Abstract Highlights

The following selected highlights explore several fascinating abstracts that were presented at the 60th European Renal Association (ERA) Congress 2023. Topics covered include vascular access in haemodialysis, renal transplantation, acute kidney injury, IgA nephropathy, and cardiovascular risk in chronic kidney disease.

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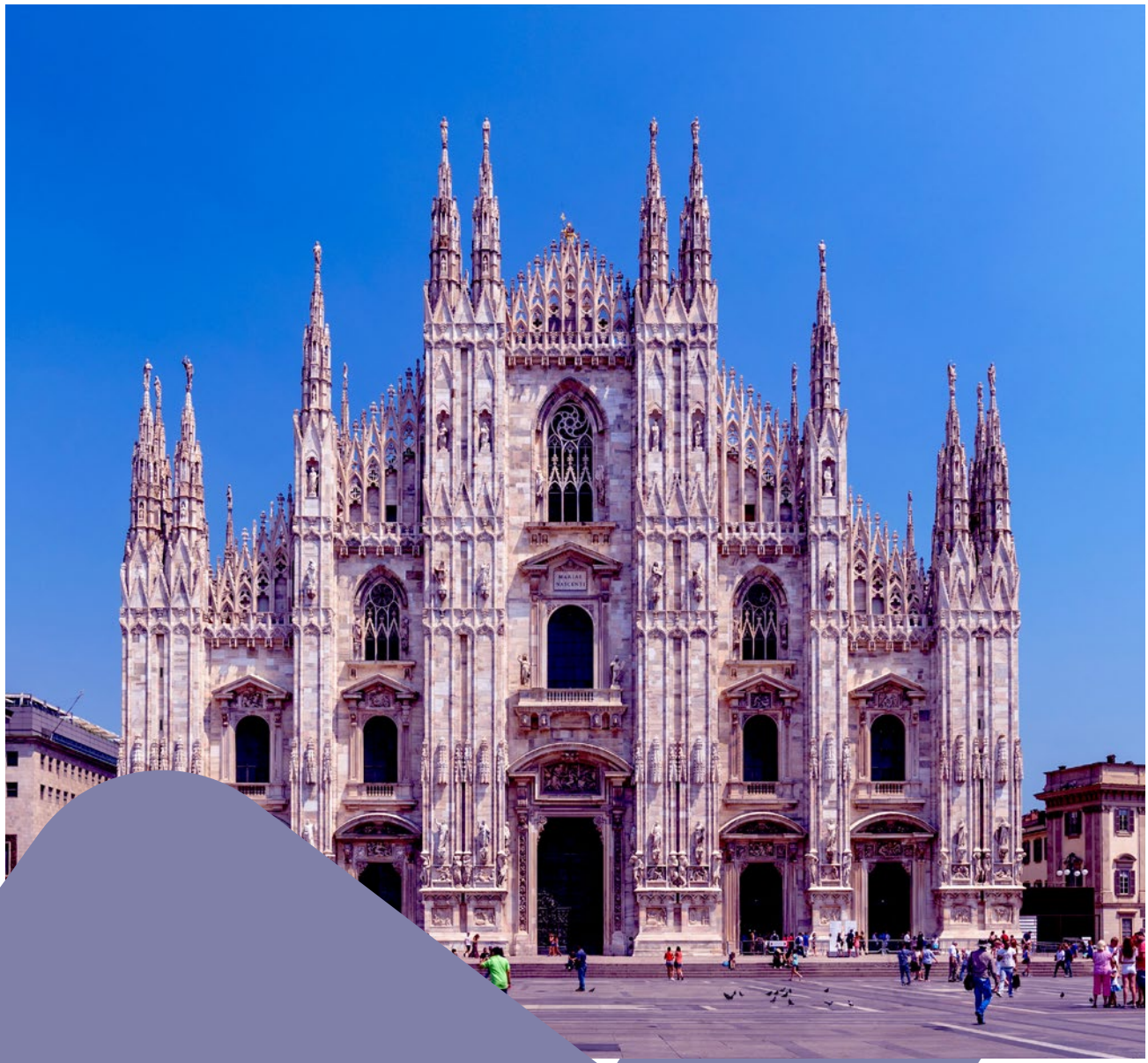


Autosomal Dominant Polycystic Kidney Disease: Identifying Early Disease Progression Risk Factors

RETROSPECTIVE analysis of longitudinal data from patients with autosomal dominant polycystic kidney disease (ADPKD) unveils early-onset hypertension (diagnosis at <18 years of age) as a risk factor for rapidly progressive disease.

