

Kidney I - Longevity of Transplant Kidney

Personalized medicine in kidney transplant

Simon Chi-Yuen CHEUNG

Kidney transplantation remains the mainstay of treatment for patients with end-stage kidney disease. With the advances in immunosuppressive therapy, there has been significant improvements in acute rejection rates and short-term allograft survival. However, this success has not been translated into the long-term benefits by the same magnitude. Optimization of immunosuppression is important in transplantation. It is important to note that each patient has unique attributes and immunosuppression management should not be a one-size-fits-all approach. The principal target is to obtain the balance between rejection prevention and over-immunosuppression.

There has been a wide variation of immunosuppressive regimens among different transplant centers. Choice should be guided by overall efficacy together with the medical and immunological risks in individual patient. In kidney transplant recipients with post-transplant cancers, the mainstay of treatment is judicious reduction of immunosuppression. Elderly transplant patients are less likely to develop acute rejection but more likely to die from infectious and cardiovascular causes than younger patients. Adjustment of standard immunosuppressive regimens are therefore advocated for this population.

Tacrolimus remains the cornerstone of immunosuppressive treatment following kidney transplantation. Due to its narrow therapeutic index and high inter- and intra-patient pharmacokinetic variability, therapeutic drug monitoring (TDM) is necessary. It has been hoped that pharmacogenetics can be used to complement TDM in optimizing drug exposure. Among the various drug-genotype pairs being investigated, tacrolimus and CYP3A5 gives the most promising results. Different studies have consistently shown that CYP3A5 expressers take longer time to achieve target blood tacrolimus levels and require a higher tacrolimus dose than nonexpressers. However, for pharmacogenetics to be widely used clinically, further trials are necessary to demonstrate the clinical benefits of genotype-guided dosing such as reduction of rejection and drug-related toxicities. Finally, the development of different biomarkers may help to reach true personalized therapy in transplant patients.