

Symposium 2.2 Challenges in Pediatric Nephrology

JAAP GROOTHOFF

Pediatric renal disease

"it's like a FOG in my head"

cognitive dysfunction

ATTENTION NETWORK TEST

ALERTNESS

EEG-Method

WHITE MATTER INTEGRITY

Alpha response

KEY FINDINGS

- CKD = complex disease
- Treatment affects brain structure
- acute state of CKD → "brain fog"

Focus: impact of cardiovascular disease on the brain

ARE YOUNG CHILDREN LESS VULNERABLE HERE?

GEMA ARICETA

TRANSITION OF ADOLESCENTS WITH CKD TO ADULT CLINICS

DIFFERENCES BETWEEN CHILDREN AND ADULTS

CRAFT FAILURE

SUPPORT DURING TRANSITION IS NEEDED

GROUPS:

- Transplant patients
- Dialysis patients
- CKD & CAKUT
- Rare kidney disease
- comorbidities

STRESSORS ALSO AFFECT FAMILIES

A TEAM PROJECT → EMPOWERMENT

CHECKLIST FOR READINESS

TRANSITION PLAN + PROTOCOL

increase privacy

RUKSHANA SHROFF

Isotope diagnostics to improve CKD-MBD management

MINERAL BONE DISORDER

REDUCED LIFE EXPECTANCY

GROWING CHILDREN NEED CALCIUM

CALCIUM BALANCE STUDIES

learn from Spacemen

RAYLEIGH PRINCIPLE

BONE FORMATION & RESORPTION

demineralisation

measure methods:

- before clinic
- in clinic
- bone scans (DEXA)

CORRELATION WITH BONE MARKERS

Ca ISOTOPES

- No EFFECT OF DIALYSIS MODALITY
- No EFFECT OF ANURIA

severe bone demineralisation at a young age

VerVieVas

Graphic Recording

Impact of severe CKD on the developing brain and neurocognitive functioning

Jaap Groothoff, Netherlands

The progression of chronic kidney disease (CKD) is associated with a myriad of systemic effects, including the impact on cognition. The research of the Amsterdam INPACT group, led by Sophie Lijdsman, found that children and young adults with CKD stage 4 and more are at risk for structural and functional brain abnormalities and neurocognitive dysfunctions. Especially in dialysis and transplant patients, there is impaired white matter integrity which is strongly associated with low full-scale IQ and basic speed and working memory performance. Impaired alertness and attention, as well as impaired alpha/theta EEG response, were found in patients with low current eGFR and longer exposure to low eGFR.

The reported cognitive problems include a lower full-scale IQ, attention deficit, impaired memory, and executive functioning, brain fog, as well as impaired memory function that may hamper the quality of life in adolescent kidney transplant recipients. To explore these issues, the group assessed structural abnormalities of the brain with magnetic resonance imaging (MRI) and diffusion tensor image

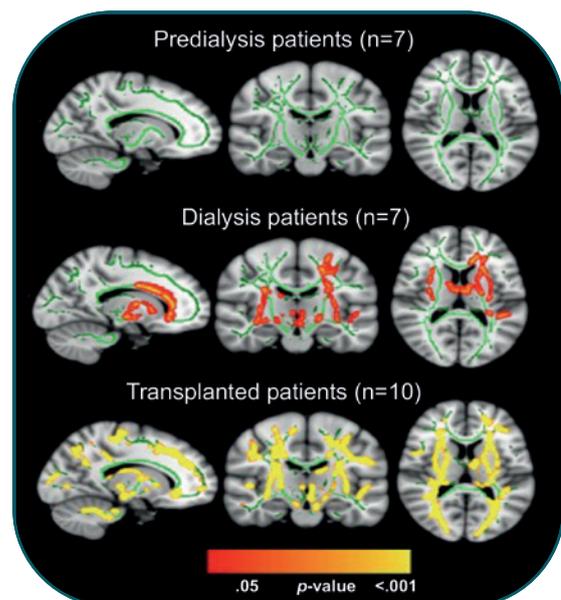


Figure 1.