The age at which patients with ADPKD reach kidney failure varies, with some patients progressing to renal failure rapidly, whilst others progress slowly. There is an unmet need for early biomarkers that enable clinicians to differentiate between patients who progress rapidly from those who progress slowly. Developing hypertension before 35 years of age was highlighted by the Predicting Renal Outcome in Polycystic Kidney Disease (PROPKD) score as a risk factor for rapid decline in renal function.

In light of this, researchers from multiple centres across the USA and Belgium sought to evaluate data from a subgroup of patients with ADPKD who developed renal failure, defined as chronic kidney disease Stage 5, or the start of renal replacement therapy, before the age of 40 years. The team reviewed data on renal function, comorbidities, and childhood history from 200 patients, and used life table and proportional hazards analysis to evaluate any associations between clinical parameters and time to renal failure.

Median age of ADPKD diagnosis was 22.3 years, and median age for onset of renal failure was 36.2 years. Of the 200 patients, 128 (64%) had a diagnosis of hypertension, and four of these had a diagnosis before the age of 10 years. The researchers found that onset of hypertension before 18 years of age correlated with significantly faster progression to renal failure (univariate hazard ratio: 2.07; 95% confidence interval: 1.32–3.25). The team also noted that median age for first urological event was 27 years, and that 71 patients (35.5%) had a history of urinary tract infections, 67 (33.5%) had haemorrhagic cysts on abdominal imaging, 66 (33.0%) presented with gross haematuria, and 40 (25.0%) presented with renal stones.

The authors concluded that early-onset of hypertension (<18 years of age) was a risk factor for rapid progression to renal failure, and suggested that ambulatory blood pressure monitoring in children with ADPKD may be useful in identifying those at risk of rapid disease progression. ●

"The team reviewed data on renal function, comorbidities, and childhood history from 200 patients."

Predicting Renal Outcomes Through Combined Activity and Chronicity Score

COMBINED assessment of acute inflammatory activity and chronic changes on kidney histology could be used to predict renal outcomes in patients with anti-neutrophil cytoplasmic antibody-associated vasculitis with glomerulonephritis (AAV-GN), according to a study presented at ERA 2023. Previous data has suggested that chronic changes on kidney biopsies could be used to stratify the risk of kidney failure with AAV-GN, and this study aimed to evaluate the impact of inflammatory activity on predictions of renal outcomes.

The retrospective cohort study included 326 patients with AAV and active renal disease who were myeloperoxidase positive, or were serum anti-proteinase 3 anti-neutrophil cytoplasmic antibody-positive and had kidney biopsies available to score. Researchers assessed inflammatory activity through the Activity Index (AI), indicating a ratio between the number of crescents and/or necrosis and the total number of glomeruli, in percent, with the following scores: 0–5=0; 6–10=1; 11–15=2; 16–20=3; 21–25=4; 26–37.5=5; 37.6–50=6; 51–65=7; 66–80=8; 80–90=9; and 90–100=10. The team also evaluated chronicity through the Mayo Clinic Chronicity Score (MCSS), and summed both scores for a combined score. The participants were classified into three classes according to the risk of progression to kidney failure, including low-, intermediate-, or high-risk.

Researchers noted that median estimated glomerular filtration rate correlated with overall risk categories. Those in the high-risk category were more likely to have an estimated glomerular filtration rate <30 mL/min/1.73 m². Those at low risk were more likely to experience renal recovery; however, those at higher risk were more likely to experience kidney failure at 12 months, and to need dialysis. Furthermore, the combined score of AI and MCSS independently predicted risk of kidney failure at 12 months, especially in patients who were classified as high risk, and patients with proteinase 3-anti-neutrophil cytoplasm antibodies.

The team concluded that combined assessment of acute inflammatory activity and chronic changes on kidney histology independently predicted renal outcomes, and that the impact of inflammatory activity is cumulative to chronic changes in patients with AAV-GN. ●

"The participants were classified into three classes according to the risk of progression to kidney failure."

