In Focus

Nurturing the benefits of pre-emptive kidney transplantation

Paolo Ferrari\textsuperscript{1,2}

\textsuperscript{1}Department of Nephrology and Transplantation, Prince of Wales Hospital, Sydney, Australia and \textsuperscript{2}Clinical School, University of New South Wales, Sydney, Australia

Correspondence and offprint requests to: Paolo Ferrari; E-mail: paolo.ferrari@sesiabs.health.nsw.gov.au

Pre-emptive kidney transplantation (PKT) refers to transplantation before the initiation of chronic maintenance dialysis. It has been suggested that PKT is associated with improved patient and graft survival, higher return-to-work rates, better quality of life and lower long-term medical costs compared with transplantation after dialysis initiation [1]. Furthermore, PKT has the advantage of dialysis avoidance, with reduced risk of catheter-associated infection, no requirement for permanent vascular access and a reduction in dialysis-associated cardiovascular events. Some theoretical disadvantages of PKT include the failure to make the most of native kidney function and the failure to take advantage of putative immunosuppressive effects of uraemia, which could theoretically help prevent allograft rejection.

Although several single-centre and registry studies have suggested PKT to be the optimal renal replacement therapy in patients with advanced chronic kidney disease, to date no evidence-based guideline recommendations with regard to PKT have been published. In this issue, the Descartes working group and the European Renal Best Practice advisory board [2] fill this gap by conducting a systematic analysis of published studies and providing a strong recommendation, albeit based on low quality of evidence (Level 1D) that programmes for PKT with living-donor kidneys should be encouraged. As such this systematic analysis is a welcome addition to existing literature and a helpful tool in advising policies and procedures at unit and national level. The two key questions addressed in this systematic review are firstly whether PKT with living-donor kidneys should be encouraged and secondly at what level of glomerular filtration rate should transplant candidates undergo PKT. Using a pre-defined search strategy, data extraction and grading methodology, the authors identified 29 observational cohort studies performed after 1990 providing data on the key outcomes of patient survival, graft survival and acute rejection rate in PKT recipients. The authors of the guidelines acknowledge that all papers had a high risk for selection bias, including lead-time bias, uncertainty whether PKT recipients were representative of the overall transplanted patients, and uncertainty in adjustment for confounders to name a few. Nevertheless, their analysis did not identify any signals of worse outcomes with PKT, and indeed they found that in PKT patient survival was better in 47%, graft survival in 57% and rejection rates in 77% of the studies reporting those outcomes. These figures should be considered as a very compelling argument to support a higher uptake of PKT, because some of the results are likely to have been diluted by inclusion of deceased donor PKT. While some organ donation agencies in a limited number of countries allow PKT from deceased donors, in many countries this practice is only an option for transplant candidates with a live donor. It is therefore important to emphasize that the recommendations by the Descartes working group are cautiously restricted to kidney transplantation from a live donor. Interestingly, in 13 articles included in this systematic review, the donors were either living or deceased and in two only deceased donors. In the USRDS analysis by Kasiske et al. patient and graft survival in recipients of deceased donor PKT were found to be better than in non-PKT recipients, but inferior to living-donor PKT recipients [3]. Furthermore, although in the ERA-EDTA registry study of 35,511 adult, cadaver and living-donor transplants from 1985 to 1992, 5-year patient and graft survival rates were not affected by PKT, living-donor graft survival was improved in PKT recipients (79% versus 69.6%) [4]. Thus, one could infer that the cautious recommendation by the guidelines authors may have been influenced by the ascertainment bias of outcome in recipients of deceased donor PKT.

The authors also took care to retrieve studies performed after 1990, because they considered that older cohorts would be outdated and would not provide relevant data as differences in transplant era may have added the bias introduced by
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comes when compared with later dialysis initiation [6]. Early

This is in line with the IDEAL trial, where the parallel trend in

early start dialysis was associated with worse or no different out-
comes when compared with later dialysis initiation [6]. Early

intervention is likely to increase costs and to prematurely ex-

pose donors and recipients to operative and immunosuppres-
sive risk associated with transplantation and thus the

recommendation that PKT should be undertaken shortly or a

few months before the need to initiate dialysis is sound, pro-

vided the pre-transplantation work-up of both donors and re-
ipients has been completed well in advance of the planned

transplantation.

While the focus of the analysis was to assess the potential ad-

vantage of PKT for recipients and from the donor perspective, it
does not make a difference whether the donation takes place be-

fore or after the start of dialysis, the authors acknowledge that it
remains important that during the informing of the donor, suf-

ficient attention is paid to explain potential short- and long-
term donor risks. The message by Abramowicz and co-authors is
clear [2]; PKT, particularly among recipients of live donor

kidneys, not only avoids the cost and risks of dialysis but is
also associated with better patient and graft survival and re-
duced incidence of rejection episodes than transplantation after commencement of dialysis and thus efforts should be
 undertaken to raise the awareness about this option of renal re-
placement therapy in patients with advanced chronic kidney
disease.

The presence of an incompatible blood group or of pre-
existing donor-specific antibodies to human leucocyte antigen
between a kidney transplant candidate and their intended
donor rule out >50% of otherwise appropriate pairs [7], and
this may be perceived as a barrier to PKT from a live donor.
Kidney paired donation (KPD) can overcome this barrier [8],
and the option of pre-emptive KPD should therefore be in-
cluded in the education of these kidney transplant candidates.

CONFLICT OF INTEREST STATEMENT

The manuscript is not under consideration for publication
elsewhere in a similar form, in any language, except in abstract
form.

(See related article by Abramowicz et al. Does pre-emptive
transplantation versus post start of dialysis transplantation
with a kidney from a living donor improve outcomes after
transplantation? A systematic literature review and position
statement by the Descartes Working Group and ERBP. Nephrol
Dial Transplant 2016; 31: 691–697)

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