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# Outcomes of Older Primary Kidney Transplant Recipients by Induction Agent and High-risk Viral Discordance Status in the United States

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**Background.** The impact of induction type or high-risk viral discordance on older kidney transplant recipients is unclear. Herein, we analyzed the association between induction type, viral discordance, and outcomes for older recipients. **Methods.** We analyzed the Scientific Registry of Transplant Recipients standard analysis file for all primary kidney transplant recipients older than 55 y who were transplanted between 2005 and 2022. All transplants were crossmatch negative and ABO-compatible. Recipients were discharged on tacrolimus and mycophenolate ± steroids. Recipients were categorized into 3 groups by induction received: rabbit antithymocyte globulin (r-ATG; N = 51 079), interleukin-2 receptor antagonist (IL-2RA; N = 22 752), and alemtuzumab (N = 13 465). Kaplan-Meier curves were generated for recipient and graft survival, and follow-up was censored at 10 y. Mixed-effect Cox proportional hazard models examined the association between induction type, high-risk viral discordance, and outcomes of interest. Models were adjusted for pertinent recipient and donor characteristics. **Results.** Induction type did not predict recipient survival in the multivariable model, whereas Epstein-Barr virus high-risk discordance predicted 14% higher mortality (1.14 [1.07-1.21], $P < 0.01$). In the multivariable model for death-censored graft survival, alemtuzumab, but not IL-2RA, was associated with an increased risk of graft loss (1.18 [1.06-1.29], $P < 0.01$) compared with r-ATG. High-risk cytomegalovirus discordance predicted 10% lower death-censored graft survival (1.10 [1.01-1.19], $P < 0.02$). Live donor and preemptive transplantation were favorable predictors of survival. **Conclusions.** In this large cohort of older transplant recipients, alemtuzumab, but not IL-2RA, induction was associated with an increased risk of graft loss compared with r-ATG. Cytomegalovirus and Epstein-Barr virus high-risk viral discordance portended poor graft and recipient survival, respectively.

(*Transplantation Direct* 2024;10: e1698; doi: 10.1097/TXD.0000000000001698.)

*Received 21 June 2024. Revision received 10 July 2024.*

*Accepted 12 July 2024.*

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*The authors declare no funding or conflicts of interest.*

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*ISSN: 2373-8731*

*DOI: 10.1097/TXD.0000000000001698*

Kidney transplantation remains the preferred choice for renal replacement therapy, proving beneficial even for older recipients. However, death with a functioning graft remains a prominent cause of graft loss. Recently, our group investigated graft failure in a cohort of nearly 6000 adult recipients,[1] revealing varied causes across different age groups. Although immunologic loss significantly diminished after the age of 55 y, death with a functioning graft exhibited a remarkable increase. The age of kidney transplant candidates continues to increase—the recent Scientific Registry of Transplant Recipients (SRTR) annual data report[2] indicates that 25.4% of active transplant candidates are older than 65 y, and the proportion of recipients older than 50 y at the time of transplantation was 60.8%.

Immunosenescence is characterized by a decline in adaptive immune capabilities and an overcompensation of innate immune responses, leading to a proinflammatory state.[3] It is strongly influenced by older age and chronic renal failure. Crepin et al[4] reported adverse kidney transplant outcomes associated with immunosenescence, and the same group published findings on the link between different induction agents and the degree of immunosenescence.[5-7]

The frequency of opportunistic infections and malignancies increases with age and may vary based on induction type.[8] Our group has studied the association between induction type

and kidney transplant outcomes in various transplant populations, including pediatric recipients,[9,10] recipients living with human immunodeficiency,[11] glomerulonephritis recipients, and second kidney transplant recipients.[12,13] Long-term outcomes, such as recipient or kidney allograft survival, can differ among specific subgroups. Recipients of second preemptive kidney transplants had an increased risk of graft loss with alemtuzumab compared with rabbit antithymocyte globulin (r-ATG), and those living with HIV had improved survival in association with nondepletional induction. In this context, our study aimed to explore the association between induction type and the long-term survival of recipients and kidney grafts among older transplant recipients. Additionally, we assessed the association between high-risk discordancy for cytomegalovirus (CMV) and Epstein-Barr virus (EBV) and long-term recipient and graft survival.