Carotid Plaque Thickness Predicts Cardiovascular Events and Death in Patients with Chronic Kidney Disease

NOVEL research presented at ERA 2023 investigated risk scoring systems in chronic kidney disease (CKD), and how they frequently underestimate elevated cardiovascular (CV) risk. The implementation of the coronary artery calcification score (CACS) has improved the prediction of CV events, and in recent years ultrasound has become an increasingly useful tool allowing for the analysis of carotid arteries to measure maximal carotid plaque thickness (cPTmax). The authors sought to investigate whether cPTmax can be used to predict CV events in patients with CKD for the first time, as well as compare the predictive value of cPTmax and CACS. cPTmax is defined as the radial distance from the media-adventitia interface to the intima-lumen interface towards the centre of the arterial lumen.

> **"The authors sought to investigate whether cPTmax can be used to predict CV events."**

The investigation included 200 patients with Stage 3 CKD. All patients had the thickest part of their carotid artery plaque measured using ultrasound between 2016 and 2017. The authors undertook statistical analysis on the highest cPTmax, giving an intra-observer coefficient of 9%. The patients were then divided into three groups based on their cPTmax score: no plaques; cPTmax 1.0–1.9 mm; and cPTmax >1.9 mm. Additionally, 175 of the patients underwent a non-contrast CT scan of their coronary arteries to calculate their CACS, and were divided into four groups: no calcification; CACS: 1–100; CACS: 101–400; and CACS: >400. The investigators then traced follow-up time, which was defined as the time of first major CV event or death of any cause (MACE).

The results of the investigators' analysis demonstrated an average follow-up time of 5.4 years. CV events were experienced by 20 patients (10%), and 28 patients died (14%). Patients with no plaque at baseline had the lowest risk of MACE, patients with cPTmax 1.0–1.9 mm showed an intermediate risk, and patients with cPTmax >1.9 mm had the highest risk. After adjustment for other factors, such as age, sex, diabetes, smoking, hypertension, and hypercholesterolemia, only patients with cPTmax >1.9 mm demonstrated a significantly increased hazard ratio (of MACE; hazard ratio: 3.2; confidence interval: 1.1-9.3; $p<0.05$). Additionally, the researchers applied C-statistics to assess whether ultrasound or non-contrast CT had a better predictive value for MACE. The analysis found predictive accuracy similar between the two methods (cPTmax [0.21; $p<0.0001$] and CACS [0.21; $p<0.0001$]).

The researchers concluded that the small study indicated that cPTmax and CACS showed equal accuracy and potential for predicting MACE in CKD. However, they highlighted that ultrasound imaging is more convenient, safer, and widely available compared to non-contrast CT. Additional study in larger cohorts is needed to further assess the value of cPTmax in predicting CV risk in CKD.

Is Kidney Replacement Therapy Affected by Arteriovenous Fistula Formation?

TO DATE, several retrospective studies have supported kidney protective effects in arteriovenous fistula (AVF) formation surgery. However, these studies have been limited by biases, including selection bias, and immortal time, in which participants have been unable to experience the study's outcome during a given period of follow-up.

A new study, carried out by the Glasgow Renal and Transplant Unit, Queen Elizabeth University Hospital, UK, aimed to investigate whether the formation of AVF can delay the start of kidney replacement therapy in patients who have Stage 5 chronic kidney disease. Researchers applied target trial emulation methods, in which the previously mentioned biases are absent.

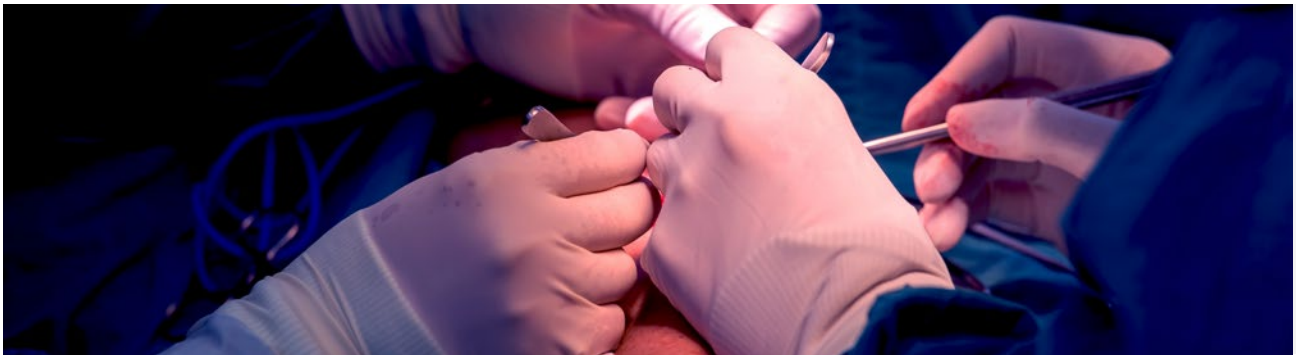
The study included 2,988 adult patients in the Strathclyde Electronic Renal Patient Record database, who attended the 'low clearance' nephrology clinic in the West of Scotland region between 1st January 2010–1st May 2022, and whose estimated glomerular filtration rate (eGFR) was <15 mL/min/1.73m². Patients were excluded if they had prior AVF, or arteriovenous graft formation. The study randomised patients (45% female; mean age: 64) to receive either an AVF immediately, or not to receive one.

