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Survival of Elderly Adults Undergoing Incident Home Hemodialysis and Kidney Transplantation

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Abstract

Background—To date, no study has compared the mortality of elderly patients with end stage renal disease (ESRD) treated with home hemodialysis (HD) versus kidney transplantation (KTx).

Design, Setting, Participants—Using data from elderly patients (65 years) who started home HD and who received KTx in the US between 2007-2011, we created a 1:1 propensity score (PS)-matched cohort of 960 elderly patients and examined the association between treatment modality and all-cause mortality via Cox proportional hazard and competing risk regression survival models using modality failure as a competing event.

Measurements—modality of renal replacement therapy.

Results—The mean±SD age of the PS-matched home HD and KTx elderly patients at baseline were 71±6 years and 71±5 years, 69% were male (both groups), 81% and 79% of patients were white and 11% and 12% were African American, respectively. Median follow-up time was 205 days (IQR: 78-364 days) for home HD patients and 795 days (IQR: 366-1,221 days) for KTx recipients. There were 97 deaths (20%, mortality rate 253 [207-309]/1000 patient-years) in the

home HD group, and 48 deaths (10%, 45 [34-60]/1000 patient-years) in the KTx group. Compared to KTx recipients, elderly patients on home HD had almost 5-times higher mortality risk (Hazard Ratio(HR): 4.74, 95% confidence interval(CI): 3.25-6.91). Similar results were seen in competing risk regression analyses (SHR: 4.71, 95%CI: 3.27-6.79). Results were consistent across different types of kidney donors and subgroups divided by various recipient characteristics.

Conclusion—KTx is associated with greater survival than home HD in elderly patients with ESRD. Further studies are needed to assess whether KTx is also associated with other benefits such as better quality of life or lower hospitalization rates.

Keywords

home hemodialysis; kidney transplantation; mortality; elderly; survival

Introduction

The proportion of elderly people (65 years) with end-stage renal disease (ESRD) has increased continuously over time; in 1990, 2000 and 2010, 39%, 44% and 44% of all prevalent dialysis patients, and 4%, 10% and 20% of all kidney transplant (KTx) recipients were older than 65 years, respectively.[1] KTx is generally regarded as the treatment of choice in ESRD irrespective of age,[2-4] given evidence of greater survival[5] and better quality of life[6] as compared to maintenance dialysis treatment. Previous data suggest that the projected increases in the life spans of KTx patients compared to conventional dialysis were 2.8 and 1.1 years for patients aged 65-69 and 70-74 years, respectively.[5] However, in 2010, the median KTx waiting time was almost 4 years in the entire nation and even longer in some states.[7] These long waiting periods may sometimes be even longer in elderly patient and may have a detrimental impact on their opportunities to receive a KTx. In addition, the life expectancy of elderly patients with ESRD may be shorter than wait times for transplant and if the home hemodialysis provides similar or better survival than KTx then transplant programs may not need to bother with working them up and listing them. This also spares precious organs for younger patients with ESRD.

Previous studies have shown that home hemodialysis (home HD) provides better survival than in-center HD in ESRD patients.[8-10] Two Canadian studies have also compared the survival of nocturnal home HD patients with KTx recipients,[11-13] and in the most recent study, which compared 173 of these Canadian nocturnal home HD patients to 1,517 Canadian KTx recipients from the same institution, patients with a KTx had a lower risk of treatment failure and death compared with home HD patients.[13] Most of these above mentioned KTx and home HD studies included ESRD patients with a mean age between 50-60 years, and studies regarding survival of elderly ESRD patients using home HD compared to other renal replacement therapies are lacking. Fast-growing dialysis therapies such as home HD may offer the same or even better survival advantages in elderly patient compared to deceased donor transplantation, the most common KTx in the elderly. Deceased donor KTx is unfortunately also associated with the burden of a major surgery, potential post-operative complications and life-long immunosuppressive therapy.[14] Home HD may thus be a better alternative to deceased donor KTx in elderly patients.

We therefore hypothesized that in the elderly, the above-mentioned small life span advantage from KTx can disappear or even reverse when compared to home HD. To address this study question, we examined the survival of incident elderly home HD and KTx patients in a large, nationally representative contemporary cohort of patients from the United States.

Methods

Data Source and Cohort Definition

The study cohort was comprised of incident home HD patients who receieved treatment from one of the largest dialysis providers in the United States, and United States incident KTx recipients who were transplanted between January 1st 2007 and December 31st 2011. Pertinent data for the two groups were obtained from electronic medical records from the large dialysis provider and from the United States Renal Data System, respectively. The study was approved by the Institutional Review Committees of the Los Angeles Biomedical Research Institute at Harbor-UCLA, University of California Irvine Medical Center, University of Washington, and University of Tennessee Health Science Center.

Home Hemodialysis cohort—The original source population was a cohort of 208,820 incident (newly initiated) dialysis patients. Patients were included in the cohort if they were 65 years old at the time of initiation of dialysis. Patients were excluded if they did not receive dialysis treatment for at least 60 days or did not have any treatment with home HD over their duration of follow up. The detailed description of dialysis modality assignment is discussed elsewhere.[15] Our final elderly home HD cohort included 638 patients (Figure 1).

