

Analysis of waiting times on Irish renal transplant list

Phelan PJ, O'Kelly P, O'Neill D, Little D, Hickey D, Keogan M, Walshe J, Magee C, Conlon PJ. Analysis of waiting times on Irish renal transplant list. Clin Transplant 2009 DOI: 10.1111/j.1399-0012.2009.01085.x. © 2009 John Wiley & Sons A/S.

Abstract: Introduction: A number of recipient variables have been identified which influence waiting list times for a renal allograft. The aim of this study was to evaluate these factors in the Irish population.

Methods: We examined patients accepted onto the transplant list from January 1, 2000 until December 31, 2005. Inclusion criteria were adults listed for kidney only, deceased donor transplants. We included patients previously transplanted. Patients were censored, but still included in the analysis, if they died while on the list, permanently withdrew from the list or if they were not transplanted at the time of the study.

Results: There were a total of 984 patients accepted onto the waiting list during the study period, of which 745 of these were transplanted. Factors significantly associated with longer waiting times included age above 50 yr, blood group O and high peak panel reactive antibodies level. Gender and patient body mass index were not associated with longer waiting times.

Conclusion: We have identified factors associated with a longer waiting time on the Irish cadaveric renal transplant list. This information can help our patients make informed decisions regarding likely waiting times and the merits of living related transplantation.

**P.J. Phelan^a, P. O'Kelly^a,
D. O'Neill^b, D. Little^c, D. Hickey^c,
M. Keogan^b, J. Walshe^a,
C. Magee^a, P.J. Conlon^a**

^aDepartment of Nephrology, Beaumont Hospital,

^bNational Histocompatibility and Immunogenetics Service for Solid Organ Transplantation (NHISSOT), Beaumont Hospital and ^cDepartment of Transplantation, Beaumont Hospital, Dublin, Ireland

Key words: ABO blood group – body mass index – kidney transplantation – panel reactive antibodies – waiting list

Corresponding author: Paul Phelan, Beaumont Hospital–Nephrology, Beaumont Rd., Dublin 9, Ireland.

Tel.: +353 1 8092732; Fax: +353 1 8092899; e-mail: paulphel@gmail.com

Accepted for publication 30 July 2009

Renal transplantation remains the optimal treatment for end-stage renal disease (ESRD) (1). Numbers waiting for allografts are increasing worldwide on a yearly basis (2, 3). The transplantation communities are struggling to meet this increasing demand using deceased donor kidneys. Some authors predict waiting times of up to 10 yr will soon be common in USA transplant programs (4). In Ireland, living donors have traditionally only made up a tiny proportion of total allograft donors although this is beginning to change with the introduction of a dedicated living donor program. There are known demographic and clinical factors that affect waiting time to transplantation (5). These include age, blood group and level of antibody sensitization. We aimed to examine the influence of these factors, in addition to sex and body mass index (BMI), on renal transplant waiting time. This would enable us to estimate likely waiting times for individual patients and counsel our patients on the merits of living

donation, especially those who are likely to wait for extended periods on the deceased donor list.

Methods

Patients

Our institution is the only kidney transplantation center in the Republic of Ireland. We studied patients who were waitlisted for renal transplantation between January 1, 2000 and December 31, 2005. Patients included were adults (≥ 19 yr), listed for a deceased donor, kidney only transplant. We included second and subsequent transplants.

Organ allocation

At our center, the following organ allocation strategy was in place during the study period, with decreasing order of priority: patients on a desensitization protocol/ABO compatible list (highest

clinical urgency), pediatric recipients, acceptable mismatched patients with high antibody sensitization (peak panel reactive antibodies [PRA] >80%), best human leukocyte antigen (HLA) matched, low matchability patients (based on our populations HLA profile) and longest waiting time. All groups are sub-sorted by time waiting and simultaneous pancreas/kidney and liver/kidney patients are pre-selected and get priority for an organ directly.