Each patient who was given AVF formation was matched to another patient who had not undergone this procedure, but who was still eligible to participate in the study. Patients were matched in age (within a 5-year range), sex, and eGFR (within 0.5 mL/min/1.73m²). Researchers also adjusted for baseline confounders, such as medication use, blood pressure, comorbidities, age, and sex, as well as serum and urine biochemical measurements (eGFR Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI], and for 6 months preceding trial; albumin; C-reactive protein; urine protein to creatinine ratio; haemoglobin; phosphate; ferritin; and adjusted calcium). The study's primary outcome was kidney replacement therapy. Hazard ratios were estimated using estimated restricted mean survival time from Kaplan–Meier curves and Cox regression. A mixed effects model analysed the eGFR slope primary endpoint.

AVF formation was found to be interlinked with a higher risk of kidney replacement therapy (hazard ratio: 1.45; confidence interval: 1.20–1.45; p<0.001), as well as a lower risk of death (hazard ratio: 0.68; p=0.001). The group who received the AVF procedure demonstrated a lower kidney replacement therapy-free survival rate, with an estimated restricted mean survival time of 265 days.

In this study, researchers were unable to identify a kidney protective effect in AVF formation. Their findings prove the usefulness in using target trial emulation to approach research avenues, in which randomised controlled trials are impractical.

"Each patient who was given AVF formation was matched to another patient who had not undergone this procedure."



Shedding Light on The Outcomes and Epidemiology of IgA Nephropathy

FINDINGS from a large retrospective observational study of patients with IgA nephropathy (IgAN) from a UK centre details the disease epidemiology as well as patient outcomes.

The authors reviewed clinical data from 401 patients with biopsy-proven IgAN at their institution between January 2000–December 2019, with the aim of describing the cohort epidemiology, determining the effect of immunosuppression, and assessing patient outcomes, including progression to end-stage kidney disease requiring renal replacement therapy (RRT) and mortality.

Of the 401 patients included, median age was 45 years, 87.5% were White, and 69.6% were male. Median cohort values for creatinine, estimated glomerular filtration rate (eGFR), and urine PCR were 142 µmol/L, 46.7 mL/min/1.73m², and 183 mg/mmol, respectively. Immunosuppression was used in 20.4% of patients in the cohort, and renin-angiotensin system blockade was used in 79.6% of patients. Median follow-up length was 51 months.

Rate of change in eGFR was used to assess chronic kidney disease progression, and all available eGFR measurements were used to generate a linear regression slope. The rate of change in urine PCR was calculated in a similar manner. The median change in urine PCR was -4.46 mg/mmol/year, and the median rate of eGFR decline was -1.31 mL/min/1.73 m²/year. Progression to end-stage kidney disease requiring RRT occurred in 29.7% of patients, and mortality occurred in almost one-fifth of patients (19.7%).

To evaluate the factors associated with mortality, a Cox regression analysis was performed. This identified increasing age, non-White ethnicity, creatinine, urine PCR, hypertension, renin-angiotensin system blockade with angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist, diabetes, cardiovascular disease, and biopsy E and T scores as factors associated with mortality. Of note, immunosuppression use was not found to be associated with mortality or need for RRT.

The Cox regression analysis further identified hypertension, creatinine, urine PCR, and use of angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist, as factors associated with need for RRT.

