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Review Article

Preemptive kidney transplant: indication, outcome and complications

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ABSTRACT

Dialysis and kidney transplantation are the only available management approaches for these patients. Estimates show that the survival rates and quality of life are significantly higher for patients that receive kidney transplantation than others with dialysis. In addition, the effectiveness of preemptive kidney transplantation was well-evidenced in the literature. It had been further demonstrated that performing preemptive kidney transplantation significantly reduces the complications of renal transplantation and dialysis and was incredibly cost-effective when compared to dialysis. Furthermore, evidence regarding its effectiveness was well-established among studies in the literature as a safe primary management approach for patients suffering from end-stage kidney disease. This literature review discussed preemptive kidney transplantation's indications, outcomes and complications. Our findings indicated the efficacy of the approach for patients suffering from end-stage kidney disease. However, the appropriate selection of the patients was a critical issue. Besides, serious efforts should be exerted to prepare the patient perioperatively. Nevertheless, kidney functions were reported to increase following preemptive kidney transplantation. Graft rejection and delayed graft functions were also reported to follow preemptive kidney transplantation. However, the estimated rates are lower than those for patients having transplantation following the start of dialysis. We encourage further relevant investigations to further elaborate on the long-term findings, prognosis, and complications.

Keywords: Preemptive, Kidney transplantation, Glomerular filtration rate, Complication, End-stage renal disease

INTRODUCTION

Patients with end-stage kidney disease are usually prone to various morbidities and life-threatening complications, in addition to the significant decrease in the aspects of quality of life. Typically, these patients do not lead an everyday life and cannot presume their daily activities after being diagnosed with the condition.[1-3] Therefore,

managing this condition is critical to save these patients' lives and enhance the quality of life.

Dialysis and kidney transplantation are the only available management approaches for these patients. Estimates show that the survival rates and quality of life are significantly higher for patients that receive kidney transplantation than others with dialysis.[4] In addition, the current literature showed the validity of performing preemptive kidney transplantation, known as performing transplantation before initiating dialysis.[5] It has been further demonstrated that performing preemptive kidney transplantation significantly reduces the complications of renal transplantation and dialysis and was incredibly cost-effective when compared to dialysis.[6,7]

Furthermore, evidence regarding its effectiveness was well-established among studies in the literature as a safe primary management approach for patients suffering from end-stage kidney disease.[8] Therefore, this study aimed to discuss the indications, complications and outcomes of preemptive kidney transplantation based on findings from relevant studies in the literature.

Methods

This literature review was based on an extensive literature search in Medline, Cochrane and EMBASE databases which was performed on 27 October 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing potential studies, a further manual search for papers was done through Google Scholar while the reference lists of the initially included papers. Papers discussing preemptive kidney transplant of indication, outcome and complications were screened for useful information. No limitations were posed on date, language, age of participants or publication type.

DISCUSSION

Indications

The current section will discuss evidence from the different investigations regarding preemptive kidney transplantation indications, complications and outcomes. Many indications were proposed in the literature for conducting preemptive kidney transplantation procedures. In addition, it has been reported that patients with end-stage kidney disease indicated to have kidney transplantation were suitable candidates for a preemptive kidney transplant. This was based on the various advantages proposed for this modality, which urged clinicians to consider it for these patients. However, this absolute indication should be regarded as in some cases. For instance, it had been debatable whether to conduct preemptive kidney transplantation for patients with short-term life expectancy and who can continue dialysis for the rest of their lives. These patients might include patients with diabetes and elderly patients. This has been indicated in a previous retrospective study by Innocenti et al which reported that the 3-year survival rates for patients with diabetes and the elderly population (>60 years of age) were similar irrespective of whether transplantation was preemptive or not.[9] On the other hand, other investigations also demonstrated that enhanced graft and patient survival rates were recorded for patients with type I and type II diabetes mellitus.[10,11] Furthermore, the favorable outcomes were reported after undergoing simultaneous preemptive kidney-pancreas transplantation or preemptive kidney transplantation alone. These outcomes were significant from other patients that underwent non-preemptive kidney transplantation procedures. Accordingly, it has been suggested that these modalities should be indicated for high-risk patients and might be sufficient evidence for conducting preemptive kidney transplantation in these patients. However, it should be noted that other investigations also reported that the outcomes of their patients do not support the use of preemptive kidney transplantation. In this context, a previous registry-based study said that allograft survival rates were significantly higher among patients undergoing non-preemptive kidney transplantation than other patients who underwent preemptive kidney transplantation procedures.[12] This has been attributed to the potential that these patients might present donor-specific antibodies during immunosuppressive modalities. Furthermore, it has been suggested that following repeat transplantation, development or relapse of BK virus nephropathy might also occured in these patients. Accordingly, future investigations were required to evaluate the effectiveness of preemptive kidney transplantation furtherly.