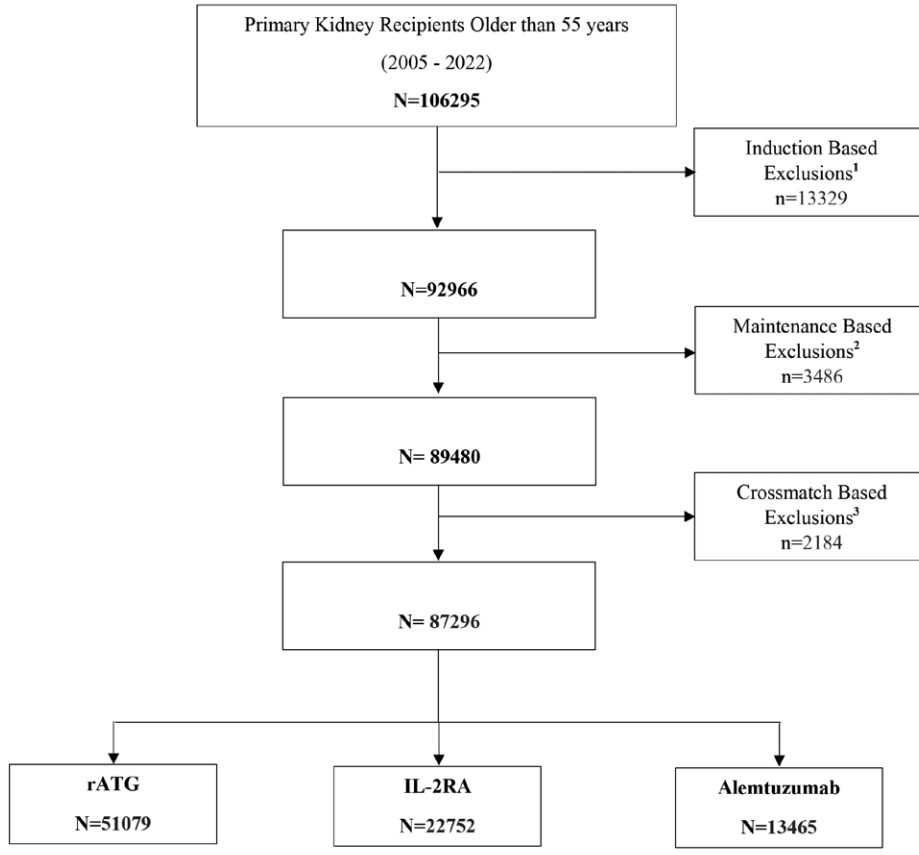
## MATERIALS AND METHODS

### Data Source

This study used data from the SRTR. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the Organ Procurement and Transplantation Network and SRTR contractors. The Mayo Clinic Institutional Review Board (INC8014532) exempted the study.

### Study Population

We analyzed the standard analysis file for all primary transplant recipients aged 55 y or older who received kidney transplants between 2005 and 2022 (N = 106 295). Recipients who did not receive induction or received induction other than r-ATG, interleukin-2 receptor antagonist (IL-2RA), or alemtuzumab were excluded (n = 13 329). Recipients discharged on maintenance regimens other than tacrolimus and mycophenolate with or without steroids were excluded (n = 3486). We also excluded recipients with a positive crossmatch or those who were ABO incompatible (n = 2184). Our cohort consisted of 87 296 recipients who received a single induction agent, of whom 51 079 received r-ATG induction, 22 752 received IL-2RA, and 13 465 received alemtuzumab (Figure 1).




1. Induction based exclusions: use of unusual agents, combination agents, missing or no-induction

2. Maintenance based exclusions: missing immunosuppression or other regimens than Tacrolimus/MMF with or without steroids

3. Missing, positive, or weakly positive crossmatch.

**FIGURE 1.** Study population.

**TABLE 1.**

**Baseline characteristics of older kidney transplant recipients**

| | r-ATG (N = 51 079) | IL-2RA (N = 22 752) | Alemtuzumab (N = 13 465) |
|---|---|---|---|
| Recipient age group | | | |
| 55–65 y | 33 323 (65.2%) | 11 871 (52.2%) | 9904 (73.6%) |
| >65 y | 17 756 (34.8%) | 10 881 (47.8%) | 3561 (26.4%) |
| Female recipients | 20 599 (40.3%) | 7323 (32.2%) | 5197 (38.6%) |
| Recipient BMI, kg/m$^2$ | 28.656 (5.1) | 28.197 (4.9) | 28.920 (5.1) |
| Recipient ethnicity | | | |
| White | 24 550 (48.1%) | 13 709 (60.3%) | 7099 (52.7%) |
| Black | 14 441 (28.3%) | 3763 (16.5%) | 3513 (26.1%) |
| Hispanic | 7466 (14.6%) | 3058 (13.4%) | 2029 (15.1%) |
| Other | 4622 (9.0%) | 2222 (9.8%) | 824 (6.1%) |
| ESRD cause | | | |
| PCKD | 4985 (9.8%) | 2204 (9.7%) | 1504 (11.2%) |
| DM | 20 099 (39.4%) | 8615 (37.9%) | 5347 (39.7%) |
| GN | 6874 (13.5%) | 3275 (14.4%) | 1802 (13.4%) |
| Other | 19 106 (37.4%) | 8653 (38.0%) | 4809 (35.7%) |
| Preemptive | 8337 (16.4%) | 5108 (22.5%) | 2727 (20.3%) |
| Dialysis vintage, y | 3.99 (2.3) | 3.47 (2.9) | 3.65 (2.9) |
| Public payer | 37 042 (72.5%) | 16 079 (70.7%) | 8828 (65.6%) |
| Vascular disease | 6518 (23.0%) | 2955 (22.5%) | 2123 (25.5%) |
| Diabetes | 24 632 (48.4%) | 10 500 (46.2%) | 6446 (48.3%) |
| cPRA | 16.6% (30.6) | 5.9% (17.2) | 12.5% (26.7) |
| HLA-MM | 4.08 (1.5) | 3.82 (1.6) | 3.95 (1.5) |
| CMV IgG D$^+$/R$^-$ | 8284 (16.6%) | 3828 (17.3%) | 2250 (17.1%) |
| EBV IgG D$^+$/R$^-$ | 2817 (6.3%) | 1368 (7.0%) | 893 (7.9%) |
| Steroid maintenance | 35 603 (69.7%) | 19 148 (84.2%) | 4393 (32.6%) |
| Live donor | 11 109 (21.7%) | 8680 (38.2%) | 4479 (33.3%) |
| Female donor | 23 504 (46.0%) | 11 465 (50.4%) | 6643 (49.3%) |
| Donor age | 44.1 (14.9) | 45.2 (14.7) | 44.5 (14.7) |
| Donor ethnicity | | | |
| White | 35 875 (70.2%) | 16 434 (72.2%) | 9522 (70.7%) |
| Black | 6978 (13.7%) | 2323 (10.2%) | 1846 (13.7%) |
| Hispanic | 6126 (12.0%) | 2757 (12.1%) | 1717 (12.8%) |
| Other | 2100 (4.1%) | 1238 (5.4%) | 380 (2.8%) |
| Donor BMI, kg/m$^2$ | 28.1 (6.5) | 27.7 (6.0) | 28.1 (6.2) |
| Donor eGFR, mL/min/1.73 m$^2$ | 97.3 (16.3) | 96.8 (16.3) | 97.3 (17.0) |
| Pre-KAS (2005–2014) | 20 110 (39.4%) | 10 755 (47.3%) | 6350 (47.2%) |
| KAS (2014–2021) | 23 486 (46.0%) | 9477 (41.7%) | 6085 (45.2%) |
| KAS-250 (2021–2022) | 7483 (14.6%) | 2520 (11.1%) | 1030 (7.6%) |

