

Pre-emptive Renal Transplantation: Optimum Treatment for End-Stage Renal Disease?

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ABSTRACT

Renal transplantation (RT) prior to having dialysis or pre-emptive renal transplantation (PRT) has been controversial because of the paucity of clinical evidence to clarify the benefits and risks of PRT. The recent emergence of evidences from major transplant centres in the United Kingdom and United States have confirmed the survival advantages for both renal allografts and RT recipients. Hence an increasing number of transplant centres are adopting the practice of PRT. This article discusses the advantages and disadvantages of PRT and highlights the clinical evidences in support of PRT.

Key Words: *Dialysis, kidney transplantation, pre-emptive renal transplantation*

INTRODUCTION

Dialysis has been the long-established initial treatment of choice for patients with end-stage renal disease (ESRD). However, with the successful outcomes of renal transplantation (RT) over the last five decades, RT is considered the optimum form of therapy for patients with stage V (GFR < 15mls/min/1.73m²) chronic kidney disease (CKD), the ESRD, because this restores the quality of life through removal of dietary restrictions, restores vitality, improves survival and is cost-effective. RT before dialysis, or pre-emptive renal transplantation (PRT), has been controversial because of the paucity of clinical evidence to clarify the benefit vs. risks of this approach. However, recent studies support the use of

PRT as a more advantageous strategy for the patients than RT after initiation of dialysis.¹

For patients with ESRD while awaiting RT, haemodialysis (HD) or peritoneal dialysis (PD) are the alternative means of PRT to sustain life. To achieve successful HD or PD, access to the vascular system or the peritoneal cavity, respectively, is required. Dialysis access remains the Achilles' heel in PRT as the patients need to undergo surgery for dialysis access on more than one occasion and the complications are often associated with considerable morbidity and mortality. For example, 20% of dialysis patients are hospitalised each year for access-related problems; greater than 50% of these admissions are related to infection of

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dialysis access. There is an increased incidence of vascular calcification in patients who are on long-term HD, which leads to increased mortality related to cardiovascular complications. Hyperparathyroidism, complement and leucocyte-mediated pulmonary dysfunction, anaemia, and transmission of hepatitis C and B are the inherent problems associated with HD.² The accelerated adverse vascular and metabolic effects of dialysis due to increased accumulation of a variety of pro-inflammatory and pro-atherogenic factors predispose them to a poorer outcome once they receive a RT.

An increasing number of patients requiring dialysis every year has posed significant strain on the renal units which mandates expansion of dialysis facilities and trained manpower. Currently, the cost of chronic HD or PD is £30,000 per patient per year in the United Kingdom, whereas a RT costs £26,000 in the first year, followed by maintenance immunosuppression worth of £7000 per year. RT provides not only financial savings to the health care providers, but also impacts significantly on the quality of life of the recipients and the family members.

The incidence of treated ESRD patients has doubled over the last decade, whereas the number of potential kidney donors has not shown a substantial growth, which has led to an increase in the waiting time to receive a RT. Traditionally, RT was carried out once the patients were on dialysis. But there is a changing trend towards PRT, which means the RT is carried out before initiation of chronic maintenance dialysis. In the United States, PRT is carried out in 25% of adult recipients of living donors and 10% adult recipients of deceased donors. Among all children who are kidney recipients, 28% of children in North America and 22% of children in the UK undergo PRT, which are mainly from living donor source. There are potential benefits of PRT, such as, avoiding time spent on dialysis with disruption of family and school life, allowing more normal growth and avoiding the need for dialysis access.³

Several studies have repeatedly confirmed the survival advantages of PRT for adults compared with transplantation after initiation of dialysis, and that increasing duration of pre-transplant dialysis is associated with increasing risk of mortality and allograft failure. Meier-Kreische et al. analysed data from 73103 primary adult RTs carried out in the United States and demonstrated significantly increased death-censored allograft failure and patient death for non-pre-emptive RTs, and that these rates increased with increasing duration of dialysis.⁴ Asderakis et al. have reported from Manchester, UK, that in a cohort of 1463 RT recipients, 161 (11%) patients had undergone PRT. The delayed graft function occurred more frequently in the dialysis

group (25% vs. 16%). The actuarial graft survival in the pre-emptive group at 1, 5, and 10 years (84, 76 and 67%) was significantly higher than the respective values in the dialysis group (83, 69, and 56%). Within the live donor recipient cohort, the survival advantage for the pre-emptive group was even more striking. They concluded that PRT not only avoided the risks, cost, and inconvenience of dialysis, but was also associated with better graft survival than transplantation after a period of dialysis, particularly within the live donor cohort.⁵

There are no published data regarding the timing of PRT. The best time to receive a PRT is the time when dialysis requirement is eminent, which is determined by the development of the symptoms of uremia and metabolic derangements, which is variable from one patient to another. Hence the decision should be made by the responsible transplant team on an individual case basis based on both laboratory and clinical parameters. According to European Best Practice Guidelines, PRT should be performed when the GFR has fallen below 15 mls/min/1.73m², which is our practice at the Sheffield Kidney Institute.⁶ Laparoscopic live donor nephrectomy, because of its several advantages over open nephrectomy, has increased the kidney donation rate significantly in our institution, which has increased the number of PRTs performed annually. Expansion of live donor pool with the introduction of paired exchanges, ABO-incompatible and positive cross-match transplantation has further encouraged PRT. PRT is carried out using kidneys from both living and deceased donor sources, although increasing number of patients are undergoing PRT from living donor sources on a planned basis. The GFR for initiation of dialysis and PRT recommended by the National Kidney Foundation – Kidney Dialysis Outcomes Quality Initiative (NKF-KDOQI) is 14 mls/min, although estimated GFR at the time of PRT was significantly less (9.9 mls/min \pm 5.3) than the recommended threshold in an analysis of 4095 PRT recipients in the United States.^{7, 8}

The theoretical disadvantages of PRT include failure to maximise the use of native kidney function and failure to take advantage of putative immunosuppressive effects of uremia, which could theoretically help prevent early post-transplant rejection. The compliance to immunosuppressive medications after RT may be reduced if patients do not experience the morbidity of dialysis. However, the potential benefits of PRT outweigh the disadvantages.⁹ These include the avoidance of morbidity associated with dialysis and dialysis access procedures, improved graft and patient survivals and reduce expenses. PRT should be offered to children in particular as this avoids dialysis, thus limiting the retardation of growth and development and has been shown to be effective.¹⁰

In conclusion, evidence to date demonstrates a significant advantage of PRT in the management of patients with ESRD. Therefore PRT should be the way forward, particularly in a developing country like Nepal, where this will not only avoid patients having to undergo dialysis access surgery and dialysis-associated comorbidities, but will also prolong the renal allograft and

patient survivals and reduce overall cost significantly. There can be considerable scepticism in accepting the concept of PRT by the transplant team, recipients, donors, and the society, but the growing body of evidence supporting PRT has led to a significant rise in the number of PRT, performed annually worldwide.

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