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Effect of Early Steroid Withdrawal on Posttransplant Diabetes Among Kidney Transplant Recipients Differs by Recipient Age

JiYoon B. Ahn, KMD, MPH,[1] Sunjae Bae, KMD, PhD,[1,2] Mark Schnitzler, PhD,[3] Gregory P. Hess, MD, MSc,[4] Krista L. Lentine, MD, PhD,[3] Dorry L. Segev, MD, PhD,[1,2] and Mara A. McAdams-DeMarco, PhD[1,2]

Background. Posttransplant diabetes (PTD), a major complication after kidney transplantation (KT), is often attributable to immunosuppression. The risk of PTD may increase with more potent steroid maintenance and older recipient age. **Methods.** Using United States Renal Data System data, we studied 12 488 adult first-time KT recipients (2010–2015) with no known pre-KT diabetes. We compared the risk of PTD among recipients who underwent early steroid withdrawal (ESW) versus continued steroid maintenance (CSM) using Cox regression with inverse probability weighting to adjust for confounding. We tested whether the risk of PTD resulting from ESW differed by recipient age (18–29, 30–54, and ≥55 y). **Results.** Of 12 488, 28.3% recipients received ESW. The incidence rate for PTD was 13 per 100 person-y and lower among recipients who received ESW (11 per 100 person-y in ESW; 14 per 100 person-y in CSM). Overall, ESW was associated with lower risk of PTD compared with CSM (adjusted hazard ratio [aHR] = $_{0.72}0.79_{0.86}$), but the risk differed by recipient age ($P_{\text{interaction}}$ = 0.09 for comparison between recipients aged 18–29 and those aged 30–54; $P_{\text{interaction}}$ = 0.01 for comparison between recipients aged 18–29 and those aged ≥55). ESW was associated with lower risk of PTD among recipients aged ≥55 (aHR = $_{0.62}0.71_{0.81}$) and those aged 30–54 (aHR = $_{0.73}0.83_{0.95}$), but not among recipients aged 18–29 (aHR = $_{0.81}1.18_{1.72}$). Although recipients who received ESW had a higher risk of acute rejection across the age groups (adjusted odds ratio = $_{1.01}1.17_{1.34}$), recipients with no PTD had a lower risk of mortality (aHR = $_{0.58}0.66_{0.74}$). **Conclusions.** The beneficial association of ESW with decreased PTD was more pronounced among recipients aged ≥55, supporting an age-specific assessment of the risk-benefit balance regarding ESW.

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Posttransplant diabetes (PTD) is a common complication after kidney transplantation (KT) and is associated with higher risk of graft failure and mortality.[1-4] Similar to the risks associated with type 2 diabetes, KT recipients with PTD are considered to be at risk of long-term complications like cardiovascular disease, retinopathy, and neuropathy.[1] The cumulative incidence of PTD is high[5] but varies, ranging from 2% to 50% at 1 y after KT,[6] because of lack of consensus on the definition of PTD before 2003.[1,7] Moreover, health care costs are higher among KT recipients with PTD according to the analysis of Medicare payments in the United States.[8]

Use of immunosuppression is known as a modifiable risk factor for PTD.[9] In particular, steroids induce insulin resistance, increase hepatic glucogenesis, and stimulate appetite,

resulting in hyperglycemia.[10-13] Therefore, steroid minimization is a common strategy to attenuate the risk of PTD.[14] Previous research suggests that KT recipients with steroid minimization are less likely to receive antidiabetic medication and less likely to experience weight gain.[15]

Age, a well-established risk factor for type 2 diabetes, also contributes to the development of PTD; the risk increases steadily for recipients aged over 40 y.[9,16,17] With increasing age, recipients experience age-related changes including decreased β-cell function[18] and impaired glucose homeostasis related to obesity.[19,20] Even with the age-related differences, there has been limited evidence that strategies for steroids use among KT recipients need to be altered by recipient age to prevent PTD and its derivatives. Early steroid withdrawal (ESW) after a few days post-KT has shown decreased PTD incidence in a population that was primarily younger adults, and this was only significant when the calcineurin inhibitor used was cyclosporine but not tacrolimus.[15,21-23] By expanding the study population to include older recipients with claims data, we aimed to examine the association of ESW with PTD and elucidate whether the association differs by recipient age.

