%) |
| DHCA(-) (n=22)    | 15 (68.2%) | 4 (18.2%) | 3 (13.6%) | 0 (0%)    |

AKI Stage (KDIGO) Among the Propensity-Matched Patients: The Distribution of AKI Stage (KDIGO) Correlated with DHCA

## Conclusion:

This study concludes that Deep hypothermic circulatory arrest (DCHA) is closely connected to acute kidney injury (AKI) up to 48 hours post-operatively and death within three months of surgery.

## References:

1. Higo M, Shimizu Y, Wakabayashi K, Nakano T, Tomino Y, Suzuki Y. Post-Operative Kidney Function Using Deep Hypothermic Circulatory Arrest (DHCA) in Aortic Arch Operation. *Int J Nephrol Renovasc Dis.* 2022 Sep 26;15:239-252.
2. Samanidis et al. Does deep hypothermic circulatory arrest with versus without retrograde cerebral perfusion affect the outcomes after proximal aortic arch aneurysm and acute type A aortic dissection repair? Different pathologies and cerebral protection techniques with similar results. *J Card Surg.* 2022 Oct;37(10):3287-3289.
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4. He L, Wei Q, Liu J, et al. AKI on CKD: heightened injury, suppressed repair, and the underlying mechanisms. *Kidney Int.* 2017;92:1071–1083.

## 3. A comparison of up-front Prostatectomy versus neoadjuvant novel hormonal therapy followed by prostatectomy for high-risk prostate cancer

### Introduction:

In order to enhance outcomes for men with high-risk prostate cancer (HRPC), neoadjuvant therapy has been suggested.<sup>1</sup> For intermediate and higher-grade illness, hormone therapy has been demonstrated to increase survival when combined with radiation therapy but not with radical prostatectomy.<sup>2</sup> In patients with high-risk prostate cancer, this study compared the effects of neoadjuvant therapy with a novel hormonal agent (NHA) before radical prostatectomy (neo-RP) with upfront radical prostatectomy (RP).

Neoadjuvant therapy with a novel hormonal agent prior to upfront radical prostatectomy was associated with longer time to biochemical recurrence (BCR) and superior metastasis-free survival (MFS) compared to up-front RP in men with high-risk prostate cancer (HRPC).

### Methods:

The neo-RP group was made up of HRPC patients who had undergone three trials of neoadjuvant NHA and RP treatment (112). The RP group (259) included a cohort of HRPC patients who underwent RP at the institution without receiving neoadjuvant therapy and who met the primary eligibility requirements for the neoadjuvant trials (i.e., 3 positive biopsy cores and Gleason 4D3[7]). When estimating treatment effects, inverse probability of treatment weighting (IPTW) was employed to reduce the likelihood of confounding variables. Time to biochemical recurrence (BCR) and metastasis-free survival (MFS) were the main results.

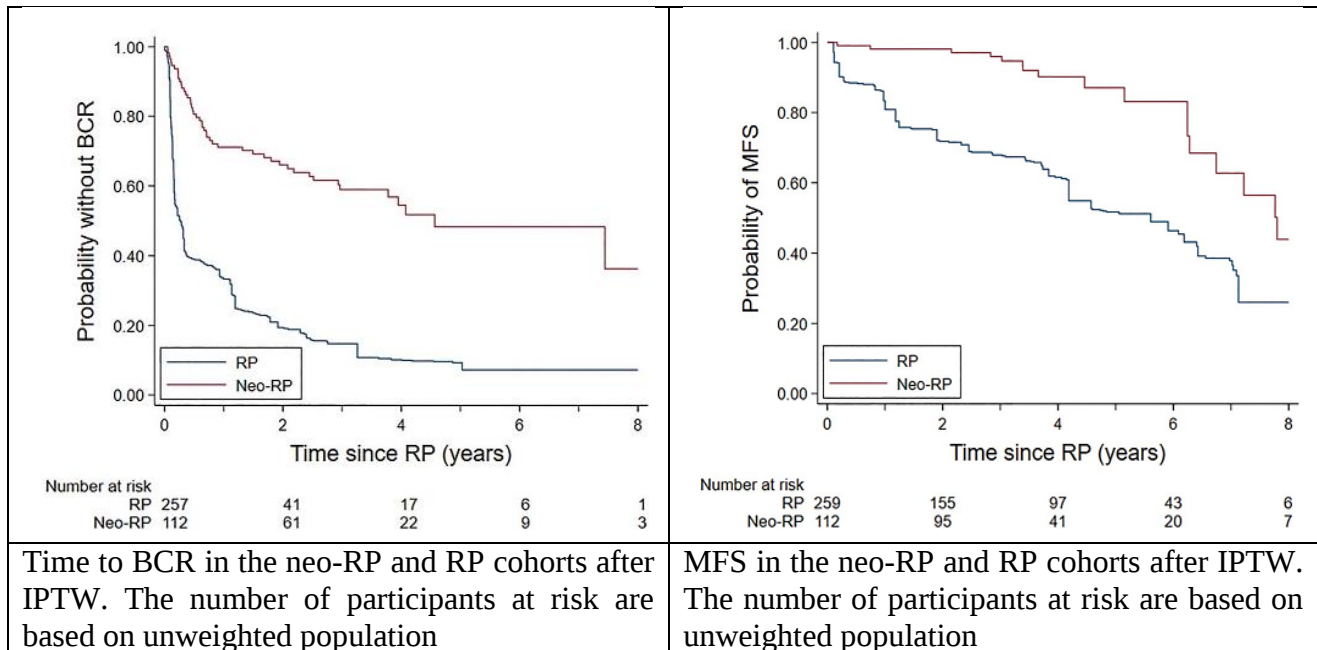
### Results:

The neo-RP cohort had greater incidences of cT3 disease (22% vs 5%), Gleason 9-10 malignancy (46% vs 24%), and PSA 20 ng/ml (14% vs 7%) before IPTW; after IPTW, the 2 cohorts were equal. Overall, the neo-RP group took noticeably longer than the RP cohort to reach BCR (HR [0.25 [95% CI 0.18-0.37]]) and MFS (HR [0.26 [0.15-0.46]]) following IPTW. The neo-RP cohort had lower rates of adjuvant (7% vs. 24%) and salvage therapy (34% vs. 46%) treatment.

### Discussion:

Prior to surgery, neoadjuvant therapy has a well-established function in the treatment of a number of solid tumours, including breast and urothelial cancer, where a positive pathological response at surgery has also been demonstrated to carry great predictive usefulness. However, the usefulness of neoadjuvant therapy before RP for HRPC is debatable because no randomised research has, to yet, demonstrated a disease-free or OS benefit with neoadjuvant therapy compared to upfront RP.<sup>1</sup> This is the first trial to compare the outcomes of upfront RP with neoadjuvant therapy before RP, and these findings point to a considerable benefit for

unselected patients with HRPC when the latter approach is used.<sup>1</sup> With multiple current studies investigating neoadjuvant therapy, including the phase 3 PROTEUS trial, these findings add significantly to the body of knowledge on neoadjuvant therapy in HRPC and confirm the disease's ongoing interest in this therapy.<sup>3</sup>



## Conclusion:

In comparison to up-front RP, neoadjuvant therapy using an NHA before RP was associated with a longer time to BCR and better MFS in men with HRPC. Despite merely hypothesis-generating, these results point to the potential advantage of neoadjuvant therapy with an NHA in HRPC, a strategy that is presently being investigated in the phase 3 PROTEUS trial.

## References:

1. Ravi P et al. Neoadjuvant Novel Hormonal Therapy Followed by Prostatectomy versus Up-Front Prostatectomy for High-Risk Prostate Cancer: A Comparative Analysis. J Urol. 2022 Oct;208(4):838-845
2. Leslie SW, Soon-Sutton TL, Sajjad H, et al. Prostate Cancer. [Updated 2022 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan
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## 4. A case report of chronic urine ascites caused by the double-J ureteral stent's proximal migration into the peritoneal cavity

### Introduction:

Particularly in gynecologic, colorectal, and vascular procedures, iatrogenic ureteral injury can be a catastrophic adverse event necessitating intra-abdominal surgery and raises the possibility of readmission to the hospital.<sup>1</sup> ureteral injuries are uncommon. Iatrogenic injuries occur during open surgery, laparoscopic, or endoscopic procedures is the most frequent cause.<sup>2</sup> The distal end of the ureter is where most surgical ureter injuries occur. The best choice for this repair is a double-J (DJ) stent ureteroneocystostomy.<sup>1</sup> Here is a case where ureteral stent displacement caused chronic urinary ascites, which was successfully addressed with endoscopic intervention.

This is the first instance of a proximally migrated ureteric catheter causing malignant urine ascites that has been effectively treated by endoscopic intervention.