Values are presented as median (IQR), n (%), or mean (SD).
BMI, body mass index; CMV, cytomegalovirus; cPRA, calculated panel-reactive antibody; DM, diabetes mellitus; EBV, Epstein-Barr virus; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; GN, glomerulonephritis; IL-2RA, interleukin-2 receptor antagonist; IQR, interquartile range; KAS, kidney allocation system; KAS-250, distance-based kidney allocation system; MM, mismatch; PCKD, polycystic kidney disease; r-ATG, rabbit antithymocyte globulin.

### Outcomes of Interest

The primary study outcomes were long-term recipient and death-censored graft survival by the type of induction received. Additionally, we analyzed death with a functioning graft, which we defined as the death date predating the graft failure date. The overall graft failure was defined as the composite of death or graft failure. Secondary outcomes included delayed graft function, rates of rehospitalization, and posttransplant lymphoproliferative disorder during the first year posttransplant.

### Statistical Analyses

Numeric variables were summarized with the mean and SD. Differences between groups were tested using ANOVA or pooled *t* tests. For categorical variables, data were summarized as counts and within-group percentages. Statistical testing was done with the chi-square test.

Time-to-event data were summarized with Kaplan-Meier estimates of incidence and curves. Log-rank tests were used to identify statistically significant differences between groups. Mixed-effects Cox models were used to evaluate the impact of induction on older recipients with adjustment for possible confounding variables. Because of changes in the kidney allocation policies during the study period, we adjusted for era based on the implementation date of the kidney allocation system[14] on December 4, 2014, and the distance-based kidney allocation system KAS-250[15] on March 15, 2012. In these models, the center was used as a random effect. Linearity in all tests was evaluated using splines for continuous variables. Plots of Schoenfeld residuals were used to test the assumption of proportionality.

All analyses were performed using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). *P* values of <0.05 were considered statistically significant.

## RESULTS

### Baseline Characteristics

Transplant recipients who were 65 y or older accounted for 36.9% of our cohort. A 33.8% of older recipients received nondepletional induction with IL-2RA. The leading cause of end-stage kidney disease in the study population was diabetes, which accounts for 39% of the entire cohort. Less than 20% of the population received preemptive transplantation before needing dialysis. A 27.8% of the population received a kidney from a live donor. EBV high-risk discordance was observed in about 7% of the cohort, whereas CMV high-risk discordance was observed in 17%. Further characteristics are detailed in Table 1. The median graft follow-up time of patients in this cohort is 3.77 y (interquartile range, 1.36–6.91 y).

### Univariable Outcomes

The median estimated posttransplant survival score increased throughout the study, reflecting the recipients' increased complexity over the years and the wide acceptance of higher-risk candidates (Figure 2). The trends of induction use have changed over the years, with increased r-ATG since 2015, whereas IL-2RA remained stable and alemtuzumab use has declined (Figure 3).

Delayed graft function was frequently observed in 25% of r-ATG recipients, compared with 18.1% of IL-2RA recipients and 19.7% of the alemtuzumab recipients ($P < 0.001$). The 1-y rejection rate ranged between 5.4% and 7.0% and was the lowest among r-ATG recipients ($P < 0.001$), whereas there was a high 1-y rehospitalization rate, ranging from 43.6% to 45.6%, of which IL-2AR recipients had the lowest rate ($P < 0.001$). The rate of posttransplant lymphoproliferative disorder did not vary by induction type ($P = 0.575$; Table 2).

In the Kaplan-Meier analysis for recipient survival (Figure 4A), compared with those aged between 55 and 65 y or younger, recipients who were 65 y or older had much lower survival (log-rank $P < 0.001$). The 1-, 5-, and 10-y