> **"Immunosuppression use was not found to be associated with mortality."**

Patients treated with immunosuppression had a higher urine PCR than those treated without immunosuppression, at 301.5 mg/mmol compared with 141 mg/mol ($p<0.001$), and were more likely to have a total MEST score of >2 (42% versus 29.1%; $p=0.041$). Furthermore, patients treated with immunosuppression saw a greater reduction in proteinuria over time compared to those treated without immunosuppression at -16.8 mg/mmol/year and -2.64 mg/mmol/year, respectively. However, no difference was seen in eGFR decline over time between those treated with or without immunosuppression at -1.18 mL/min/1.73 m²/year and -1.32 mL/min/1.73 m²/year ($p=0.703$), respectively.

Overall, the researchers concluded that this large study provides real-world data that will be useful for practicing clinicians, and that whilst immunosuppression was associated with a larger reduction in proteinuria, this did not lead to mitigation of renal function decline.

Which Vascular Access is Best for Older Patients Receiving Haemodialysis?

DETERMINING the best approach for vascular access in patients >75 years of age with end-stage renal disease (ESRD) is challenging. Researchers from the General University Hospital of Alexandroupolis, Athens, Greece, and the Papageorgiou General Hospital of Thessaloniki, Greece, performed a meta-analysis to assess the outcomes following different vascular access procedures in patients ≥75 years with a diagnosis of ESRD.

The authors used MEDLINE and Scopus electronic databases to search for eligible articles published up to October 2021. In total, 12 articles met the inclusion criteria, all of which were retrospective cohort studies. The initial step of the analysis looked at five studies that focused on primary patency rates of autologous versus prosthetic vascular access for haemodialysis. The second step of the analysis reviewed articles that compared primary and secondary patency rates of forearm (distal) versus upper arm (proximal) fistulas.

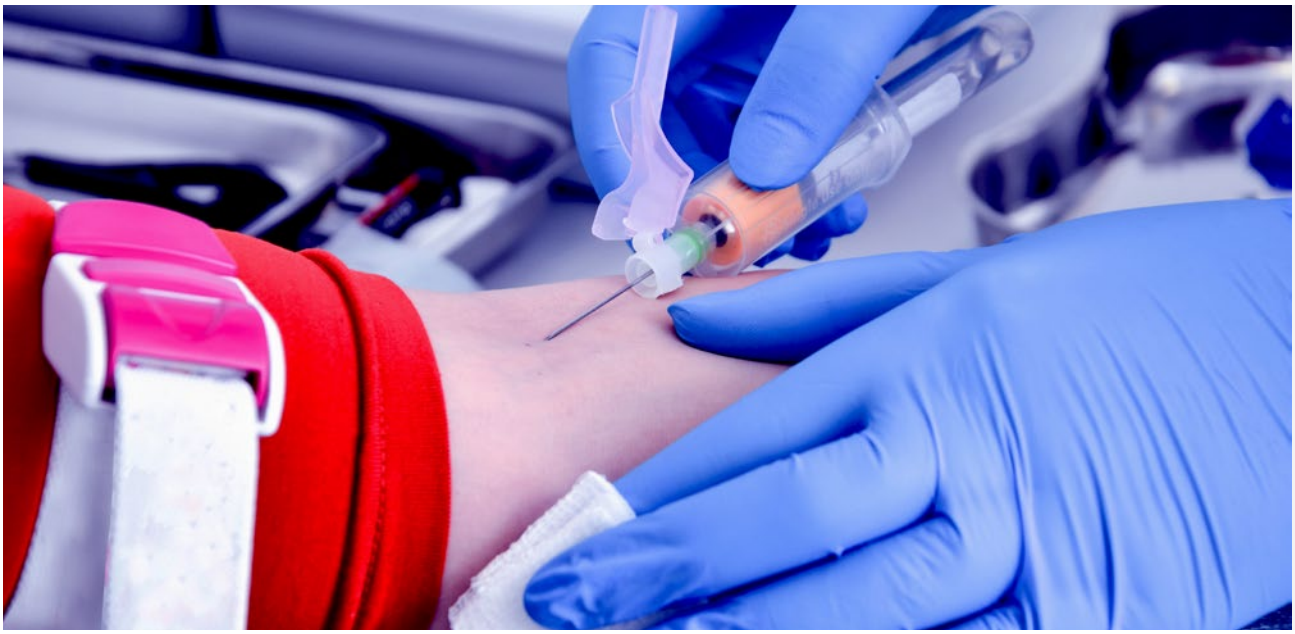
The analysis for the first step showed that 24-month primary failure rate favoured autologous arteriovenous fistula (AVF) access compared with prosthetic vascular access (odds ratio [OR]: 0.56; 95% confidence interval [CI]: 0.38–0.83; p=0.003).