Statistical analysis

Waiting time was calculated from initiation onto the active waiting list until time of transplantation. Patients were censored if they died while on the pool, permanently withdrew from the pool or were not transplanted by the date of study analysis in February 2008. Censored patients were still, however, included in the analysis. The following factors were examined as part of a multi-factorial model: patient age > 50 yr, sex, BMI above and below 25, ABO blood group and PRA divided into $\leq 10\%$, 11–49%, >50%. PRA was determined by use of the complement-dependent cytotoxicity (CDC) assay, NIH Basic technique.

A combination of paper records, our renal patient database (CLINICAL VISION 3.4a Version 1.1.34.1) and the National Histocompatibility and Immunogenetics Service for Solid Organ Transplantation (NHISSOT) database was used to access patient details. Cox proportional hazards models were used to analyze outcome where the notion of hazard was reversed from its normal definition to encompass the event of transplantation. The model was tested for proportional hazards assumption (6), and this assumption was contradicted when BMI of subjects was included. For this reason, a stratified proportional hazards model was used with discrete years on transplant pool used as the stratified groups. STATA (version 8; Stata Corp., College Station, TX, USA) was used for the analysis, and a p-value of less than 0.05 was deemed to be significant.

Results

There were 984 patients meeting the inclusion criteria accepted onto the transplant list during the study period, of which 745 were transplanted. Of all those accepted onto the list, almost 63% were male with a mean age of 45.2 yr (range 19–76 yr). Sixty percent were above the age of 50 yr (see Table 1 for baseline demographics). A total of 54 patients who had been approved for the waiting list

Table 1. Baseline waiting list patient characteristics

Age	
Mean (SD)	45.3 (14.3)
% >50 yr	60.0%
Sex (% M/F)	62.8%/37.2%
BMI, mean (SD)	
Male	25.19 (4.25)
Female	24.31 (3.46)
PRA	
$\leq 10\%$	65.1% (n = 633)
11–49%	9.1% (n = 89)
$\geq 50\%$	25.8% (n = 251)
ABO blood group	
A	29.7% (n = 289)
B	10.9% (n = 106)
AB	3.2% (n = 31)
O	56.2% (n = 548)

died without being transplanted. Of these, 13 were active on the list at time of death and 41 had been suspended from the list due to poor health before death.

In a multifactorial model, there was no significant difference in waiting times for males as compared to females ($p = 0.699$); however, those less than 50 yr had significantly shorter waiting times than over 50 yr of age ($p = 0.008$). Patients < 35 yr ($n = 274$) had the shortest waiting time as compared to the older patient groups (35–49 yr [$n = 315$], 50–64 yr [$n = 309$] and > 65 yr [$n = 86$]; $p = 0.001$).

The mean BMI was 25.19 (± 3.46) for male patients and 24.31 (± 4.25) for females. We compared overweight/obese patients (BMI ≥ 25) to those with normal weight/underweight (BMI < 25) as part of the multifactorial model. This showed no significant difference in waiting times between the two groups ($p = 0.166$).

ABO blood group

Over 56% of those on the list were blood group O, 29.7% were group A, 10.9% were group B and 3.2% were group AB. This breakdown was similar to actual donor characteristics and Irish

Table 2. Blood group comparisons for Irish population, donors and wait list patients

Blood group	% Irish population ^a	% Donor population (2000–2005)	% Transplant list (2000–2005)
O	55	56.0	56.2
A	31	31.0	29.7
B	11	11.2	10.9
AB	3	1.8	3.2

^aIrish Blood Transfusion Service.

population figures in general (see Table 2). ABO blood group was also a significant factor regarding waiting times, with blood group O patients waiting the longest ($p = 0.007$, see Fig. 1). In our study, 7% of group O allografts were allocated to non-O recipients (18 to group A, 11 to group B and none to AB; see Table 3).

PRA

Most of the pool had a low level of antibody sensitization, with 65.1% having a PRA $\leq 10\%$. Fewer than 26% had a PRA $\geq 50\%$. For the three levels of sensitization (PRA $\leq 10\%$, 11–49%, $\geq 50\%$), there was a stepwise increase in transplant waiting time that was highly significant ($p < 0.001$, see Fig. 2).