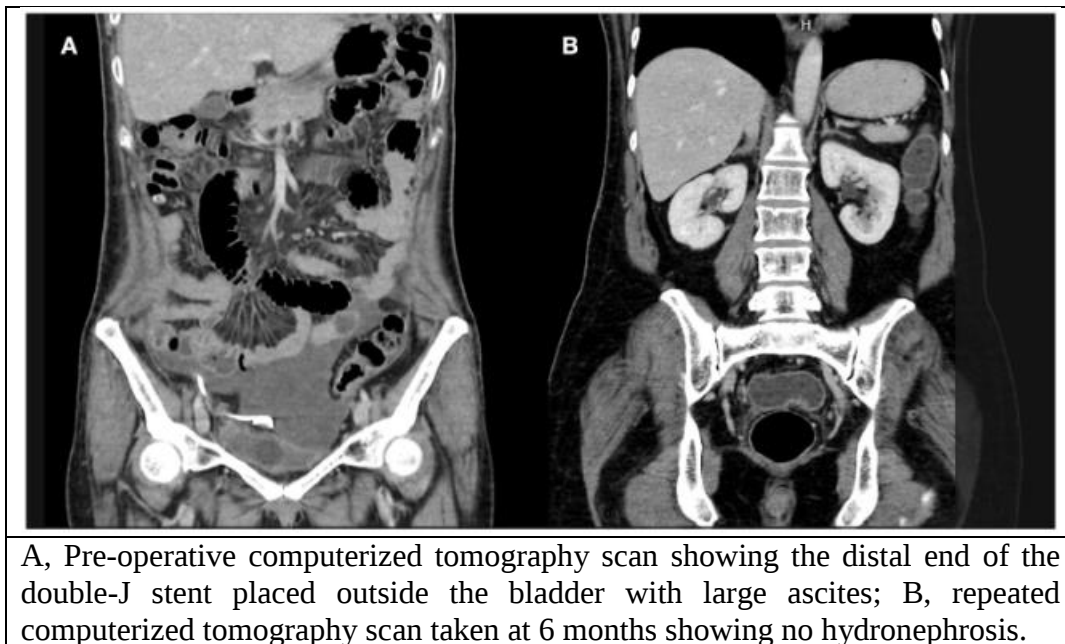
### Case Presentation:

A 50-year-old female patient with chronic weight loss and a large ascites was referred to the urology department. She had an open abdominal hysterectomy three months prior due to severe diffuse uterine adenomyosis and concomitant ureteral reimplantation following an accidental right distal ureter damage at another institution. The surgical surgery went smoothly overall, and recovery went smoothly in the first few days. However, she steadily deteriorated during a follow-up appointment with the primary surgeon due to unexplained weight loss, a persistent low-grade fever, and stomach discomfort; as a result, she needed a second medical opinion. The patient was found to be dehydrated, lethargic, and to have abdominal distension with varying dullness. Her body temperature (38.2 °C) was higher than normal but her hemodynamic values were otherwise normal. Blood tests also showed leukocytosis, with neutrophils at 84.6% and a leukocyte count of 13.2 10<sup>5</sup>/m. Her urine analysis found increased leukocytes and red cells, whereas her serum creatinine was only slightly higher (from 0.5 to 1.0 mg/dl). The distal point of the ureteric stent was found inside the peritoneal cavity and there was substantial ascites fluid, according to an abdominal computed tomography. The yield from abdominal paracentesis was 2.8 L of straw-colored fluid. The analysis of ascitic fluid found a high creatinine level of 5.76. These clinical findings suggested that there may be abdominal urine leakage. Consequently, doctors implanted a nephrostomy tube and gave the patient intravenous antibiotics (ampicillin plus gentamicin). Her clinical condition had improved two weeks later as a result of adequate diet. After considering several surgical possibilities, it was determined that endoscopic surgery should be carried out. The dorsal lithotomy position was applied to the patient. The placement of the stent and the bladder were both visualised by retrograde cystography. In order to properly examine for anomalous intra-vesical findings, rigid cystoscopy was used. Suspicious regions of the bladder mucosa were excised under direct vision and fluoroscopic guidance. A 20 W holmium laser with a 550 m core laser fibre was used for tissue cutting with a power of 1 J and a frequency of 10 Hz. The DJ stent's identified distal tip was brought into the intravesical space using grasper forceps. The patient's surgical

recovery went without issue. Three months after being discharged, the stent was removed cystoscopically. At six months, the renal scan and subsequent CT scan images showed no hydronephrosis, and kidney function was stable.

## Discussion:

It is still difficult to diagnose ureteral damage during surgery. Urinary tract problems must be promptly identified and corrected in order to achieve great surgical results and avoid late complications. Unrecognized injuries or a delay in diagnosis can result in extended morbidity, which can impede renal function, create fistulas, or even result in death.<sup>1</sup> Depending on the location of the stent retained, the presence of intraabdominal adhesions, and surgical expertise, the care of misplaced stents currently includes of open surgical procedures, interventional radiological techniques, and endourologic management.<sup>3</sup> In this instance, the lower portion of the stent was deeply linked to the bladder serosa, while the upper portion appeared to be in the correct renal pelvis location. Additionally, chronic urine irritation can result in highly inflammatory processes and the development of intra-abdominal adhesions, which can significantly impede open abdominal surgeries by making it impossible to reach the abdomen and distorting its structure. As a result, it was conceivable and practical to try endoscopic surgery safely. During the follow-up phase, outstanding imaging data allowed us to confirm this achievement.<sup>1</sup>



## Conclusion:

Urinary ascites is a crucial clinical condition to recognise since it can be detected and treated instantly. This is the first instance of a proximally migrated ureteric catheter causing malignant urine ascites, which was effectively treated with endoscopic intervention.

## Reference:

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