Kidney transplant cohort—The United States Renal Data System includes all patients who received a KTx between 1963 and 2012. Patients 65 years old at time of transplant and who received their first kidney between January 1st 2007 and December 31st 2011 were included in our cohort. Patients were excluded if they were potentially also represented (based on age, race/ethnicity, date of transplant and gender) in the home HD cohort yielding a cohort with 12,668 KTx patients (Figure 1).

For the main analyses we created a 1:1 propensity score (PS) matched cohort consisting of 480 home HD and 480 KTx elderly patients (Figure 1).

Exposure, Covariates, Outcome

Data on age, gender, race/ethnicity, ESRD etiology and vintage, access type, primary insurance, body mass index, serum albumin, blood hemoglobin and coexisting conditions was obtained from the two data sources and refined. The following nine coexisting conditions were considered: diabetes mellitus, hypertension, alcohol abuse, atherosclerotic heart disease, other cardiac disease (pericarditis and cardiac arrhythmia), congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, and malignancy. Exposure was defined as home HD versus KTx, and the outcome was all-cause mortality. Expanded criteria donors (ECD) were defined as: donors are normally aged 60 years or older, or over 50 years with at least two of the following conditions: history of hypertension, serum creatinine > 1.5 mg/dl or cause of death from cerebrovascular accident. The Kidney

Donor Profile Index (KDPI) combines a variety of donor factors into a single number that summarizes the risk of graft failure after kidney transplant and it is currently used for donor allocation in United States.[16]

Statistical Analysis

Data were summarized using proportions, means ± SD, or median (interquartile range (IQR)) as appropriate. PS matching was used to account for baseline differences arising from dissimilarities in clinical and demographic characteristics of home HD and KTx patients. We created PS-matched cohorts for the overall cohort. STATA's "psmatch2" command suite was used to generate 1:1 PS-matched cohorts using nearest neighbor matching without replacement. The following variables were included in a logistic regression model to calculate the propensity scores: age, gender, race/ethnicity, primary insurance, type of vascular access at the time of transplantation/home HD, cause of ESRD, previous time with ESRD, body mass index, blood hemoglobin, serum albumin, comorbidities at baseline (diabetes, hypertension, cardiovascular disease, atherosclerotic heart disease, heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, malignancy, and alcohol abuse). Home HD and KTx patients before and after matching were compared using standardized differences.[17]

Associations between renal replacement modalities (home HD vs. KTx) and all-cause mortality were assessed using the Kaplan-Meier method, and Cox proportional hazard models (for time to event analyses). Models in PS-matched cohorts were not additionally adjusted for covariates. For the main analyses, the start of the follow-up period was the start date of home HD modality or the date of kidney transplantation. Patients were followed until date of death, date of censoring [transfer to a different dialysis modality, kidney transplantation, transfer to a different facility or other reason for home HD patients; or date of allograft loss (re-transplantation, first date of dialysis) for KTx patients], or the end of the follow-up period (December 31st, 2011). In sensitivity analyses, we used an alternative censoring method where home HD patients were not censored at time of transfer to a different dialysis modality and continued to be followed until death, end of follow up, or other causes of censoring.

As a significant proportion of home HD patients were transplanted during the follow-up period, there is a potentially significant degree of informative censoring due to the selective removal of a healthier group of transplant eligible home HD patients. We therefore performed a competing risk model analyses to take this into account. Our event of interest was all-cause mortality and the competing event was kidney transplantation in the home HD group and graft loss in the KTx group. In our study we used the Fine and Gray model,[18] which extends the Cox proportional hazards model to competing-risks data by considering the subdistribution hazard.

Finally, we also performed sensitivity analysis using the entire cohort population (n=13,306). In this Cox proportional hazards model we adjusted for the following confounders: age, gender, race/ethnicity, primary insurance, type of vascular access at the time of transplantation/home HD, cause of ESRD, previous time with ESRD, body mass index, blood hemoglobin, serum albumin, comorbidities at baseline (diabetes, hypertension,

cardiovascular disease, atherosclerotic heart disease, heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, malignancy, and alcohol abuse).

Effect modification by different patient characteristics was tested in the association of treatment modality with all-cause mortality. Statistical analyses were performed using Stata MP version 13 (Stata Corporation, College Station, TX, USA) and SAS, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics

Baseline characteristics of home HD and KTx patients before and after matching are shown in Table 1. Before matching, home HD patients were older, more likely to be male, diabetic, and white, had a higher prevalence of atherosclerotic heart disease, congestive heart failure, and other cardiovascular disease and had a higher serum albumin and shorter total ESRD time before modality initiation. After PS matching, all baseline variables were well balanced between home HD and KTx patients (Table 1).