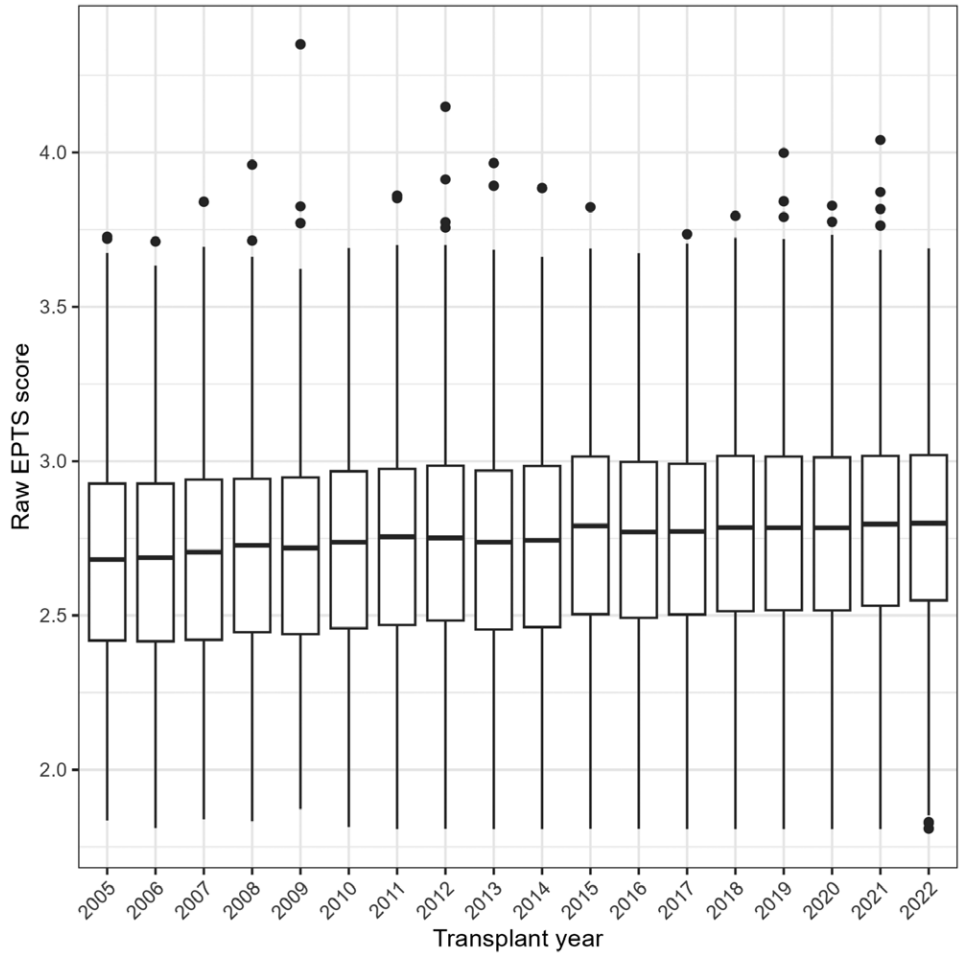



**FIGURE 2.** EPTS scores of older kidney transplant recipients by year of transplant. EPTS, estimated posttransplant survival.

survival rates were 96.8% versus 94.7%, 84.9% versus 74.4%, and 62.1% versus 40.1% in the 55–65 y or younger group versus 65 y or older group, respectively. In the death-censored kidney graft survival analysis by recipient age (Figure 4B), the graft survival did not differ between the 2 age groups (log-rank $P = 0.443$). The 1-, 5-, and 10-y survival rates were 97.7% versus 97.3%, 91.5% versus 91.5%, and 80.8% versus 82.6%, respectively, in recipients aged between 55 and 65 y or younger versus those who were 65 y or older.

Alemtuzumab appeared to have better unadjusted survival in the univariable Kaplan-Meier analyses for recipient survival and death with functioning graft by induction type (Figures 5A and B). IL-2RA had the best overall graft survival ($P = 0.02$; Figure 5C). The death-censored graft survival (Figure 5D) was the lowest among alemtuzumab recipients, followed by r-ATG, with IL-2RA recipients having the highest death-censored graft survival ($P < 0.001$).

## Adjusted Primary Outcomes

### Determinants of Patient Survival

In this cohort of older transplant recipients, we analyzed the association between long-term recipient survival and recipient age and induction type; we adjusted the model for pertinent donor, recipient, and immunologic factors. Recipient age older than 65 y was associated with a 69% increased risk of death compared with those aged 55–65 y (hazard ratio [HR] 1.69 [1.63-1.75], $P < 0.01$). Compared with r-ATG, neither IL-2RA nor alemtuzumab induction was a predictor of mortality. Interestingly, EBV high-risk discordance (EBV $D^+/R^-$) was associated with a 14% increased risk of death (HR 1.14 [1.07-1.21], $P < 0.01$) compared with EBV $D^+/R^+$ status. Preemptive kidney transplant and live kidney donor transplant were positive predictors of survival (HR 0.78 [0.73-0.82], $P < 0.01$ and HR 0.67 [0.64-0.71], $P < 0.01$). Steroid maintenance was associated with an increased risk of mortality (HR 1.12 [1.07-1.18], $P < 0.01$). Since 2005, a recent transplant year has been associated with an increased risk of death compared with the previous year (HR 1.04 [1.03-1.05], $P < 0.01$; Table 3).

### Determinants of Death-Censored Kidney Graft Survival

Increased age at transplantation was not a predictor of death-censored graft loss. Compared with r-ATG, alemtuzumab induction was associated with an 18% increased risk of graft loss (HR 1.18 [1.07-1.30], $P < 0.01$). Graft loss risk in recipients of IL-2RA did not differ statistically from those who received r-ATG. CMV high-risk discordance status was associated with a 10% increased risk of graft loss (HR 1.10 [1.02-1.19], $P < 0.01$) compared with those with $R^+/D^+$ status. Preemptive transplantation (HR 0.72 [0.65-0.79], $P < 0.01$)