MATERIALS AND METHODS

Study Population

Using the United States Renal Data System, we studied first-time kidney-only adult (≥18 y) transplant recipients from deceased-donor from January 1, 2010, to December 31, 2015. The population was restricted to recipients who had Medicare as primary payer during 1 y before KT and who, at the time of KT, had immunosuppression data and initiated tacrolimus and mycophenolate (Figure 1). We excluded recipients with known pre-KT diabetes using Centers for Medicare and Medicaid Services Medical Evidence Report (CMS-2728) or pre-KT Medicare claims using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (250) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) (E11-E13).[5,24]

This study was reviewed by the institutional review board at Johns Hopkins School of Medicine and was determined to qualify for an exemption under 45 CFR 46.101(b), since study participants cannot be identified directly or through linked identifiers. All clinical and research activities being reported are consistent with the Declaration of Helsinki and the Declaration of Istanbul.

Early Steroid Withdrawal

ESW was defined as withdrawal of steroid by the time of discharge after KT. Since the exact date of steroid withdrawal cannot be obtained using the data, we excluded to recipients who were not discharged within 30 d post-KT (n = 267, 0.5%) to exclude late steroid withdrawal cases and their continued steroid maintenance (CSM) counterparts.[25] This study population included 12 488 first-time KT recipients without known pre-KT diabetes.

Posttransplant Diabetes

We identified recipients with PTD by applying the algorithm used in previous studies[5,8] in linked Medicare claims
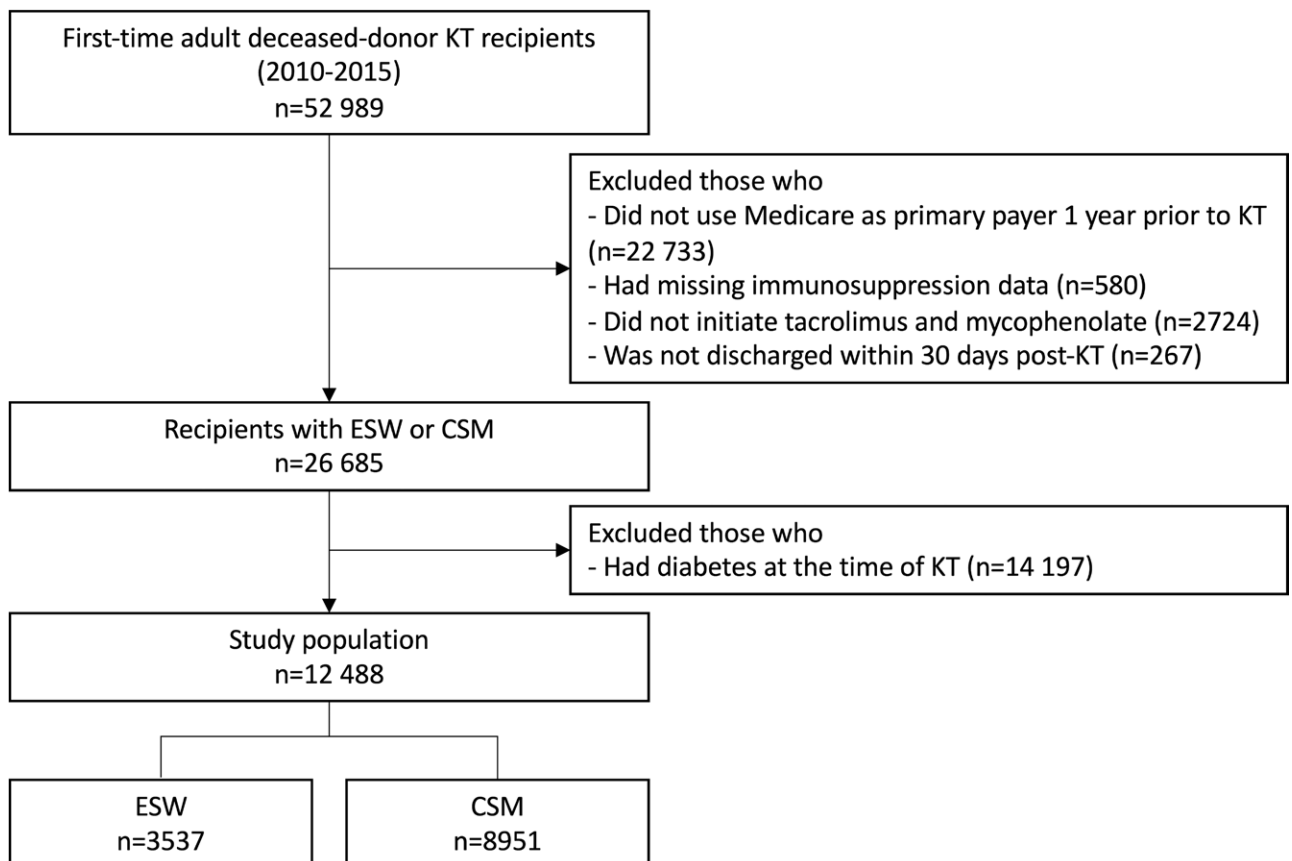