These results signify a patency benefit in use of autologous AVF in patients aged ≥75 years with ESRD.

The analysis for step two revealed that 12-month primary failure rate was in favour of proximal fistulas (OR: 2.1;, 95% CI: 1.53–2.97; p=<0.00001). The secondary patency rate was also superior in proximal autologous fistulas (OR: 1.76; 95% CI: 1.12–2.78; p<0.01), suggesting that proximal AVFs are favourable as the vascular access of choice in patients ≥75 years of age with ESRD.

> **"The secondary patency rate was also superior in proximal autologous fistulas."**

The researchers concluded that whilst there remains no clear answer regarding the best vascular access approach for haemodialysis in older patients, the study analysis highlighted that proximal autologous AVFs have better patency rates compared with distal AVFs, and that creation of autologous vascular access in patients ≥75 years of age should not be excluded. ●



Using Middle Molecule Blood Tests in Incremental Dialysis

A RETROSPECTIVE analysis was conducted to assess the impact of incremental versus conventional haemodialysis initiation. The use of incremental dialysis has shown potential benefits, including improved patient quality of life, reduced treatment burden, and health economic benefits.

The Kidney Disease Outcome Quality Initiative (KDOQI) has recommended the option of incremental dialysis when renal urea clearance (KRU) is ≥2 mL/min, and patients must undertake frequent interdialytic urine collections to monitor residual kidney functions and avoid underdialysis. Due to the inconvenience of this process, some alternative methods of RKF monitoring have been studied, including the assessment of blood levels of middle molecules through β_2 microglobulin (B2M) and β-trace protein.

The study included an analysis of data from 55 patients from a multicentre feasibility randomised controlled trial.

The participants were followed up for up to 12 months, with monthly interdialytic urine collections to assess RKF, as well as monthly B2M and β-trace protein measurements. A middle molecule-based KRU equation and B2M cut-off level was used to predict RKF, and results were compared with the interdialytic reading to assess reliability in identifying patients with the cut-off point of KRU >2mL/min.

Results from the study revealed that the middle molecule-based KRU equation had 62% sensitivity and 84% specificity, and the B2M cut-off level of 0.5 L/day combined predicted KRU >2, with 70% sensitivity and 98% specificity. Overall, this result revealed that 1.8% of patients would have had underdialysis using these methods of monitoring. The researchers concluded that the use of blood B2M level alongside urine volume assessment was a reliable and safe predictor of RKF for incremental dialysis, which would mitigate the need for urine collection. ●

"The study included an analysis of data from 55 patients from a multicentre feasibility randomised controlled trial."

Racial Disparities in Living Kidney Donors

SOME races and ethnicities are disproportionately affected by kidney disease. A new retrospective cohort study, presented at ERA 2023, aimed to determine whether this disparity exists in living kidney donors, by evaluating the association between race/ethnicity and kidney function after donation.

The study included data from the Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR) on 136,814 living kidney donors undergoing donation between June 1972–September 2022. Researchers used multiple Cox proportional hazard regression analyses to examine time-to-event of >35% rising post-donation serum creatinine from pre-donation serum creatinine. Of the participants, 70% were White, 14% Hispanic, 11% Black, 4% Asian, 0.61% multi-racial, 0.47% American Indian/Alaska Native, and 0.25% Hawaiian/other Pacific Islander. In total, 75% of donors experienced an event during the follow-up time (median 6.27 months), with an incidence rate of 0.09 person-months.

Black patients had a significantly higher risk of increased post-donation serum creatinine >35%, while Hispanic and multi-racial groups had a significantly lower risk (hazard ratio [HR] Black: 1.03; 95% confidence interval [CI]: 1.01–1.06; HR Hispanic: 0.95; 95% CI: 0.93–0.97; HR multi-racial: 0.92; 95% CI: 0.84–0.99). This remained the case after adjusting for gender, USA citizenship, age, pre-donation BMI, education, systolic and diastolic blood pressure, post-donation proteinuria, serum creatinine, history of pre-donation hypertension, and interaction term between race/ethnicity and age. There were no significant differences in risk among other races/ethnicities. The team also noted that age was an effect modifier, leading to attenuated risk for increased serum creatinine >35% in older Asian, Hispanic, and multiracial groups.