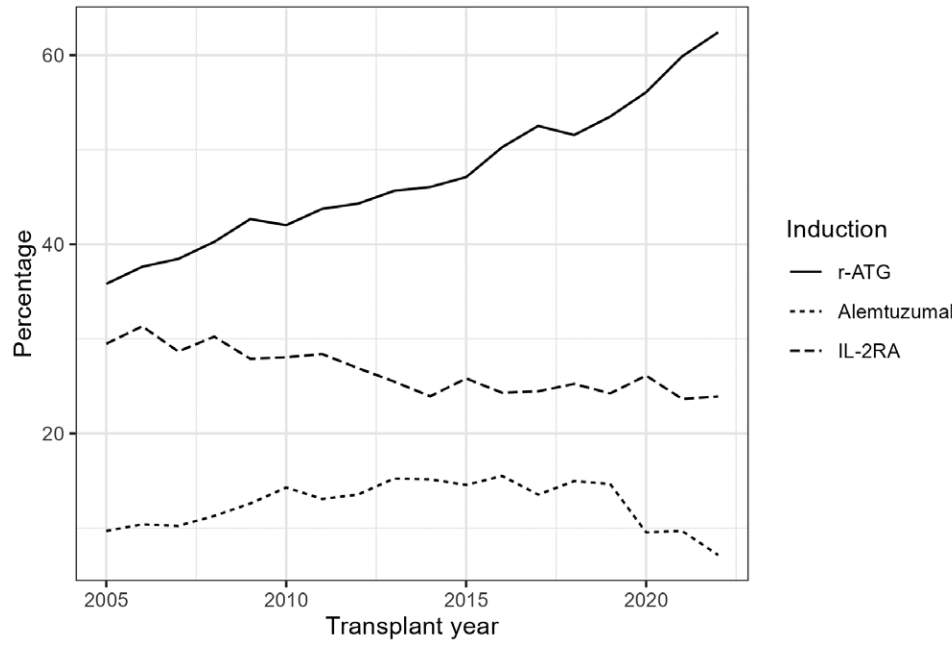



**FIGURE 3.** Trends of induction used among kidney transplant recipients.

**TABLE 2.**

**Short-term outcomes for older kidney transplant recipients**

| | r-ATG | IL-2RA | Alemtuzumab | *P* |
|---|---|---|---|---|
| Delayed graft function | 12 763 (25.0%) | 4112 (18.1%) | 2646 (19.7%) | <0.001 |
| One-year rejection | 2519 (5.4%) | 1484 (7.0%) | 823 (6.5%) | <0.001 |
| One-year PTLD | 108 (0.2%) | 56 (0.2%) | 33 (0.2%) | 0.575 |
| One-year rehospitalization | 20 563 (45.6%) | 8725 (43.6%) | 5356 (43.7%) | <0.001 |

Delayed graft function is defined as requiring dialysis in the first 7 d. Rejection is defined as biopsy-proven or treated.
IL-2RA, interleukin-2 receptor antagonist; PTLD, posttransplant lymphoproliferative disorder; r-ATG, rabbit antithymocyte globulin.

and live donor (HR 0.50 [0.46-0.55], $P < 0.01$) recipients had a lower risk of graft loss. Steroid maintenance was not associated with a lower risk of graft loss. The risk of graft loss improved over time (HR 0.96 [0.94-0.97], $P < 0.01$), and we observed a 4% lower risk per recent year since 2005. Similar associations were observed in the death with function model and the overall graft failure model.

### Causes of Graft Loss and Death

Because of significant missing data for categorizing graft loss and death causes at the registry level, meaningful statistical analysis was impossible. The causes of graft loss are detailed in Table 4. Chronic rejection is the most frequently documented cause of graft failure, accounting for 25.3%, 28.5%, and 23.4% in the r-ATG, IL-2RA, and alemtuzumab, respectively. BK polyomavirus as a cause of graft loss was documented in 3.9%, 3.2%, and 4.2% in the r-ATG, IL-2RA, and alemtuzumab groups, respectively.

For causes of death being reported specifically, besides the categories other and unknown, cardio-cerebrovascular etiology was the most frequently encountered cause at 19.6%, 18.5%, and 19.9%, followed by infection at 11.3%, 12.0%, and 11.2%, and malignancy at 10.5%, 10.7%, and 10.2% in the r-ATG, IL-2RA, and alemtuzumab, respectively (Table 5).

## DISCUSSION

Our study details the predictors of outcomes in older trans plant recipients in the United States. The results can be summarized as follows: (1) recipient age more than 65 y strongly predicts increased mortality, death with functioning graft, and overall graft failure but was not a predictor of death-censored graft failure. (2) Compared with r-ATG, alemtuzumab induction but not IL-2RA was associated with increased death-censored graft loss. (3) EBV increased risk discordance and steroid maintenance were associated with a higher risk of death, death with function, and overall graft failure. In contrast, CMV increased risk discordance was associated with an increased risk of death-censored graft loss. (4) Living donation and preemptive transplantation are favorable predictors of recipient and graft survival among recipients aged 55 y or older.

Our results are consistent with previous reports of outcomes of older kidney transplant recipients,[16,17] highlighting age as a strong predictor of mortality and death with functioning graft.[1,18–21] In our analysis, preemptive transplantation and kidneys from live donors were favorable predictors of improved outcomes. As transplant candidates continue to get older,[2] considerations for preemptive transplantation and the live donor option are highly encouraged on the basis of our results and others.[22–24]