FIGURE 1. Population (n = 12 488) was selected to study the effect of early steroid withdrawal (vs CSM) on posttransplant diabetes among KT recipients by recipient age. CSM, continued steroid maintenance; ESW, early steroid withdrawal; KT, kidney transplant.

and national transplant registry data, which requires at least 1 inpatient or 2 outpatient claims within 1 y using ICD-9-CM (250) and ICD-10-CM (E11-E13).[24] We defined the onset of PTD as the earliest date of the claims. We only considered claims that occurred >60 d after KT so that we would not include transient posttransplantation hyperglycemia in our case definition of PTD. During this first 60 d, transient post-transplantation hyperglycemia is common but normalizes often without intervention. Furthermore, PTD is only diagnosed when recipients have stable kidney function.[1] We followed this study population until one of the following events: PTD, graft failure, death, 3 y after post-KT, end of Medicare coverage, or the end of follow-up (December 31, 2016).

Effect of ESW on PTD by Recipient Age

We treated ESW as a time-fixed exposure and analyzed data by using an analog of the intention-to-treat in randomized trials.[26] We compared risk of PTD among recipients who received ESW with those who received CSM using Cox regression. We used the inverse probability weighting method to adjust for confounding. Probability of being treated with ESW was estimated using a generalized estimating equation with logit link to adjust for center-level confounding. We included recipient factors (age, sex, race/ethnicity, education level, body mass index [BMI], cause of kidney failure, years on dialysis, hepatitis B virus core antibody [HBV], hepatitis C virus [HCV], cytomegalovirus [CMV], previous malignancy, calendar year of KT, human leukocyte antibody mismatch, peak panel reactive antigen, preemptive transplant, cold ischemic time, and induction agent) and donor factors (age, sex, race/ethnicity, expanded criteria donor, donation after cardiac death) in the model (**Figure S1** and **Table S1, SDC**, http://links.lww.com/TXD/A388). We included education level as a marker of socioeconomic status, which is known to have inverse association with the prevalence of type 2 diabetes.[27]

We aimed to characterize the interaction between ESW and age using a flexible technique with fewer modeling assumptions. We estimated adjusted hazard ratios (aHRs) of PTD using recipient age at the time of transplant as a continuous variable using restricted cubic splines with 3 knots. Knots were placed at percentiles based on Harrell's recommendation.[28] Based on the feature, we grouped the study population into the 3 age groups (18–29, 30–54, and ≥55 y) and tested whether the effect of ESW on PTD differed across the age groups. To test the effect measure modification by recipient age, we included an interaction term of ESW and age in the model and used a Wald test to evaluate the statistical significance of the interaction terms. Interaction P value <0.05 suggested that the effect of ESW on PTD differed across the age groups.

Stratification

Then, we conducted stratified analysis by potential risk factors for PTD: recipient sex, race/ethnicity (White, Black, other, and Hispanic), BMI (<25, 25–29.9, and ≥30), HBV, HCV, CMV, previous malignancy and induction agent (antithymocyte globulin, interleukin 2 receptor antagonist [IL2Ra], alemtuzumab, no induction, and other).[9]

ESW and Acute Rejection

We used data collected by United Network for Organ Sharing, which provides information on acute rejection on specific periods (0–6 mo, 7–12 mo, and then annually) rather than exact dates, and defined acute rejection as experiencing any of acute rejection

episodes during 1 y after KT.[29,30] Logistic regression was used to compare the risk of acute rejection between recipients who received ESW and those who received CSM. To test the effect measure modification by recipient age, we included an interaction term of ESW and age in the model and used a Wald test to evaluate the statistical significance of the interaction terms. Interaction P value <0.05 suggested that the effect of ESW on acute rejection differed among recipients across the age groups.