Combining the results for ABO blood group and PRA, patients in group O waited significantly longer across all levels of antibody sensitization. Median waiting times in patients with PRA $\leq 10\%$ for blood group A, B, AB and O were 10.6, 8.0, 7.9 and 14.9 months, respectively. For the intermediate PRA patients (11–49%), the waiting times were 12.5, 18.8, 19.9 and 31.6 months, respectively. For those with the highest PRA, group O patients waited almost double the time of group B patients (24.2 vs. 47.2 months, see Fig. 3). Group A had a median wait of 32.8 months, and there were no transplants in group AB patients with a PRA $\geq 50\%$.

Discussion

This study demonstrates patient factors that are associated with an extended waiting time on the deceased donor renal transplant pool. Up to now, it has been difficult for us to predict likely

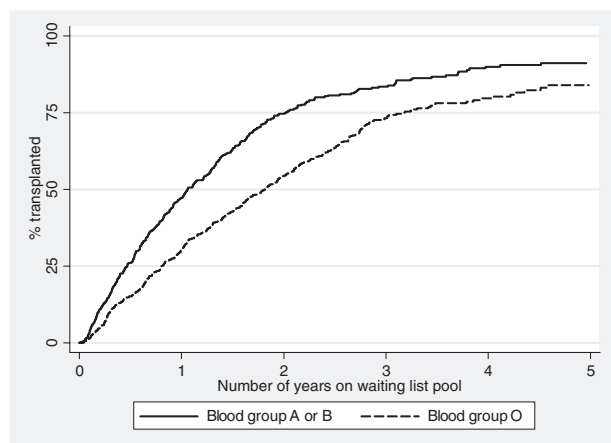


Fig. 1. Numbers transplanted by ABO blood group (log rank test, $p < 0.001$).

Table 3. Allocation of transplanted kidneys by blood group

Recipients	Donor kidneys				Total
	A	AB	B	O	
Blood group					
A	224	0	0	18	242
AB	5	13	5	0	23
B	0	0	78	11	89
O	0	0	0	385	385
Total	229	13	83	414	739

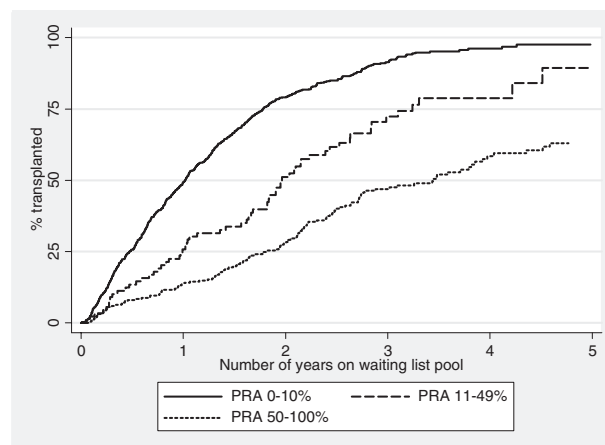


Fig. 2. Numbers transplanted by PRA level (log rank test, $p < 0.001$).

waiting times for individual patients. It is encouraging to see no difference in time waiting on the pool between males and females. Previous studies have shown longer waiting times for females (7), and also have findings to suggest females face barriers in being activated on the list to begin with (7, 8). It must be noted that 62.8% of our pool was male, which may be accounted for by a larger proportion of males developing ESRD. Indeed, the national renal review (Ireland) states the gender distribution of ESRD patients in Ireland is 59% male and 41% female (Renal Disease in Ireland – A Strategic Review [unpublished]). This is similar to recent reports from the UK, where 62% of incident patients starting renal replacement therapy were male (9). However, our study does not examine access to the transplant list and we must be careful in presuming equality to transplantation access on the basis of similar waiting times alone.

