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Preclinical Xeno-Kidney Transplantation of Pig to Cynomolgus Non-Human Primate: 2 Years of Experience

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Introduction: Xenotransplantation is gaining much attention as an alternative means to resolve the worldwide organ shortage. Pigs are currently considered the best donor animal, and recent clinical application of kidney xenotransplantation in a decent model was encouraging. However, there are a lot more to learn and preclinical study using non-human primates is valuable in moving to a successful clinical trial. We present our 2-year experience with renal xenotransplantation using cynomolgus primate recipients in South Korea. Our primary aim was to investigate the immunological changes following xenotransplantation.

Methods: A total of sixteen cynomolgus monkeys received kidneys from pigs of various genetic modifications, including DKO (GGTA1, B4galNT2), DKO (GGTA1, CMAH), TKO, QKO (TKO + iGb3S), and DKO (GGTA1, B4galNT2) with CD46, TBM. A standardized immunosuppressive regimen was used, with anti-thymocyte globulin and rituximab as induction, followed by aCD154, sirolimus and steroids as maintenance. Serial biopsies were performed after transplantation, and histology was reported by a renal transplant specialist pathologist.

Results: The mean overall survival was 43.1 days. A significant proportion of recipients (n = 10, 62.5%) died of systemic complications including systemic oedema, septic shock, and asphyxia. AMR and TCMR were present in two cases each, and one borderline rejection was identified. There was no mortality secondary to post-operative bleeding. A subgroup analysis was performed to compare outcomes between donor groups, but a meaningful conclusion could not be drawn due to small numbers.

Conclusion: Our experience demonstrates that rejection-free kidney xenograft survival is possible with adequate genetic modifications and immunosuppression. However, the rate of systemic complications was unacceptably high, although they might be related to immunological reasons. To achieve longer survival, a better understanding of histopathological changes in xenotransplantation and improved management of such complications would be necessary, in addition to further development of organ-specific optimal target gene modifications and refinement of immunosuppressive regimen.