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Original Article

Clinical outcome of type 2 diabetic patients after kidney transplantation: Systematic review

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ABSTRACT

Aim: To conduct a systematic review to summarize the outcome of adult patients with history of type II DM after renal transplantation [RTx] in following category of patients: (1) type 2 DM; (2) type 2 DM vs Non-DM; (3) type 2 DM vs Dialysis; (4) Preemptive Kidney Transplant (prekTx) vs non prekTx.
Method: MEDLINE, EMBASE, Renal transplant registries were searched for observational/cohort/case-control studies from 1980 to 2015.
Results: We identified 10 studies reporting outcome of kidney transplantation in patients with type 2 DM [type 2 DM (2), type2 DM vs Non-DM (6), type 2 DM vs Dialysis (1), prekTx vs non-prekTx (1)]. One and five year graft survival ranged from 76% to 100% and 53% to 96% respectively. 8, 4, 8, and 2 studies showed 1, 3, 5 and 10 yr patient survival respectively. Recent study with type 2 DM patients showed at 10 yrs, graft survival did not differ between Non-DM and type 2 DM but Non-DM patient survival was better ($p < .001$) than type 2 DM patients after RTx. At 5 yrs, patient survival ranged from 29% to 97%. Graft and patient survival did not differ between type 2 DM and Non-DM patients in three and two studies respectively. A study showed at 10 yrs, survival after RTx was significantly ($p < .001$) better than patients on dialysis. Preemptive transplant study reported lower adjusted graft failure and mortality risk for type 2 DM transplant recipients from living donors compared to deceased donors.
Conclusion: Results from these few single center studies demonstrate the need for multicenter rigorous studies to look at long term survival of type 2 diabetes patients after renal transplant.

1. Introduction

Diabetes mellitus (DM) is the single most important cause of renal disease worldwide.[1] Type 2 DM is a growing cause of end stage renal failure worldwide.[2] With increasing prevalence of diabetes, diabetic nephropathy has become a worldwide epidemic which is the most common cause of end-stage renal disease (ESRD).[3] According to the US Renal Data System (USRDS) 2014 report (with 2012 data), 44% of total ESRD causes are diabetic nephropathy (DN).[4] Mode of treatment for DN patients is still not very clear.

Till 1990, type 2 DM patients were less likely to be referred for renal transplantation as they are older, obese and present significant comorbidities.[5] Preexisting CVD burden in diabetic patients showed high mortality in dialysis and kidney transplant patients. Consequently, proportion of patients who used to survive for a long time to experience the nephropathy risk was small. However, by analyzing kidney transplant patients from USRDS and comparing them with adult kidney waitlisted patients, Herwig-Ulf Meier-Kriesche had shown that restoring renal function by kidney transplant might lower the risk of CVD over time.[6]

For transplants performed before 1988, the survival rate was significantly lower in diabetic groups as compared to other groups; but, survival of diabetic patients showed comparable results to survival of non-diabetics after adoption of a series of new procedures after 1988.[3] Individual studies have indicated that kidney transplant is a better option even for diabetic patients compared to other modes of RRT and is associated with lower risk of mortality.[7] Wolfe in his longitudinal study on dialysis patients showed that among diabetic patients, projected years of life with transplant were higher than projected years of life without transplant (on dialysis).[8]

There has been little systematic exploration of how beneficial renal transplant is with pre-type 2 diabetic patients. We conducted a systematic review to summarize the outcome [survival] of renal transplant on adult patients with a history of type 2 diabetes. Since

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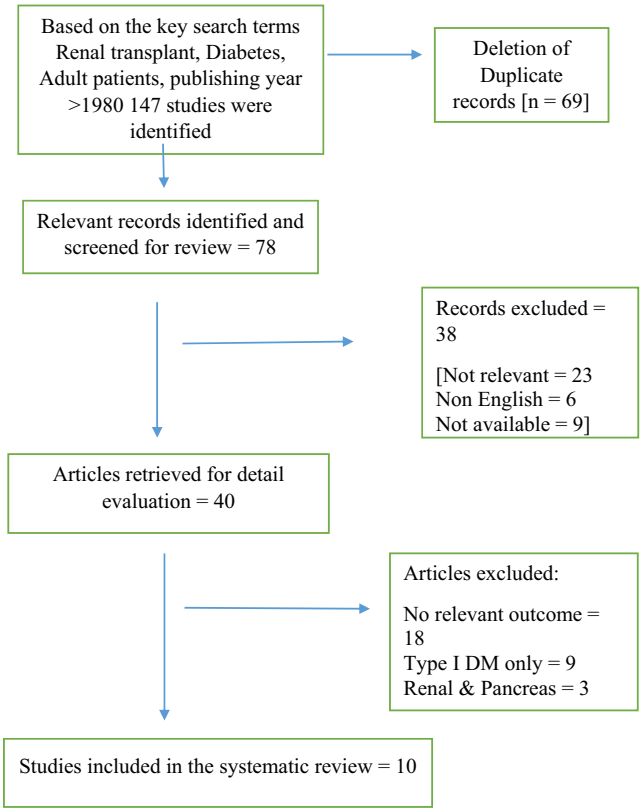