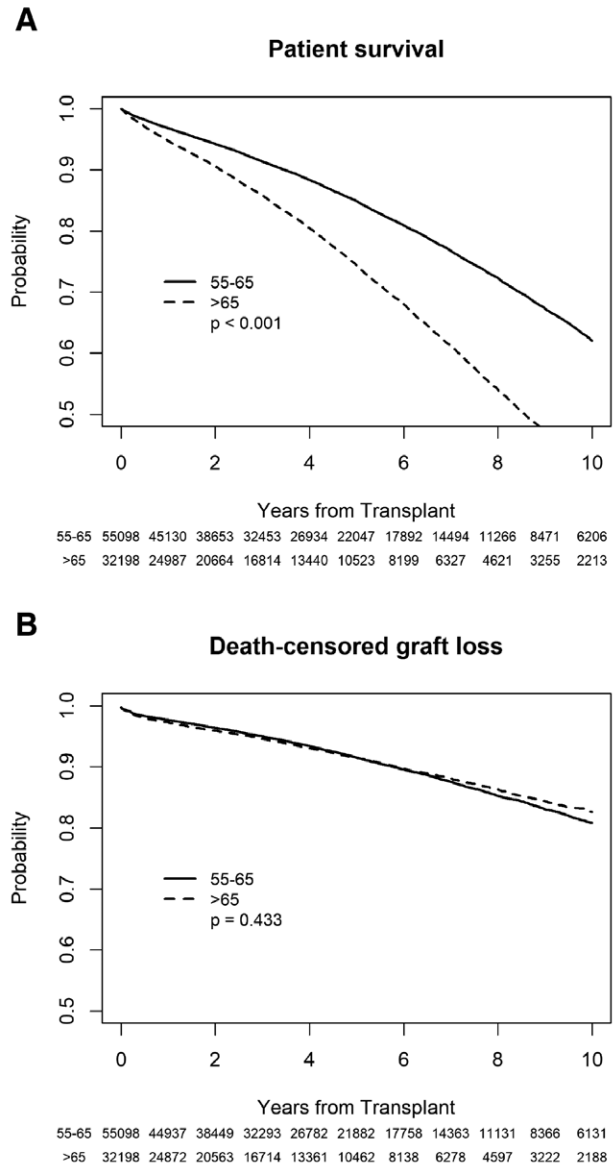



**FIGURE 4.** Recipient and graft survival by recipient age.

Infection and malignancy are frequent complications in older adults,[25] more so in those with end-stage kidney disease,[4,5,26] and have been linked to immunosenescence. Infection as a cause of death accounted for over 11% of all-cause mortality in our cohort. Unfortunately, the cause of death is not very well tracked in the transplant follow-up forms, which limited our analysis. Nonetheless, our findings are consistent with our previous multicenter report,[1] identifying cancer and infection among the leading causes of death. Although the choice of induction did not influence recipient survival or rates of infection, alemtuzumab was associated with increased graft loss in this older population of transplant recipients. This finding echoes the findings of Koyawala et al[27] and our previous findings of increased graft loss associated with alemtuzumab use in the preemptive second[12] kidney transplant population. Alemtuzumab primarily affects T cells more profoundly and durably than B cells while not clearing plasma cells. Some studies link alemtuzumab use to an elevated risk of antibody-mediated rejection or posttransplant development of donor-specific alloantibody.[28] The reasons for this association, whether because of reduced maintenance immunosuppression regimens or patient-specific factors, remain unclear. The B cell–depleting effect triggers a homeostatic response, elevating B cell–activating factor and activated B cells, potentially explaining the rise in alloantibody production after alemtuzumab induction,[29] thereby explaining the worst graft survival we observed herein. Additionally, older recipients are affected by immunosuppression differently,[30] and less intense immunosuppression regimens,[31] such as steroid avoidance, were associated with better survival in older recipients, concordant with our findings. In all, resources should be devoted to tailoring immunosuppression protocols, taking into consideration the mechanistic intersection between immunosenescence and aging kidney transplant candidates.

Death related to cardiovascular and cerebrovascular accounted for nearly one-fifth of all death causes, which is consistent with previous reports.[32–34] Underscoring the importance of developing strategies to offset these risks with an emphasis on exercise,[35,36] which can be implicated with additional benefits of healthy aging.

Our findings highlight the known complications[37–40] associated with high-risk EBV and CMV donor-recipient serostatus discordance ($D^+/R^-$). In our study, EBV $D^+/R^-$ status was associated with an increased risk of mortality and overall graft loss, confirming the findings of Dinesh et al[41] in their report of a single-center study. These findings may be explained by the increased risk of posttransplant lymphoma[39,42] in high-risk EBV discordant, especially older recipients. Similar to the findings by Zona et al[40] and others,[43,44] CMV $D^+/R^-$ status was an independent risk factor for death-censored graft loss in this cohort of older transplant recipients. Based on our findings, avoiding high-risk donor-recipient viral discordance status may be a modifiable factor to help reduce the risk of mortality and graft loss. Lockridge et al[45] conducted a study to assess the feasibility of allocating kidneys based on CMV serologic matching within a single organ procurement organization that supplied 3 transplant centers. These centers agreed to adopt the variance for CMV matching. The study found that implementing CMV serologic matching did not negatively impact transplantation rates. However, further analyses will be needed to evaluate the feasibility of this strategy in the setting of the competing risk of delaying a transplant in the older population.

## Strengths and Limitations

This study is the most extensive study to date to document the long-term outcomes of older kidney transplant recipients by induction type. Our study was designed to isolate the association of induction type by including a standardized maintenance regimen of tacrolimus and mycophenolate with or without steroids. We only considered conventional risk recipients who were ABO-compatible and had crossmatch negative transplants. We chose a combination of well-tracked primary outcomes by the SRTR. Nonetheless, our study is not free of limitations. The retrospective nature of cohort studies does not allow full adjustment because of unmeasured confounders.