PTD and Mortality

To examine the association between PTD and mortality, we used a Cox regression treating PTD as a time-varying exposure after adjusting for confounders listed above.

Sensitivity Analysis

We conducted stratified analysis by impaired glucose tolerance, which was obtained using ICD-9-CM (790.2x) and ICD-10-CM (R730x) codes. Also, we varied the criteria to exclude transient posttransplantation hyperglycemia in early post-KT (15, 30, 45, 60, and 90 d) since there is no time window in agreement.

Statistical Analysis

Missing covariates were imputed using chained equations[31-34] throughout the analysis. A P value <0.05 was considered statistically significant. Confidence intervals are reported as per the method of Louis and Zeger.[35] All analyses were performed using Stata 16.0/MP for Linux (College Station, TX) and R version 3.6.2.

RESULTS

Population Characteristics

Of 12 488 study population with no known pre-KT diabetes, 3537 (28.3%) received ESW, of whom 968 are 18–29 y old, 1967 are 30–54 y old, and 602 are 55 y old and above, and 8951 (71.7%) received CSM, of whom 2499 are 18–29 y old, 4973 are 30–54 y old, and 1479 are 55 y old and above. Median age was 50 y, 40.6% are female, 39.9% are Black, 9.0% are HBV positive, 68.2% are CMV positive, 7.2% have previous malignancy, and 17.0% received IL2Ra. Compared with those with CSM, recipients with ESW are less likely to be female (35.7% versus 42.5%), Black (38.1% versus 40.5%), HBV positive (7.6% versus 9.5%), CMV positive (65.1% versus 69.4%), have previous malignancy (7.8% versus 6.9%), and receive IL2Ra (5.2% versus 21.6%) (Table 1).

Incidence Rate of PTD

The incidence rate of PTD was 13.2 per 100 person-y and lower among recipients with ESW compared with those with CSM (10.8 per 100 person-y versus 14.3 per 100 person-y). Compared with those with CSM, recipients with ESW had lower incidence rates of PTD across the age groups. The incidence rates of PTD were 6.1 per 100 person-y in ESW and 6.5 per 100 person-y in CSM among recipients aged 18–29; 10.0 per 100 person-y in ESW and 12.6 per 100 person-y in CSM among those aged 30–54; 13.1 per 100 person-y in ESW and 18.8 per 100 person-y in CSM among those aged ≥55 (Table 2).

Effect of ESW on PTD by Recipient Age

After adjusting for confounding, the risk of PTD was lower among recipients with ESW (aHR = $_{0.72}0.79_{0.86}$) compared

TABLE 1.

Study population characteristics of adult kidney transplant recipients in 2010–2015 by steroid maintenance (n = 12 488)

	ESW (n = 3537)	CSM (n = 8951)
Recipient factors		
Age (y)	50 (40–60)	50 (39–60)
Female	35.7%	42.5%
Race/ethnicity		
White	40.8%	36.2%
Black	38.1%	40.5%
Other	6.8%	7.2%
Hispanic	14.3%	16.1%
Attended college	46.1%	45.6%
BMI (kg/m²)	27.1 (23.6–31.4)	26.8 (23.5–30.9)
HBV+	7.6%	9.5%
HCV+	4.8%	5.2%
CMV+	65.1%	69.4%
Previous malignancy	7.8%	6.9%
Cause of ESKD—GN	28.9%	30.5%
Cause of ESKD—HTN	38.9%	38.1%
Transplant factors		
Preemptive transplant	1.2%	2.1%
Y on dialysis	4.8 (3.3–6.7)	4.8 (3.2–6.8)
Cold ischemic time (h)	16.2 (11.2–23.0)	15.7 (10.8–21.3)
Peak PRA	0.0 (0.0–18.0)	0.0 (0.0–34.2)
Zero HLA mismatch	3.6%	4.4%
Transplant y		
2010	16.9%	14.7%
2011	15.2%	15.1%
2012	15.1%	15.7%
2013	16.4%	16.8%
2014	16.2%	17.2%
2015	20.3%	20.5%
Induction agent		
ATG	44.2%	51.7%
IL2Ra	5.2%	21.6%
Alemtuzumab	37.5%	6.8%
No induction	7.2%	13.6%
Other	5.9%	6.3%
Delayed graft function	23.2%	26.3%
Donor factors		
Age (y)	39 (24–51)	38 (24–50)
Female	40.8%	38.9%
Race/ethnicity		
White	68.9%	72.6%
Black	15.2%	14.9%
Other	3.4%	2.6%
Hispanic	12.5%	9.9%
ECD	13.3%	12.7%
DCD	16.8%	18.3%