We did not show a longer waiting time for patients with a higher BMI. Obesity has been associated with longer waiting times in other programs. Segev et al. recently reported that the likelihood of receiving a kidney transplant, for

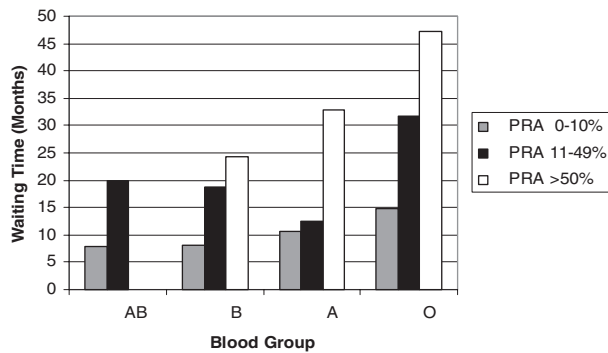


Fig. 3. Median waiting time in months based on PRA level and blood group.

those already on the transplant pool, decreased with increasing degrees of obesity, measured by BMI. They also showed that the likelihood of being bypassed when an allograft became available increased in a graded manner with category of obesity, beginning with a BMI > 25 (10). Moreover, a survey of UK transplant units showed that 60% of centers exclude those with a high BMI, the average cut-off being BMI > 35 (11). In Ireland, a BMI cut-off of 32 has recently been introduced in assessing candidates for renal transplantation and patients can face delays being accepted onto the pool if they are very overweight.

We confirmed that increasing recipient age resulted in a lower likelihood of receiving an allograft. This was despite excluding pediatric patients < 19 yr of age who are prioritized in most transplantation programs including our own. When we examined this age effect a little closer, it was particularly those aged < 35 yr who had significantly shorter waiting times as compared to older wait-listed patients. In a study by Schold and Meier-Kriesche, increased candidate age was associated with the likelihood of not receiving a transplant during the period on the waiting list. This was as a result of mortality and also related to morbidity and delisting (12). In this study, the age effect remained even after censoring for mortality. This leaves patient co-morbidity and delisting as the likely reason for this effect.

Our study confirms previous work showing longer times waiting for blood group O patients (13). However, our blood group B patients had waiting times similar to the other non-O groups which is different to other populations (14). Group O had significantly longer times on the list across all levels of PRA. ABO compatible (non-identical) transplantation may occur if deemed clinically urgent or if the recipient is highly sensitized (PRA > 50%,

approximately 26% of our waiting list), although this is not routine. However, it is routine for pediatric transplantation. Therefore, some group O allografts are donated to non-group O recipients, which amounted to 29 kidneys in our study.

Higher levels of PRA severely decreased the chances of receiving an allograft. This was evident even with a moderate increase in PRA. In blood groups AB, B and O, there was more than a doubling of waiting times compared in the PRA 11–49% range compared to the ≤ 10% PRA group. Blood group O patients waited particularly long on the pool with higher levels of sensitization (median wait over 47 months for Group O with ≥ 50% PRA). A possible limitation of the study is that during the study period only complement fixing antibodies were included in PRA (CDC assay) rather than newer, more sensitive techniques of antibody detection which have more recently become available (15). PRA measured by CDC on peripheral blood mononuclear cells, as used in this study, does not detect HLA class II or non-complement fixing antibodies.

Our study demonstrates that the majority of our listed-patients eventually get transplanted. Moreover, our overall waiting times appear to be less than those in North America, which were reported for new candidates as ranging around 1100–1200 d between 1998 and 2003 (16). Deceased-donor organ donation is similar in Ireland and the USA (approximately 20 donors per million population [p.m.p.] in 2002) and compares well internationally (17). However, the difference in waiting times is undoubtedly due to differences in ESRD prevalence. For example, in 2004, prevalence of dialysis patients (HD and PD) in North America was 1030 p.m.p. (18) as compared to 304 p.m.p. in Ireland (19).

We have shown that certain groups of individuals wait longer for a deceased donor transplant. The characteristics associated with longer waiting times are readily available; thus, these, results should prove useful in providing newly-listed patients with an approximate idea of how long they will be required to wait for a deceased donor kidney transplant. It has been demonstrated that increased waiting times from one to three yr decreased the overall survival benefit of renal transplantation from 7.1 to 5.6 yr in a database of over 60 000 patients (20). These results are thus an important reminder to us to minimize sensitizing events, specifically blood transfusions, in potential renal transplant recipients. The results also suggest that we should be targeting our patients with likely long waiting times and actively promoting the merits of living donor transplantation.

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