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Factor	High PRA	Low PRA	Signif cance
Overall	125 (18.7%)	543 (81.3%)	
Mean age	50.8	52.7	-
Elderly (>65)	17 (13.6%)	105 (19.3%)	-
Sex (male)	72 (57.6%)	170 (31.3%)	**
White	91 (72.8%)	384 (70.7%)	-
Black	28 (22.4%)	122 (22.5%)	-
Hispanic	4 (3.2%)	27 (5.0%)	-
Asian	2 (1.6%)	10 (1.8%)	-
Mean PRA	55.8	1.6	**
Retransplant	56 (44.8%)	124 (22.8%)	**
* p<0.05, ** p<0.005			

Table 1: Recipient demographic and general information.

At the time of the procedure, patients were treated with 25 mg of diphenhydramine intravenously (IV), induction immunosuppression with methylprednisolone 500 mg intravenously (IV) (Solu-Medrol, Pfizer, New York, NY), mycophenolate sodium 540 mg by mouth (PO) (Myfortic, Novartis Pharmaceuticals, Basel, Switzerland), and ALE 30 mg IV was administered.

The post-operative steroid taper consisted of: methylprednisolone 250 mg IV on post-operative day 1, methylprednisolone 125 mg IV on post-operative day 2, prednisone 60 mg PO on post-operative day 3, prednisone 40 mg PO on post-operative day 4, and, finally, prednisone 20 mg PO on post-operative day 5.

Starting on post-operative day 1, Tacrolimus 1.5 mg PO (Prograf, Astellas Pharma, Tokyo, Japan) and mycophenolate sodium 540 mg PO twice per day were given (Novartis, nutley, NJ). Tacrolimus levels were measured and titrated to the correct dose. Side effects permitting, mycophenolate sodium was increased to 720 mg PO at discharge. Steroids were generally tapered to off by one month.

Antimicrobial prophylaxis was started post-operatively with sulfamethoxazole (800 mg)-trimethoprim (160 mg) 1 tab PO (Bactrim DS, AR Scientific, Philadelphia, PA) 3 times per week and clotrimazole troche 10 mg dissolved in the mouth 4 times per day following oral care. Valgancyclovir 450 mg PO (Valcyte, Hoffman-La Roche, Basel, Switzerland) was prescribed based on established risk factors.

Statistical analyses were performed using SPSS, Version 21 (IBM, Armonk, New York). For categorical variables we used Pearson's Chi-squared test. For continuous variables we used independent T-test. Survival curves were calculated using the life table method. P-values of less than 0.05 were considered significant.

A total of 668 patients underwent kidney transplantation, alemtuzumab induction, and recorded serum PRA profiles. 125 of the 668 patients measured a pretransplant PRA >20%. Baseline characteristics for patients (Table 1) and donor kidneys (Table 2) were stratified according to the PRA level group. Donor characteristics were comparable between groups. The low PRA group had a higher percentage of CMV+ mismatch donors than the high PRA group (p=0.036).

Recipient demographics between the two groups were similar, as shown in Table 2. The most notable differences were a higher percentage of males and patients undergoing retransplant in the high PRA group (44.8%) compared to low PRA (22.8%). Baseline characters for reasons for renal complications requiring transplantation were also similar for both groups, with the exception of significant difference in the proportion of patients requiring transplantations due to previous graft failure: 9.7% for the high PRA group, 1.7% for the low PRA group. Mean PRA in the high PRA group was 55.8 while the low PRA group was 1.6. The mean recipient age at time of transplant for high PRA and low PRA was 50.8 years and 52.7 years, respectively.

Overall patient survival was 88% for the high PRA group and 83.6% for the low PRA group with no statistically significant difference between them (p=0.274). Patient survival rates at 1 year were 98.2% in the high PRA group and 95.5% in the low PRA group (p=0.286); at 3 years 92.7% high PRA, 89.0% low PRA (p=0.426); at 5 years 87.3% high PRA, 83.4% low PRA (p=0.476), with no significant difference at each time point (Figure 1).

Overall death censored-graft survival (Figure 2) was significantly lower in the high PRA group (77.6%) compared to low PRA (87.5%) (p=0.007). At 1 year, death-censored graft survival presented as 93% in the high PRA group and 95% in the low PRA group with no statistical significance (p=0.343). Death censored-graft survival up to 3 years, however, was 79.3% for the high PRA group and 91.3% for the low PRA group (P=0.003). At 5 years: 73.2% in the high PRA group and 85.9% in the low PRA group (P=0.013).

Overall graft rejection survival rates (Figure 3) were 33.6% in the high PRA group and 25.4% in the low PRA group (p=0.073). However, at 1-, 3-, and 5-years, there was no significant difference between groups (p=0.556, p=0.199, p=0.229, respectively).

Graft loss in both groups was primarily due to death and acute rejection, but while loss due to death was 20% and 51.1% in the high PRA group and low PRA group, respectively (p<0.05), loss due to acute

Factor	High PRA	Low PRA	Signif cance
Mean KDPI	36.7	40.7	0.121
Deceased donation	96 (76.8%)	402 (74%)	0.57
ECD	13 (13.7%)	46 (11.4%)	0.596
DCD	87 (90.6%)	362 (90.0%)	1
Donor CMV+	62 (53%)	290 (54.4%)	0.838
Donor race mismatch	38 (30.4%)	180 (33.1%)	0.598

Table 2: Donor information.