Significantly lower white matter integrity in CKD, dialysis, and transplant patients compared to healthy controls on maps for fractional anisotropy (from ref. 1)

analysis (DTI) and evaluated brain function by electroencephalogram (EEG) temporal resolution. Cognitive functioning was analyzed using the comprehensive neurocognitive test battery. This included the estimated full-scale IQ and several neurocognitive components, among which a special test on alertness - the attention network test (ANT). The renal factors are taken into consideration as determinants were the eGFR, illness duration, and age at diagnosis, as well as the type of treatment (pre-dialysis, dialysis, and transplantation).

The research found a widespread disruption of white matter integrity throughout the group, with no significant differences between the dialysis and transplant groups. Older age at diagnosis and longer dialysis vintage at the time of transplantation negatively affected the neurocognition, including intelligence, basic speed, and working memory. On the other hand, no evidence was found to prove a difference between the predialysis group and healthy controls. To the surprise of the researchers, neurocognition was unaffected by eGFR and the duration of severe CKD. Concerning brain function and attention, the researchers concluded that problems in alertness and attention difficulties occur in patients with current low eGFR and longer exposure to low eGFR, and are most likely reversible after kidney transplantation. These functional abnormalities were reflected by altered EEG patterns. The conclusion is that the impact of severe CKD in children and young adults is complex. Severe CKD and its management may affect brain structure, especially the white matter integrity, which may impact global cognition, memory and basic speed.

Also, CKD and exposure to uremic toxins impact brain function and provokes attention difficulties, but this issue is likely reversible after transplantation. Future research should focus on the impact of cardiovascular disease on the brain in young renal transplant patients, the impact of the CKD course and uremic toxins, as well as on exploring the aspect of physical exercise benefits for enhancing white matter function.

Transition of adolescents with CKD to adult clinics?

Gema Ariceta, Spain

The adolescent CKD group is characterized by the highest risk of poor self-management and unfavorable outcomes. Emerging adulthood has been recognized as a high-risk period for kidney transplant graph loss and recent evidence suggests that adolescents and young adults with CKD also have unfavorable prognoses in comparison with younger and older patients in a similar clinical setting. Therefore, novel research focuses on transitioning this vulnerable population to adult clinics.

Congenital anomalies of the kidney and urinary tract (CAKUT), glomerulonephritis, but also a substantial number of rare and genetic or inherited disorders are the most common causes of CKD. Therefore, the transition process must account for all these unique requirements. Although it has recently been reported that the incidence of children progressing to renal failure during their pediatric age has decreased in the CAKUT group, many of those patients continue to progress and reach renal failure in their 30s and 40s. This highlights the need to transition not only for patients with advanced CKD or post-transplant and dialysis patients but also for patients with milder CKD, to avoid a lack of adequate follow-up.

Transition needs to consider different patient profiles, such as patients with CAKUT who have associated uropathy and the associated need for lifelong urologic care. This indicates that the transition must not only include nephrology but urology as well. At the same time, there is a conflict between the need to provide independence to the patient in terms of self-management and the limitations that the patient may present, not only because of comorbidities but also due to the complexity of providing adequate care.

One of the main issues is that transition is not only a medical process. Instead, it is also influenced by many psychological and social factors, since it occurs when brain maturation is still incomplete. Adolescents with CKD face not only the typical challenges of emerging adulthood, but they must also learn to manage a lifelong condition on their own. Delicate peer interaction, extended school absence, strict immunosuppressant drug regimes, post-traumatic stress symptoms, and family instability owing to financial hardship may all worsen psychosocial challenges and lead to poor treatment adherence.