Center reporting patterns are a fundamental limitation in the SRTR standard analysis file, limiting the ability to study

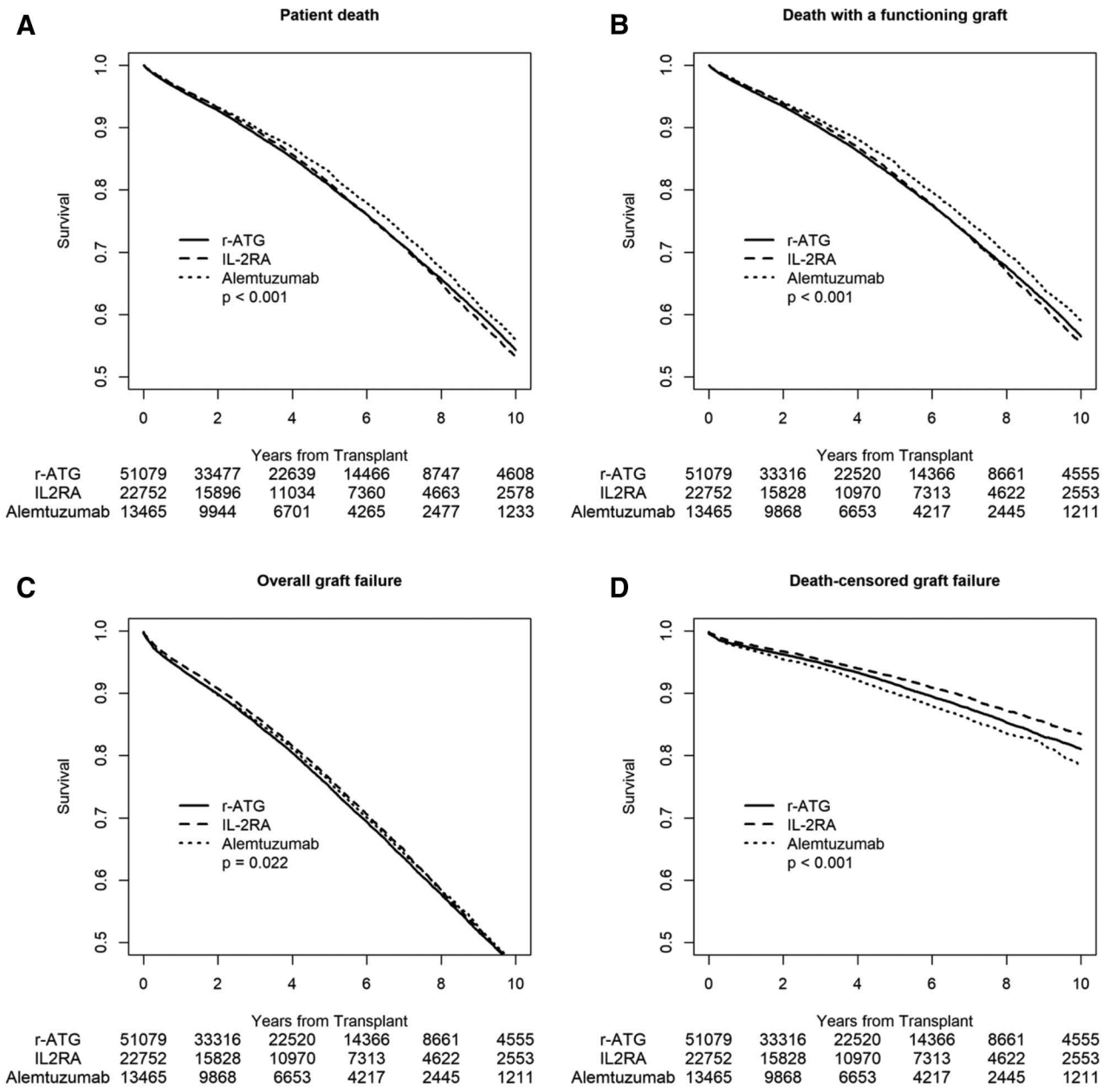



**FIGURE 5.** Recipient survival (A), death with functioning graft (B), overall graft survival (C), and death-censored graft survival (D) by induction type in older kidney transplant recipients.

causes of death or graft loss. Although we restricted the cohort to recipients discharged on tacrolimus and mycophenolate, the standard analysis file does not include consistent data on subsequent immunosuppression change after discharge. Variances in immunosuppression exposure, that is, drug levels, are unavailable; therefore, we could not include these in our analysis.

Immunosuppression side effects are not typically tracked in the standard analysis file; therefore, we could not comment on immunosuppression tolerability in older recipients. Longitudinal data on donor-specific antibody formation or late rejection episodes are not recorded in the database. Finally, the lack of biorepository or T-cell profiling did not allow us to explore the association between induction type and the effect on the immune system in older transplant recipients.

## CONCLUSION

In this large cohort of older transplant recipients, age more than 65 y is a strong predictor of mortality, death with a functioning graft, and overall graft failure. Alemtuzumab induction was associated with a higher risk of graft loss than r-ATG, whereas IL-2RA was not associated with better recipient or graft survival. Living donation and preemptive transplantation are favorable predictors. EBV and CMV high-risk discordances are associated with worse recipient and graft survival, respectively.

Clinicians are encouraged to reconsider using alemtuzumab in older recipients while carefully considering the immunologic risk over age when selecting an induction type. Making further efforts to avoid higher-risk EBV and CMV discordance in older recipients may be additionally beneficial.