Fig. 1. Flow chart of articles search strategy.

renal transplantation for type 1 diabetic patients is now widely accepted,[1,8] and results of kidney transplantation with type 2 diabetes is scarce,[1] we decided to explore survival of patients with a history of type 2 diabetes. We looked at survival of type 2 DM patients after RTx and compared survival of type 2 DM with Non-DM after RTx. Third and fourth comparisons were type 2 DM vs dialysis and preemptive KidneyTx (prekTx) vs nonprekTx. We reviewed outcome in terms of 1, 3, 5, and 10 yr graft and patients survival, immunosuppressant used and author's remarks. Additionally we looked at adverse events, death, and infections.

2. Methods

A comprehensive search was conducted to identify all relevant studies by using Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).[9] Studies conducted in English language were included. Databases such as MEDLINE, EMBASE and evidence based medical reviews were searched. The detail search strategy is shown in Fig. 1. Study was selected for further review after an agreement between the two experts.

2.1. Study selection

Study eligibility criteria were predetermined by two reviewers. Studies were appropriate for inclusion if the study reported important clinical outcomes such as patient and graft survival, infections, rejections, cardio vascular events, malignancies and cause of death in renal transplant and dialysis population. Studies with pediatric, adolescents (age $<$ 16 yrs) and studies on multi organ or pancreas transplantation were excluded. Preference was given to studies including more than thirty participants in each treatment modality group to increase the statistical power and to minimize bias. However due to unavailability of enough published literature on renal transplant with diabetic patients, we had to compromise by including studies with sample size less than 30 in each group. The results reported here are only for single transplant. Observational/Cohort/Case–control studies from year 1980 to 2014 were included.

2.2. Risk of bias assessment

We assessed and reported risk of bias in included studies using items from the Downs and Black checklist.[10] These include items of study design, statistical analysis, and results. We included two items specifically relevant to the time-to-event analyses in these studies: (1) selected time of origin, and (2) adverse events. Two reviewers independently assessed each included study.

2.3. Data extraction

The following properties were extracted from each study: characteristics (country, data source, study period, duration of follow-up, subgroups and populations, sample size), participants' age, gender, and co morbidities, renal replacement modality (living or deceased donor: LD or DD, hemodialysis, peritoneal dialysis, etc.) and survival outcome (1 yr, 3 yr 5 yr and 10 yr survival). Other outcomes observed were: rejections, infections, cardiac events, and malignancies.

2.4. Data synthesis

The studies were few and from diverse populations; it was not possible to pool the data from these various studies. To facilitate comparison, we have presented individual study summary statistics for the variables in Tables 1a and 1b.

3. Results

3.1. Search result

As shown in Fig. 1, from 147 identified citations, 78 articles were recovered for detailed evaluation of which 10 studies were suitable for this review (only type 2 DM = 2,[2,11] type 2 DM vs Non-DM = 6,[1,12–16] transplant vs Dialysis = 1,[17] and Preemptive vs non preemptive = 2).[18] Study sample size ranged from 7 to 808.

3.2. Population studied

All studies have used retrospective data. All studies were carried out in single center except one that had used data from Scientific Registry of Transplant Recipients (SRTR). Some studies had recruited type I, type II and Non-DM,[18] or IDDM, NIDM, PTDM, Non-DM and coexisting DM[14] or PreDM, or pancreas – kidney transplant[18] patients. However for this systematic review, outcome after kidney transplant related to type 2 DM, type 2 DM vs Non-DM was studied. Age of participants was 35 yrs and over. There were more male than female patients. Three studies used matched controls. Treatment of immunosuppressant was reported by 8 out of 10 studies. 1–10 yr survival of RTx patients is shown in Table 1a.

3.3. Risk of bias assessment

The risk was assessed by scoring if aims/objective, method, interventions and study design were clearly described. Patient characteristics were included. Study findings such as adverse events were reported with clarity, and study outcome was well explained.

It was observed that studies provided demographic information (90%), screening procedure (71%), method (96%), immunosuppressant (87.5%), pre transplant risk factors (RF) (58%),