

Abstract

Improving the short-term results of kidney transplantation did not result in improving the long-term function and survival of kidney allograft. Organ shortage and increasing number of marginal donors remains the key problem in transplant today. The quality of donor organ is critical for graft function development and survival. The aim is to improve understanding to ischemia/reperfusion injury and its consequences, predict delayed graft function and rejection, improve organ allocation strategy and identify patients suitable for safe drug minimization or complete withdrawal of immunosuppressive therapy.

Analysis of donor kidneys identified poor tubular cell quality and low survival factor, Netrin-1 expression levels, to be associated with delayed graft function. We confirmed that reperfusion phase of ischemia/reperfusion injury leads to minimal morphological but significant molecular abnormalities. Dissociation observed in histology and molecular pathology finding calls for an integrated approach in donor quality organ evaluation and allocation for transplantation. Significant heterogeneity within donors with expanded criteria was shown and subgroup of organs at low risk of delayed graft function was identified. We suggested donor biopsies to be performed as a routine praxis in all kidneys irrespective of ECD classification. Decreased expression of NF-kappaB signalling pathway after Thymoglobulin induction was observed when compared to ATG-F, which could be indicative of more effective alloimmune regulation and explain success of this biological treatment in clinical practice. The up-regulation of several operational tolerance-related genes in the peripheral blood and kidney graft tissues of rejection-free patients in kidney transplant patients was observed.

Key words

delayed graft function, ischemia/reperfusion injury, kidney transplantation, organ quality, prediction, transcriptom