Outcomes and complications

Among the different investigations in the literature, most of these studies reported that preemptive kidney transplantation was correlated with favorable outcomes including enhanced patient and allograft survival rates. These outcomes were also reported for adult and pediatric populations. For example, in previous research by Amaral et al the authors concluded that after conducting preemptive transplantation for pediatric patients suffering from end-stage renal diseases, enhanced allograft and patient survival rates were significantly noticed among this population.[13] However, it should be noted that among the patients indicated to have preemptive kidney transplantation, 4.4% died and 17.5% had graft failure at 13 years of follow up. The favorable events were furtherly displayed when these findings were compared with patients that had dialysis before transplantation. The authors indicated that the preemptive group had significantly lower death rates and graft rejection than the other group. These results were furtherly adjusted for the different demographics and other baseline variables with no change in the significance of the findings. Thus, evidence furtherly indicated the favorable events regarding allograft and patient survival rates following preemptive kidney transplantation. Most of the included

studies in the literature report consistent primary outcomes. However, some findings of these investigations might be mixed.[14-22]

It should be noted that some studies reported that the donor source could alter the transplantation outcomes. For example, previous research in North America reported that the long-term graft survival rate was significantly shortened for living donor kidney transplant recipients after pre-transplantation dialysis. On the other hand, the authors also noted that no significant outcomes were recorded for deceased kidney transplant recipients following the same intervention.[21] Another investigation that was conducted in Europe and included 1,111 participants between 1990 and 2000 reported contradicting outcomes. The authors showed that performing preemptive kidney transplantation was not associated with remarkable benefits for living donor kidney transplant recipients. On the other hand, the same intervention for reduced donor kidney transplant recipients correlated with enhanced graft survival rates. However, this favorable outcome was not noticed on the whole period of the study and disappeared within the 2nd five decades since the study started.[14] Another registry-based investigation obtained their information from the organ procurement and transplantation network database and included 3606 patients who received kidney transplantation. Among these, 28% had preemptive kidney transplantation and the group was associated with the lowest acute graft rejection rates after one year of follow up. However, it had been reported that the favorable outcomes of preemptive kidney transplantation were reported for the recipients of living and not deceased donor kidney transplantations.[19] On the other hand, research by Amaral et al reported that the favorable benefits of reduced graft rejections and mortality rates for preemptive kidney transplantation were noticed irrespective of the donor type.[13]

Despite the favorable events from preemptive kidney transplantation, not many patients were indicated to have transplantation. Estimates from different investigations suggested that the rate of conducting kidney transplantation ranged between 22.2% and 37%.[23] Evidence also indicated that the dialysis effect on pediatrics suffering from end-stage kidney disease should not be minimized, although children were less frequently exposed to having dialysis than adults. Moreover, a previous report estimated that mortality rates were 30 times higher among patients suffering from end-stage kidney disease than other patients without it.[24] The effect of transplantation was furtherly elaborated in another investigation. The authors showed that the overall 5-year survival rate was 95% following kidney transplantation compared to 82% only for peritoneal dialysis and hemodialysis. Moreover, conducting hemodialysis was correlated with an increased risk of infection. In this context, previous research estimated that infection affected 81% of patients that had hemodialysis.[23]