Median (interquartile range) was presented for continuous variables.
ATG, antithymocyte globulin; BMI, body mass index; CMV, cytomegalovirus; CSM, continued steroid maintenance; DCD, donation after cardiac death; ECD, expanded criteria donor; ESKD, end-stage kidney disease; ESW, early steroid withdrawal; GN, glomerulonephritis; HBV, hepatitis B virus; HCV, hepatitis C virus; HTN, hypertension; IL2Ra, interleukin 2 receptor antagonist; PRA, panel reactive antigen.

TABLE 2.

Crude incidence rates of posttransplant diabetes by steroid maintenance (early steroid withdrawal vs continued steroid maintenance) and age (18–29, 30–54, and ≥55 y)

	Overall			ESW			CSM		
	N	PY	IR	N	PY	IR	N	PY	IR
Overall	2886	21 826	13.2	698	6476	10.8	2188	15 351	14.3
Recipient age (y)									
18–29	137	2143	6.4	40	653	6.1	97	1490	6.5
30–54	1374	11 601	11.8	333	3340	10.0	1041	8261	12.6
≥55	1375	8082	17.0	325	2483	13.1	1050	5599	18.8

Incidence rate was calculated as (the number of cases)/(person-y) × 100.
CSM, continued steroid maintenance; ESW, early steroid withdrawal; IR, incidence rate; and PY, person-y.

TABLE 3.

Effect of early steroid withdrawal (vs continued steroid maintenance) on posttransplant diabetes among kidney transplant recipients by recipient age (18–29, 30–54, and ≥55 y)

	N	aHR	$P_{interaction}$
Overall	12 488	$_{0.72}0.79_{0.86}$	–
Recipient age (y)			
18–29	1123	$_{0.81}1.18_{1.72}$	Reference
30–54	6567	$_{0.73}0.83_{0.95}$	0.09
≥55	4798	$_{0.62}0.71_{0.81}$	0.01

aHR, adjusted hazard ratio.
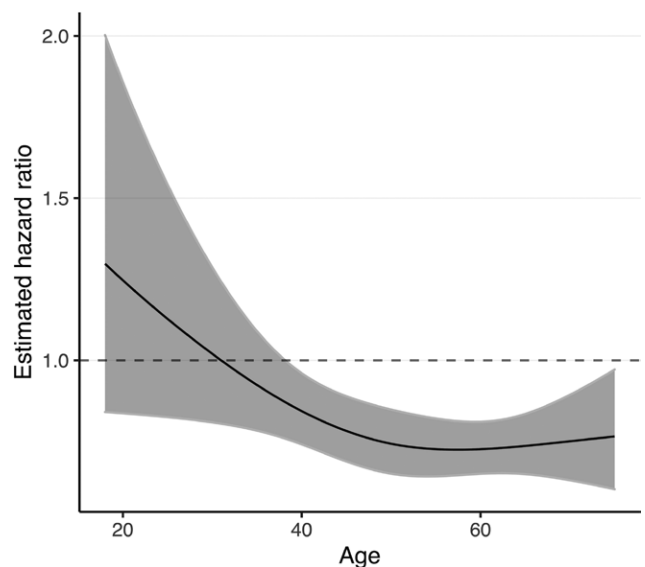
FIGURE 2. Hazard ratio of posttransplant diabetes among kidney transplant recipients comparing early steroid withdrawal with continued steroid maintenance using restricted cubic splines (n = 12 488). Recipient age was treated as a continuous variable. 95% confidence intervals are indicated as gray colored area.

with those with CSM (Table 3); however, this association differed by recipient age. The hazard ratios (HRs) of PTD comparing ESW with CSM decreased from age 18 to mid-50s and slightly increased after mid-50s (Figure 2). The risk of PTD was highest in the youngest age group and then declined and plateaued. The HR was not different from one in the youngest ages. Based on the HRs by age, the study population was divided into 3 age groups (18–29, 30–54, and ≥55 y).

