Update on primary hyperoxaluria in Italian patients

Alessandra Pelle

1 University of Turin, Italy
2 SSD Genetica Medica, Italy
3 AOU San Luigi Gonzaga, Italy

Primary hyperoxalurias (PH) are a group of rare autosomal recessive diseases commonly arising in childhood and presenting with nephrolithiasis, nephrocalcinosis, progressing to chronic renal failure. 3 responsible genes are known: Alanine-glyoxylate aminotransferase (AGXT, PH1), glyoxylate reductase/hydroxypyruvate reductase (GRHPR, PH2) and 4-hydroxy-2-oxoglutarate aldolase (HOGA1, PH3). Out of over 200 patients from all Italy referred until April 2016 to the multidisciplinary network established in Torino in the 80s, PH1 had been diagnosed in 82, PH2 in 3, PH3 in 2 DZ twins and one additional patient homozygous for a novel HOGA1 variant of unknown significance (c.341-81delT). A defined suspicion of PH strictly depends on a reliable dosage of urinary oxalate that it is strongly influenced by the analytical procedure (free vs. bound Uox), in particular in the advanced phase of the disease. This may in part explain why PH is underdiagnosed. 21 patients suspected to have PH on clinical grounds were negative for mutations in the 3 genes. Negative findings might be ascribed in a few cases to mutations of difficult identification by Sanger sequencing. Alternatively, new genetic subtypes of PH can also be hypothesized, caused by mutations in other genes encoding proteins of glyoxylate metabolism (e.g. HAO1, SLC26A1). To explore this possibility, whole exome sequencing and SNPs array techniques and further phenotype–genotype studies are needed. This approach requires a closer interaction between clinicians and geneticists in evaluating the clinical and biochemical data: A multiple step diagnostic algorithm based on clinical and biochemical data could be proposed to achieve this goal.

alessandraelisapelle@gmail.com

Expanded criteria donor kidneys for retransplantation UNOS

Hina J Panchal

Icahn School of Medicine at Mount Sinai, USA

We analyzed outcomes of retransplantation from expanded criteria donors (ECD) over the last 2 decades to determine the benefits and risks of using ECD kidneys for retransplantation. Data from the United Network for Organ Sharing database were collected and analyzed. Graft survival, death censored graft survival, and patient survival for retransplantation with ECD kidneys (re-ECD) were reported and compared with primary transplantation with ECD kidneys (prim-ECD) and retransplantation with standard criteria donor kidneys (re-SCD). Re-ECD kidneys had higher risk of graft failure compared with prim-ECD (HR=1.19) and to re-SCD (HR=1.76). Patient survival was better in re-ECD compared with prim-ECD (HR=0.89) but was worse than re-SCD (HR=1.82). After censoring the patients who died with a functioning graft, re-ECD had a higher mortality risk compared with prim-ECD (HR=1.45) and re-SCD (HR=1.79). Transplantation improves quality of life and reduces healthcare costs, and due to the risk associated with resumption of hemodialysis and the longer waiting list times for SCD kidneys, there is a benefit to accepting ECD kidneys for select patients requiring retransplantation. Although this benefit exists for select patients, retransplantation with ECD kidneys should be undertaken with trepidation, and appropriate informed consent should be obtained.

hinaben.panchal@icahn.mssm.edu