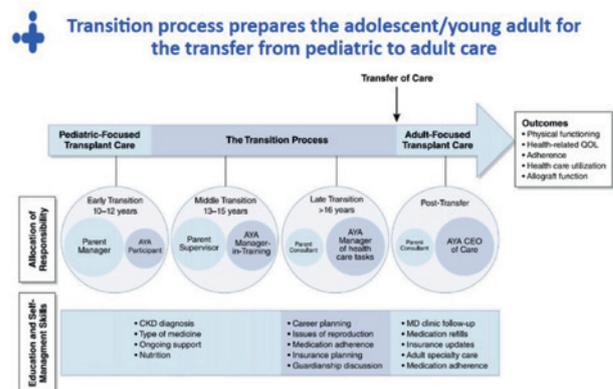


Figure 2.

The transition process of CKD patients from pediatric to the adult clinic (from ref. 2)

Successful transition lies in the individualized approach, identification of the most suitable specialists, and communication on all levels, as well as careful planning and adapting the existent protocols to the specific needs of the patient.

Isotope diagnostics to improve CKD-MBD management

Rukshana Shroff, United Kingdom

Chronic kidney disease in children is a substantial challenge and bone mineral disorders can be extremely difficult to manage in this population. Nearly 30% of children with CKD stage 2 and >90 % of children on dialysis have insufficient mineralization, which manifests with the occurrence of bone deformities and a much higher risk of fractures than in healthy age-matched children. The assessment of bone health poses a significant problem for physicians treating this vulnerable group.

Calcium is measured by imprecise and invasive methods such as serum calcium levels, bone biopsies, radiological changes, biomarkers, and parathyroid hormone (PTH). Calcium isotopes ^{42}Ca and ^{44}Ca , which are non-radioactive, are found in the human diet and are stored in bodily compartments via kinetic isotope fractionation principles. Isotopically light ^{42}Ca is mostly absorbed into bone tissue, whereas heavier ^{44}Ca is excreted in the urine and feces. When bone mineralization exceeds resorption, the $^{44}/^{42}\text{Ca}$ serum ratio rises, indicating a positive calcium balance in the bones.

A recent study in a healthy population showed that children have the highest calcium isotope ratios due to rapid growth, followed by young adults and finally elderly subjects, with elderly osteoporotic women having the lowest calcium isotope ratio. In a further study in children with CKD and on dialysis, we using a somewhat different model that took into consideration the calcium loss through the kidneys in subjects with preserved diuresis, calcium exchange on dialysis, and possible extraosseous calcification. Compared to healthy age-matched children, subjects with CKD and those on dialysis have a significantly lower calcium isotope ratio. This points to substantial bone demineralization, similar to elderly osteoporotic subjects, signifying that children with CKD and on dialysis are at the extreme of bone demineralization.

Therefore, the naturally occurring stable calcium isotope ratio in serum is a significant and independent predictor of bone calcium balance in children with CKD and on dialysis. It is more sensitive and accurate than the routinely measured biomarkers as well as bone mineral density measured by dual-energy x-ray absorptiometry (DXA) or peripheral quantitative computed tomography (pQCT). This isotope measurement can be used in many different groups, such as in children with inherited bone diseases, adults with CKD, and on dialysis, as a prognostic marker of fracture risk in older people and for sensitive monitoring of the effects of medications like steroids and anti-resorptive treatments that affect the bone.

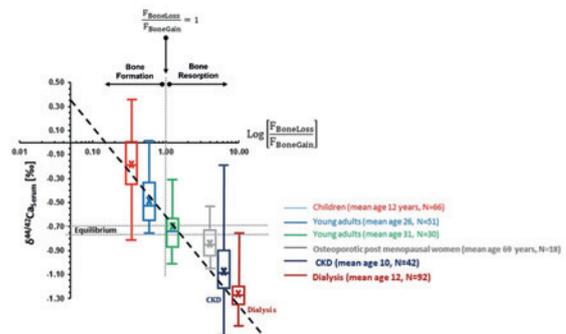


Figure 3. Calcium isotope ratios and bone mineralization-demineralization status in different populations

Further readings

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All the speakers reviewed and approved the content.