The effect of ESW (versus CSM) on PTD differed by age ($P_{interaction}$ = 0.09 for comparison between recipients aged 18–29 and those aged 30–54; $P_{interaction}$ = 0.01 for comparison between recipients aged 18–29 and those aged ≥55). The risk

of PTD was lower for those with ESW compared with those with CSM among recipients aged 30–54 (aHR = $_{0.73}0.83_{0.95}$) and those aged ≥55 (aHR = $_{0.62}0.71_{0.81}$) but not among recipients aged 18–29 (aHR = $_{0.81}1.18_{1.72}$) (Table 3).

Stratification

When stratified by recipient sex, race/ethnicity, BMI, HBV, HCV, CMV, and previous malignancy, the effect of ESW on PTD was consistent across the strata. The effect of ESW on PTD differed by recipient age among those who are male, Black, HBV negative, HCV negative, and CMV positive; have BMI of 30.0 kg/m2 and above; and have no previous malignancy (Figure 3).

ESW and Acute Rejection

The incidence of acute rejection 1-y post-KT was 9.6% and higher among recipients who received ESW (10.3% in ESW versus 9.3% in CSM). After adjusting for confounding, the risk of acute rejection was higher among recipients who received ESW compared with those who received CSM (adjusted odds ratio = $_{1.01}1.17_{1.34}$) and this association was consistent across the age group ($P_{\text{interaction}}$ = 0.08 for comparison between recipients aged 18–29 and those aged 30–54; $P_{\text{interaction}}$ = 0.13 for comparison between recipients aged 18–29 and those aged ≥55).

PTD and Mortality

The risk of mortality was lower among recipients without PTD compared with those with PTD after adjusting for confounding (incidence rate = 1.9 per 100 person-y among those without PTD; 3.3 per 100 person-y among recipients with PTD, aHR = $_{0.58}0.66_{0.74}$).

Sensitivity Analysis

We observed consistent results when stratified by pre-KT impaired glucose tolerance (**Table S2, SDC**, http://links.lww.com/TXD/A388) and varied the criteria to exclude temporal hyperglycemia in early post-KT (**Results S1, SDC**, http://links.lww.com/TXD/A388).

DISCUSSION

Using the national registry data, we observed that ESW was associated with lower risk of PTD compared with CSM (aHR = $_{0.72}0.79_{0.86}$), but this association differed by recipient age ($P_{\text{interaction}}$ = 0.09 for comparison between recipients aged 18–29 and those aged 30–54; $P_{\text{interaction}}$ = 0.01 for comparison between recipients aged 18–29 and those aged ≥55) among KT recipients with no known pre-KT diabetes. ESW was associated with lower risk of PTD among recipients aged 30–54 (aHR = $_{0.73}0.83_{0.95}$) and those aged ≥55 (aHR = $_{0.62}0.71_{0.81}$) but not among those aged 18–29 (aHR = $_{0.81}1.18_{1.72}$). Although recipients who received ESW had a higher risk of acute rejection across the age groups (adjusted odds ratio = $_{1.01}1.17_{1.34}$), these findings suggest that ESW had the benefit to prevent PTD especially among older recipients, which is associated with lower risk of mortality (aHR = $_{0.58}0.66_{0.74}$).

In the modern era of immunosuppression, limited and conflicting evidence is available on the effect of steroid withdrawal in the early posttransplant period on PTD.[21] ESW was associated with a decreased risk of PTD that was defined as requirement for insulin[36] but not when PTD was defined as 2

occurrences of fasting glucose ≥126 mg/dL[37] or requirement for insulin for over 30 consecutive days.[38]

In this study, we applied the validated method to identify patients with diabetes in claims data developed by Hebert et al,[24] which was used in the previous observational studies of PTD in linked Medicare claims and national transplant registry data and observed the beneficial effect of ESW on preventing PTD. Using the registry data, we included recipients older than 70 y who are excluded in completed[37] and ongoing trials registered on clinicaltrials.gov. Furthermore, we expanded the current literature on PTD by testing whether the effect of ESW differed by recipient age; our findings will help inform the choice or modification of immunosuppression strategy, particularly for older recipients.

Previous research supported that renal function[39] and graft survival[22] among recipients with ESW is comparable with among those with CSM. A randomized clinical trial data by Woodle et al[40] observed no difference of long-term death-censored graft failure and all-cause graft failure between ESW and CSM.

In addition, we observed that recipients without PTD had lower risk of mortality compared with those with PTD (aHR = $_{0.58}0.66_{0.74}$), which supports the previous evidence.[41] This suggests that ESW had the benefit to prevent PTD and the downstream long-term consequences.