**TABLE 3.**

**Multivariable Cox proportional hazard outcome models for older kidney transplant recipients**

| | Death, HR (95% CI) | P | Death with function, HR (95% CI) | P | DCGS, HR (95% CI) | P | Overall graft failure, HR (95% CI) | P |
|---|---|---|---|---|---|---|---|---|
| Age >65 y[a] | 1.69 (1.63-1.75) | <0.01 | 1.70 (1.64-1.77) | <0.01 | 0.96 (0.90-1.01) | | 1.45 (1.40-1.49) | <0.01 |
| Induction type r-ATG (ref) | | | | | | | | |
| IL-2RA | 1.01 (0.96-1.05) | 0.77 | 1.00 (0.95-1.05) | 0.98 | 1.00 (0.93-1.08) | 0.97 | 1.00 (0.96-1.04) | 0.93 |
| Alemtuzumab | 0.99 (0.93-1.05) | 0.73 | 0.96 (0.90-1.03) | 0.30 | 1.18 (1.07-1.30) | <0.01 | 1.03 (0.97-1.09) | 0.35 |
| EBV $D^+/R^-$[b] | 1.14 (1.07-1.21) | <0.01 | 1.13 (1.06-1.21) | <0.01 | 1.07 (0.96-1.18) | 0.22 | 1.11 (1.05-1.18) | <0.01 |
| CMV $D^+/R^-$[c] | 1.03 (0.98-1.08) | 0.20 | 1.02 (0.97-1.08) | 0.36 | 1.10 (1.02-1.19) | 0.02 | 1.05 (1.00-1.09) | 0.04 |
| Living donor | 0.67 (0.64-0.71) | <0.01 | 0.69 (0.65-0.72) | <0.01 | 0.50, (0.46-0.55) | <0.01 | 0.63 (0.60-0.66) | <0.01 |
| Preemptive transplant | 0.78 (0.73-0.82) | <0.01 | 0.79 (0.75-0.84) | <0.01 | 0.72 (0.65-0.79) | <0.01 | 0.77 (0.73-0.81) | <0.01 |
| Steroid maintenance | 1.12 (1.07-1.18) | <0.01 | 1.11 (1.06-1.17) | <0.01 | 1.05 (0.98-1.14) | 0.18 | 1.10 (1.05-1.15) | <0.01 |
| Transplant year | 1.04 (1.03-1.05) | <0.01 | 1.05 (1.04-1.06) | <0.01 | 0.96 (0.94-0.97) | <0.01 | 1.02 (1.01-1.03) | <0.01 |

Models were further adjusted for recipient ethnicity, payer type, ESRD cause, peripheral vascular disease, dialysis duration, cPRA, HLA-MM, level of education, cold ischemia time, donor age, sex, ethnicity, KAS era, and BMI.
[a]Reference 55–65 y.
[b]Reference EBV donor/recipient positive.
[c]Reference CMV donor/recipient positive.
BMI, body mass index; CI, confidence interval; CMV, cytomegalovirus; cPRA, calculated panel-reactive antibody; DCGS, death-censored graft survival; ESRD, end-stage renal disease; HR, hazard ratio; IL-2RA, interleukin-2 receptor antagonist; KAS, kidney allocation system; MM, mismatch; r-ATG, rabbit antithymocyte globulin.

**TABLE 4.**

**Causes of graft failure among older kidney transplant recipients**

| Cause of graft failure | r-ATG, 4751 (9.3%)[a] | IL-2RA, 2021 (8.9%)[a] | Alemtuzumab, 1507 (11.2%)[a] |
|---|---|---|---|
| Acute rejection | 449 (9.5%) | 222 (11.0%) | 188 (12.5%) |
| Chronic rejection | 1203 (25.3%) | 575 (28.5%) | 353 (23.4%) |
| Hyperacute rejection | 2 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| BK viremia | 186 (3.9%) | 64 (3.2%) | 63 (4.2%) |
| Infection | 296 (6.2%) | 108 (5.3%) | 81 (5.4%) |
| Graft thrombosis | 135 (2.8%) | 55 (2.7%) | 28 (1.9%) |
| Primary failure | 187 (3.9%) | 66 (3.3%) | 73 (4.8%) |
| Primary nonfunction | 260 (5.5%) | 76 (3.8%) | 63 (4.2%) |
| Urological complication | 29 (0.6%) | 18 (0.9%) | 6 (0.4%) |
| Recurrent disease | 286 (6.0%) | 152 (7.5%) | 116 (7.7%) |
| Unknown | 1718 (36.2%) | 685 (33.9%) | 536 (35.6%) |

Causes of graft loss within 10 y from transplant presented as n (%) within-group percentage.
[a]N (%) represents the entire group percentage.
IL-2RA, interleukin-2 receptor antagonist; r-ATG, rabbit antithymocyte globulin.

**TABLE 5.**

**Causes of death among older kidney transplant recipients**

| Cause of death | r-ATG, 10562 (20.7%)[a] | IL-2RA, 5227 (23.0%)[a] | Alemtuzumab, 2833 (21.0%)[a] |
|---|---|---|---|
| Cardiovascular | 1636 (15.5%) | 746 (14.3%) | 437 (15.4%) |
| Cerebrovascular | 321 (3.0%) | 164 (3.1%) | 96 (3.4%) |
| Graft failure | 42 (0.4%) | 45 (0.9%) | 18 (0.6%) |
| Hemorrhage | 118 (1.1%) | 60 (1.1%) | 30 (1.1%) |
| Infection | 1195 (11.3%) | 626 (12.0%) | 317 (11.2%) |
| Malignancy | 1111 (10.5%) | 558 (10.7%) | 288 (10.2%) |
| Other | 3333 (31.6%) | 1518 (29.0%) | 812 (28.7%) |
| Unknown | 2806 (26.6%) | 1510 (28.9%) | 835 (29.5%) |

Causes of death within 10 y from transplant presented as n (%) within-group percentage.
[a]N (%) represents the entire group percentage.
IL-2RA, interleukin-2 receptor antagonist; r-ATG, rabbit antithymocyte globulin.

## ACKNOWLEDGMENTS

The data reported here have been supplied by the Hennepin Healthcare Research Institute as the contractor for the SRTR.

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