Despite the remarkable benefits of preemptive kidney transplantation, evidence showed that not all pediatric patients were eligible candidates.[25] For instance, it had been demonstrated that an infant with end-stage kidney disease should have a suitable weight (around 10 kg) to maintain the success of the process. In addition, preemptive kidney transplantation might also be precluded by pre-existing medical conditions including lupus and active nephrotic syndrome.[13] Finally, favorable advantages for conducting preemptive kidney transplantation also include significant cost savings. Unfortunately, despite all of these good events, only one-third of kidney transplantation procedures were presumed preemptively in the United States.[26-28]

The cause of the favorable events usually associated with preemptive kidney transplantation was not adequately understood among the various studies in the literature. A previous study by Ishani et al included 40-46 participants who received a first kidney transplantation procedure from a living donor.[29] The authors reported that based on the modification of diet in renal disease equation, graft survival rates were not remarkably correlated with the pre-transplantation estimated glomerular filtration rate (eGFR). Moreover, it was indicated that no correlation was noticed between 6-month post-transplantation and pre-transplantation eGFR. Another similar investigation also assessed these outcomes among patients with diabetes mellitus.[30] In addition, the authors reported that patient and graft survival or function did not significantly improved by having a higher pretransplantation eGFR. These effects were furtherly noted for patients with and without end-stage kidney disease. Another retrospective investigation also compared the outcomes of conducting preemptive kidney transplantation among patients suffering from end-stage kidney disease. The authors demonstrated that not conducting preemptive kidney transplantation was correlated with a substantially more enhanced posttransplantation eGFR at six months since the begging of the study.[31] However, it should be noted that the reported differences were not significant between patients that had preemptive kidney transplantation and others that had pre-transplantation dialysis. It has been furtherly reported that living donor recipients were associated with less frequent events of acute rejections. This indicated the importance of the donor factor as previously discussed, in addition to the potential immune reaction that might result from pre-transplantation dialysis.

Some barriers were also reported for conducting preemptive kidney transplantation. In this context, policies regarding cadaver kidney allocation were the primary barriers to performing this approach.[32,33] In addition, a late referral from nephrologists to the centers of transplantation also represented another barrier to achieving preemptive kidney transplantation for patients suffering from end-stage kidney disease. A previous questionnaire-based investigation aimed to assess nephrologists' perspectives about preemptive kidney

transplantation for patients with end-stage kidney disease in the United States. It has been found that most participants (71%) reported that preemptive kidney transplantation was the therapy of choice for patients suffering from end-stage kidney disease. Losing a source of revenue might be a potential reason for the delayed referral of patients from dialysis to the centers of transplantation.[34] Furthermore, it had been evidenced that preemptive kidney transplantation might be delayed due to the different concepts of the indicated patients. These included financial issues and health-related concerns about the efficacy of the procedure of transplantation. In addition, compliance with immunosuppressive medications might be reduced among patients that had preemptive kidney transplantation because these patients do not initially suffer from the various related morbidities of dialysis. Delayed graft function was also reported to occur as a complication following preemptive kidney transplantation frequently.[8,9,31,35] However, reports showed that this complication rate was remarkably variable and ranges between 2-3.7%. On the other hand, the reported rates of delayed graft functions were significantly higher among patients that had kidney transplantation after the initiation of dialysis, with an estimated rate of 4-9.7%.[9,31] We suggested that further investigations should be conducted in this context to better assess and evaluate the complications and outcomes for patients with end-stage renal disease. These adverse events should include the incidence of infections, cardiovascular diseases, and cancer. Besides, evaluation of the kidney functions and patient's quality of life is also essential on a long-term basis. Finally, these outcomes should correlate with the glomerular filtration rate following preemptive kidney transplantation to better demonstrate this modality's efficacy.

CONCLUSION

Evidence regarding the effectiveness of preemptive kidney transplantation is continuously growing. The efficacy of the approach for patients suffering from end-stage renal disease. However, the appropriate selection of the patients is a critical issue. Besides, serious efforts should be exerted to prepare the patient perioperatively. Nevertheless, kidney functions were reported to increase following preemptive kidney transplantation. Graft rejection and delayed graft functions were also reported to follow preemptive kidney transplantation. However, the estimated rates are lower than those for patients having transplantation following the start of dialysis. We encourage further relevant investigations to be conducted for further elaboration on the long-term outcomes and complications.

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