However, there is a need to balance the risk of acute rejection with PTD when tapering steroid in early post-KT. In Cochrane review by Haller et al,[22] ESW was associated with higher risk of 1-y acute rejection (risk ratio [RR] = $_{1.21}1.77_{2.61}$) but not 1-y biopsy-proven acute rejection (RR = $_{0.78}1.32_{2.22}$).[22] Recent studies conducted in the 20th century observed no difference between ESW and CSM in combination with cyclosporine (RR = $_{0.25}1.40_{7.97}$ by Matl et al[42]; RR = $_{0.21}1.00_{4.75}$ by Pelletier et al[43]). Since tacrolimus was approved for the prevention of acute rejection by the Unites States Food and Drug Administration,[44] lower risk of acute rejection with tacrolimus was observed compared with cyclosporine.[45] With advances in immunosuppression strategies, studies reported no differences in risk of acute rejection comparing ESW with CSM in combination with tacrolimus.[39,46,47]

Through our real-world evidence study, we included older population (even aged ≥70) who is often excluded in trials and expanded our knowledge by asking clinically useful questions.[48] However, our study has some limitations. First, misclassification may affect the magnitude of the association between ESW and PTD. Use of claims to define PTD is a possible limitation of this study because it may be defined differently in other studies[49] or in clinical practice and undetected.[50] Second, unmeasured confounders and confounding by indication may bias the results. We applied the inverse probability weighting method and adjusted for many of clinical factors available in the United States Renal Data System data to minimize the limitation. Third, detailed dosage of steroid and the exact date of steroid withdrawal was not attainable. Lastly, although the combination of tacrolimus and mycophenolate is common in modern era,[51] our finding might not be generalizable to those who receive maintenance agents other than tacrolimus and mycophenolate.

