

## Pre-emptive renal transplantation versus transplantation after a period of dialysis in paediatric patients: a systematic review and meta-analysis

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**Introduction:** Kidney transplantation is the treatment of choice for many patients with end-stage renal disease. However, whether or not dialysis prior to kidney transplantation in children should be avoided at all is still unclear. Research has reported mixed findings on whether pre-emptive kidney transplantation (PKT) is associated with better outcomes when compared to kidney transplantation after a period of dialysis (nPKT). The aim of the study was to systematically review the clinical outcomes of PKT versus nPKT in paediatric patients.

**Methods:** A bibliographic search was carried out using free text and controlled vocabulary terms to search the following databases: EMBASE, MEDLINE (OvidSP), PubMed Publisher, Cochrane Central Register of Controlled Trials (CENTRAL), Cinahl, Web-of-science and Google Scholar. Studies that compared first or subsequent, living or deceased donor PKT versus nPKT in paediatric patients were included. Any study design was included except for case reports as long as the study reported any of the predefined clinical outcomes, including patient and graft survival, delayed graft function and acute rejection. The screening, selection of articles for inclusion, quality assessment and data extraction were carried out by two independent reviewers. The Downs and Black Checklist was used for assessing the methodological quality. Where possible, data were combined using the random-effects model to produce a summary estimate and 95% confidence interval (CI). The  $I^2$  statistic was calculated to assess heterogeneity. The review was registered with PROSPERO [CRD42014010565].

**Results:** The search identified a total of 4,743 unique references and 21 studies met the inclusion criteria. A total of 20,800 paediatric patients were included in the analysis, of which 5,044 (24.3%) received PKT and 7,540 (36.3%) had a living donor kidney transplant. The study designs included registry analyses, retrospective cohorts, and case-control and cross-sectional studies with a follow-up range of 1-20 years. The methodological quality varied between studies and the quality scores ranged from 10 to 19 out of a maximum score of 28. The meta-analyses comparing PKT versus nPKT revealed that there was no difference in the risk of patient death (9 studies; Relative Risk (RR) 0.68; 95% CI 0.41-1.13;  $I^2 = 41.5\%$ ) and delayed graft function (3 studies; RR 0.57; 95% CI 0.22-1.50;  $I^2 = 81.5\%$ ). However, the risk of graft loss was significantly lower in PKT compared to nPKT (15 studies; RR 0.58; 95% CI 0.50-0.68;  $I^2 = 51.1\%$ ). There was a trend towards a reduction in the risk of acute rejection (7 studies; RR 0.77; 95% CI 0.58-1.03;  $I^2 = 77.7\%$ ) in PKT patients. Moderate to substantial levels of heterogeneity between studies were observed and subgroup analyses were conducted to explore the reasons for heterogeneity. Limiting analysis to studies that corrected for confounding variables yielded similar results to the overall analysis.

**Conclusion:** PKT in paediatric patients appears to be superior to non-PKT with regards to graft loss. No differences were found in terms of patient death, delayed graft function and acute rejection.