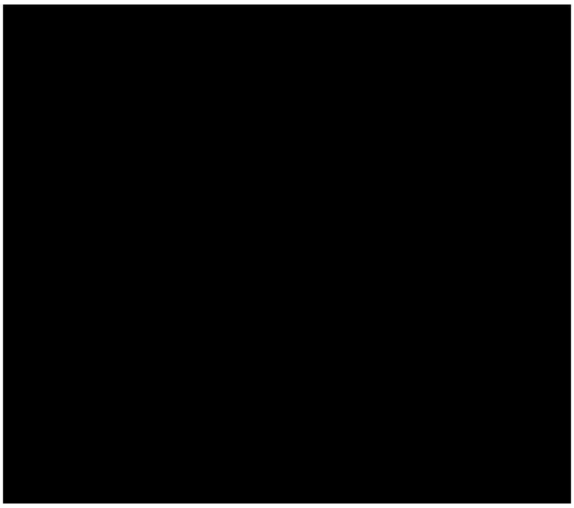

Figure 1: Kaplan–Meier overall survival curve in days in the set of 668 patients stratiýed according to PRA level.

rejection was 34.1% in the high PRA group and 10.1% in the low PRA group ($p<0.05$). These results are shown in Table 3.

Time (in days) to negative outcomes was also recorded. Of those who experienced a negative outcome, there was no significant difference between the two groups in mean time to graft rejection (high PRA: 336.4, low PRA: 279.9, p=0.466), graft loss (high PRA: 722.5, low PRA: 960.6, p=0.122) and patient death (high PRA: 1329, low PRA: 1067, p=0.533).

Hazard ratio analyses are displayed in Table 4. Age (HR 0.98, CI 0.967-0.994, SI: 0.004), KDPI (HR 1.013 CI 1.005-1.021 SI 0.001), and expands on other studies that suggest that the use of alemtuzumab and subsequent steroid freedom for kidney transplant convey early protective effects, but these effects may not translate to long term graft survival and tend to delay occurrences of acute rejection [17-19]. Overall, alemtuzumab allows for high risk patients to experience a short-term period where their rate of graft loss is equivalent to that of their low risk counterparts. After this honeymoon period, however, the protective effects of alemtuzumab taper and the patient is left at risk. We therefore see the benefits of maintaining these high risk patients on a long-term steroid regimen in attempt to avert an otherwise expedited decline in graft function.

Some studies have demonstrated the potential of immunosuppressive induction therapy to reduce the disparity between negative outcomes of extended versus standard criteria (including deceased vs living) donor kidneys [20-22]. Khalafi-Nezhad et al. found no distinct difference in rejection rates from deceased or living donor kidney recipients [23]. Similarly, we report no significant difference in rejection rates between deceased or living donor kidney recipients in both high and low PRA groups. However, we found donor type to be

When comparing patient outcomes between high PRA and low PRA patients, an interesting unrelated trend was observed. Our analysis shows that being of black ethnicity was actually protective in terms of patient death for the control low PRA group (p=0.026) but not for the high PRA group. For the high PRA group, being black played no significant role in patient death, graft loss, or rejection, suggesting that alemtuzumab may equalize some disparities in ethnicity. It is reasonable to assert that alemtuzumab may be a good choice for high risk black transplant recipients. Although, alemtuzumab already has proven its usefulness in this regard in previous study [25,26].

Previous studies have demonstrated the benefits of Alemtuzumab and minimal steroid usage in kidney transplant. However, few have acknowledged the long term consequences of such a protocol within high risk recipient populations. Our research contributes meaningful findings on this matter while concurrently expanding the analysis to include many groups of high risk recipients, including those with elevated PRA. Additionally, with the proportion of highly sensitized patients in our study being comparable to others (18.7%), a respectable sample size was maintained and used for this analysis. Furthermore, uniform pre- and post-operational transplant protocols were used throughout.

While the effectiveness of alemtuzumab in this study shows promising results, there are three main limitations: first, the retrospective nature of this study leads to difficulties in drawing absolute conclusions. Secondly, our sample lacks a direct comparison of other induction methods, including no induction at all, to alemtuzumab. Lastly, as a result of our single center study, these results may not be applicable to all centers.

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Alemtuzumab is effective at eliminating the negative outcome disparities between high PRA and low PRA kidney recipients. Patient survival and rejection rates of high risk, high PRA patients were similar to their low PRA counterparts. However, the short-term effectiveness of alemtuzumab in improving graft survival may not directly translate to long-term elimination of this disparity, and require further study of whether this is a result of alemtuzumab itself, or subsequent steroid freedom. Other transplant outcome risk factors, in addition to elevated PRA, also play key roles in determining the efficacy of alemtuzumab in kidney transplantation. This analysis suggests that kidney recipients presenting with elevated PRA in addition to other compounding high risk factors may still benefit from alemtuzumab without complete steroid withdrawal.

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Stanton, A: Drafting Article/Data interpretation

Naji, M: Drafting Article/Data interpretation

Mitro, G: Statistical analysis

Rees, M: Paper review

Ortiz, J: Study design, paper review and editing

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