In conclusion, ESW is associated with a decrease in PTD among recipients aged 30–54 and those aged ≥55 but not among those aged 18–29, with an increased risk of acute rejection across the age groups. Our findings suggest that the effect of ESW on preventing PTD, which leads to improved
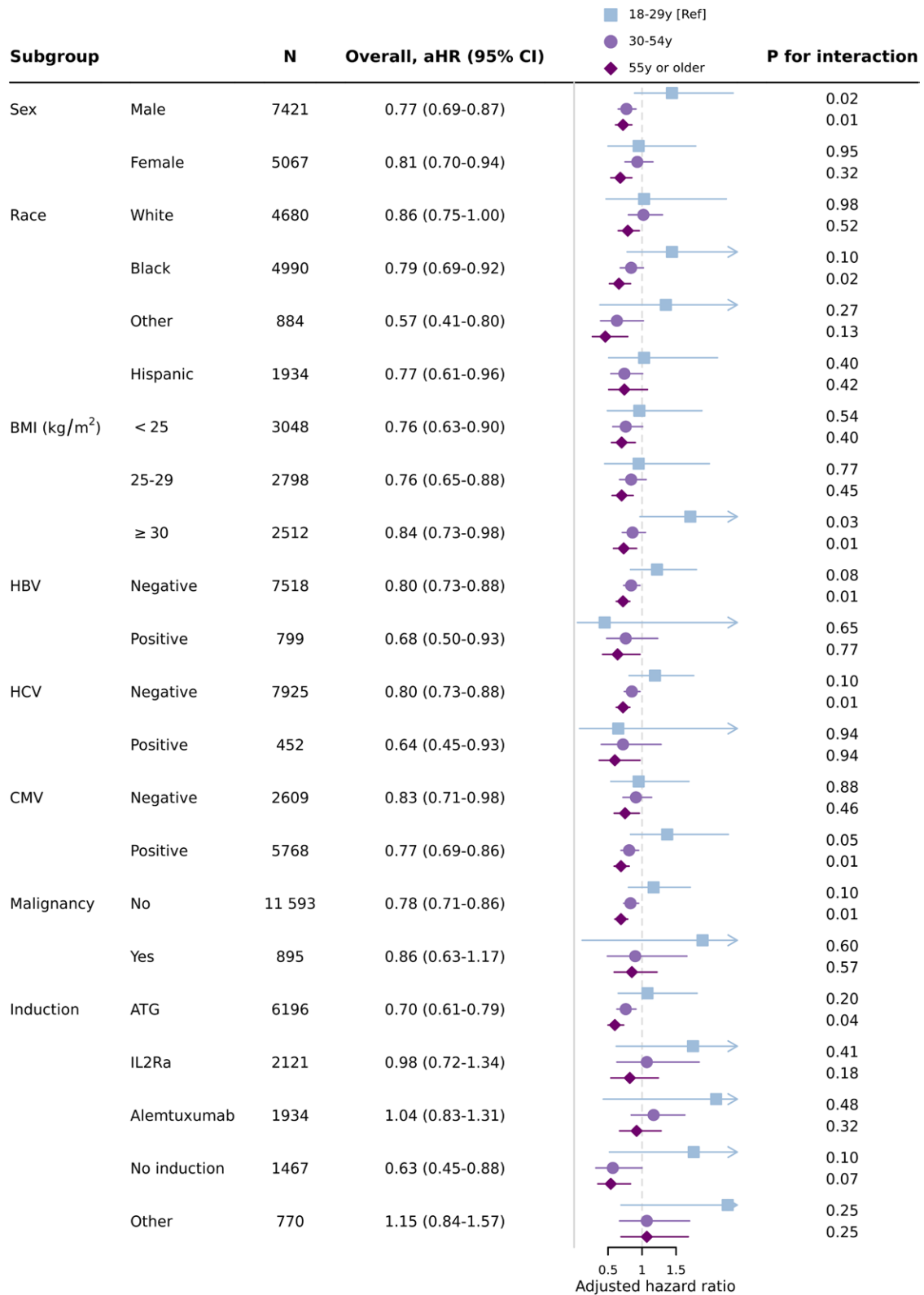
Subgroup		N	Overall, aHR (95% CI)	Forest Plot	P for interaction
				■ 18-29y [Ref] ● 30-54y ◆ 55y or older	
Sex	Male	7421	0.77 (0.69-0.87)		0.02 / 0.01
	Female	5067	0.81 (0.70-0.94)		0.95 / 0.32
Race	White	4680	0.86 (0.75-1.00)		0.98 / 0.52
	Black	4990	0.79 (0.69-0.92)		0.10 / 0.02
	Other	884	0.57 (0.41-0.80)		0.27 / 0.13
	Hispanic	1934	0.77 (0.61-0.96)		0.40 / 0.42
BMI (kg/m^2)	< 25	3048	0.76 (0.63-0.90)		0.54 / 0.40
	25-29	2798	0.76 (0.65-0.88)		0.77 / 0.45
	≥ 30	2512	0.84 (0.73-0.98)		0.03 / 0.01
HBV	Negative	7518	0.80 (0.73-0.88)		0.08 / 0.01
	Positive	799	0.68 (0.50-0.93)		0.65 / 0.77
HCV	Negative	7925	0.80 (0.73-0.88)		0.10 / 0.01
	Positive	452	0.64 (0.45-0.93)		0.94 / 0.94
CMV	Negative	2609	0.83 (0.71-0.98)		0.88 / 0.46
	Positive	5768	0.77 (0.69-0.86)		0.05 / 0.01
Malignancy	No	11 593	0.78 (0.71-0.86)		0.10 / 0.01
	Yes	895	0.86 (0.63-1.17)		0.60 / 0.57
Induction	ATG	6196	0.70 (0.61-0.79)		0.20 / 0.04
	IL2Ra	2121	0.98 (0.72-1.34)		0.41 / 0.18
	Alemtuxumab	1934	1.04 (0.83-1.31)		0.48 / 0.32
	No induction	1467	0.63 (0.45-0.88)		0.10 / 0.07
	Other	770	1.15 (0.84-1.57)		0.25 / 0.25

Adjusted hazard ratio: 0.5   1   1.5

FIGURE 3. Effect of early steroid withdrawal (vs continued steroid maintenance) on posttransplant diabetes among kidney transplant recipients differed by recipient age (18–29 [reference], 30–54, ≥55 y). Stratified analysis was conducted by risk factors of posttransplant diabetes. Interaction *P* values are presented to see whether the association differs across the age groups. aHR, adjusted hazard ratio; ATG, antithymocyte globulin; BMI, body mass index; CI, confidence interval; CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; IL2Ra, interleukin 2 receptor antagonist.

patient survival by reducing microvascular and macrovascular disease in later life,[52] may be weighed against the risk of acute rejection.

reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the US Government.

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