"Black patients had a significantly higher risk of increased post-donation serum creatinine >35%."

The team concluded that being Asian was protective, and Black patients were at risk of increased post-donation serum creatinine, compared with White groups. Furthermore, outcomes were not worsened in elderly Asian, Hispanic, and multi-racial living kidney donors compared to younger patients with the same race/ethnicity. ●

Acute Kidney Injury in Hospitalised Patients Remains Unrecognised

UNDIAGNOSED acute kidney injury (AKI), which leads to a higher risk of complications and mortality, is an unrecognised issue in hospitalised patients, according to data presented at ERA 2023. While attempts to point attention to the condition and uniform its diagnosis have been made, recognition of this condition remains a problem.

The study aimed to evaluate the impact of underdiagnosed AKI in hospitalised patients at the IRCSS Policlinico San Martino, Genoa, Italy, between 1st January 2016–31st December 2019. Data including clinical data, length of hospital stay, serum creatinine (sCr), comorbidities, death, and primary diagnoses were analysed. Patients with Stage 4–5 chronic kidney disease were excluded. In the 56,820 remaining patients, the team defined and graded AKI following the Kidney Disease Improving Global Outcomes (KDIGO) criteria, comparing lowest sCr during hospitalisation, representing baseline kidney function, to peak sCr. The cohort was divided into three groups: those with no AKI; those with AKI calculated by sCr changes and formally codified in hospital discharge form (diagnosed AKI); and those with AKI calculated by sCr changes but not codified in hospital discharge form (undiagnosed AKI). Clinical characteristics and outcomes of the three groups were compared.

Data showed an incidence of AKI of 24.5%, with only a small percentage reported in some wards, including 13% in surgical wards, 27% in medical wards, and 19% in intensive care units, compared with 78% in the emergency department. Prevalence of comorbidities, including heart failure, diabetes, and heart failure, as well as sepsis and myocardial ischaemia, was higher in those with AKI (diagnosed and undiagnosed), compared with those without AKI. These patients also had major mortality risk and significantly longer hospitalisation.

> **"These patients also had major mortality risk and significantly longer hospitalisation."**

The team concluded that recognition of AKI in hospitalised patients remains a problem that needs to be faced, as this category of patients is at high risk of complications and mortality. ●

Screening Tool Can Predict Stenotic and Thrombotic Vascular Events

VASCULAR access (VA) risk score could be a useful screening tool to assist decision making, according to research presented at ERA 2023. Alshymaa Eltahan, Salford Renal Department, Northern Care Alliance NHS Foundation Trust, Greater Manchester, UK, and colleagues studied the accuracy of predicting stenotic/thrombotic vascular events with remote monitoring technology that uses VA data routinely collected during haemodialysis treatment. They calculated the access risk score retrospectively in a blinded fashion, using data from all haemodialysis sessions from two satellite units for 12 months.

The researchers identified patients with significant VA events, such as thrombosis, and those without an event through electronic records. They calculated the Access Risk Score as an average of the scores from three consecutive treatments, with a high-risk score (HRS) defined as ≥7. Clinically detected malfunctioning fistula information was retrieved from the last clinic letter and multidisciplinary meeting notes before the event. For patients who were event-positive, VA data from the previous 2 months was generated, while data for 5 consecutive months and 1 month follow-up was included for negative patients.

Of the 141 patients with Vasc-Alert (Vasc-Alert LLC, Lafayette, Indiana, USA) data, 60 were dialysed by a tunnelled line. A total of 10 out of 81 patients with arteriovenous fistula or graft had ≥2 HRS 2 months before the vascular event. Of the 46 patients without a vascular event, 15 had ≥2 HRS, while four patients had only the one HRS.

The positive predictive value of HRS ≥2 was 40.0%, while the negative predictive value was 93.9%, with a sensitivity and specificity of 83.3% and 67.4%, respectively. A history of clinically detected malfunctioning fistula and previous access to stenosis was associated with vascular events.

While this research can be a useful tool when screening patients for VA risk stratification, prospective studies are needed to evaluate its usefulness in the VA surveillance pathway. ●

"Prospective studies are needed to evaluate its usefulness in the VA surveillance pathway."