Mortality in the PS matched cohort

Median follow-up time was 205 days (IQR: 78-364 days) for home HD patients and 795 days (IQR: 366-1,221 days) for KTx recipients. There were 97 deaths (20%, mortality rate 253 [207-309]/1000 patient-years) in the home HD group, and 48 deaths (10%, 45 [34-60]/ 1000 patient-years) in the KTx group. Figure 2 shows the probability of 5-year survival of home HD and KTx patients in the PS matched group. Home HD patients had a 4.7 fold higher mortality risk compared to KTx patients (hazard ratio (HR): 4.74, 95% confidence interval (CI): 3.25-6.91) over the entire follow-up period. Similar results were seen in sensitivity analyses using alternative censoring (HR: 4.71, 95%CI: 3.25-6.84) (Figure S1) or competing risk regression (SHR: 4.71, 95%CI: 3.27-6.79) or in the entire cohort (Figure S3) after adjusment for important confounders (HR: 3.51, 95%CI: 2.82-4.36).

Mortality in the PS matched subcohorts

Figure 3 shows that home HD patients had higher mortality risk compared to KTx patients in all PS matched subcohorts, except in African-American patients and KTx recipients transplanted from donors with a KDPI<20. However, no significant effect modification was detected between different subgroups based on testing for interaction using interaction terms. Similar results were also seen in sensitivity analyses using alternative censoring (Figure S2) and in the entire cohort (Figure S4).

Discussion

In this contemporary cohort of incident elderly home HD patients and elderly KTx recipients in the United States, we examined the association between type of renal replacement modality with all-cause mortality. Patients who received a KTx had significantly better survival regardless of recipient or donor characteristics.

There is an ongoing discussion about what the ideal renal replacement therapy (RRT) is for elderly ESRD patients, ranging from conservative treatment (no RRT) to kidney transplantation.[19] Large epidemiological studies from different countries have shown that there is no significant difference in survival[20-22] or quality of life[23, 24] in elderly patients being treated with hemodialysis versus peritoneal dialysis. However, in United States, higher risk for death was showed in sub-groups of elderly patients treated with peritoneal dialysis compared to hemodialysis.[25] Nevertheless, some studies suggest that compared to dialysis patients, elderly KTx recipients, and in particular recipients of expanded criteria deceased (ECD) donor kidneys, have greater survival.[2-5, 26, 27] Moreover, a recent study showed that age is a strong, independent risk factor for death after KTx. Although lower mortality was observed with living kidney transplantation among elderly recipients, living-donor rates decrease with increasing recipient age.[28]

It has been argued that transplantation may offer substantial clinical benefits to older patients at a reasonable financial cost, especially if transplantation waiting times were short.[5, 29-37] In a recent study including 2000 deceased-donor KTx recipients older than 70 years, elderly KTx recipients had a 41% lower mortality risk compared to elderly patients who remained on the KTx waitlist.[3] Unfortunately, one of the largest studies comparing KTx recipients to waitlist patients in 230,000 dialysis patients did not include patients older than 70 years, but did show that mortality risk was significantly lower in KTx recipients (3.8 vs. 6.3/100 patient-years).[5] KTx in the elderly can increase risk of infectious complications,[38] and risk of early mortality due to a higher burden of comorbidity[39]. Older age may also be associated with different adaptive immunity and pharmacokinetics,[40] which can have negative effects on post-transplant survival.

Compared to the European system (elderly recipients are prioritized for elderly donor kidneys ("old for old" program)), where an effective allocation system has been developed and used for elderly patients;[41] the new allocation system in the US penalizes older recipients, as their Estimated Post Transplant Survival (EPTS) score cannot be low. For example, the EPTS score of a 70 years old candidate without diabetes waiting for the first pre-emptive transplant is 55% (based on a reference population as of 9/30/2013), excluding this candidate from receiving the best quality donor kidney. Our results indicate that KTx is associated with a better chance of survival compared to home HD in elderly patients with ESRD, consequently KTx may still be the best choice of treatment regardless of age in patients with ESRD.

To the best of our knowledge no study has compared to date survival in elderly patient treated with home HD with that of KTx recipients. Home HD may provide certain advantages in elderly ESRD patients, including improved blood pressure control,[42-45] reductions in total peripheral resistance and plasma norepinephrine levels,[46] reduction in left ventricular mass,[42, 45, 47, 48] better anemia[49] and phosphorus control,[45, 50-52] and better control of sleep disorders,[53] which might diminish the previously described survival difference between KTx and regular dialysis patients.

In our study, despite all the potential benefits of home HD, elderly home HD patients had an almost 5-times higher risk of mortality compared to their KTx counterparts. Similar results

were found in almost all subgroups of patients. Even elderly KTx recipients with ECD donors and severe comorbidity showed better survival than home HD patients with similar comorbidities. Prior studies in Canadian patients similarly showed a survival benefit of KTx compared to home HD.[11, 13] However, the mean±SD age of the recent Canadian study was 45±13 years indicating that only few home HD patients were older than 65 years[13], and therefore these results may not be applicable to elderly ESRD patients from the United States. Our study results confirm that KTx should remain the treatment of choice for elderly patients with ESRD, even compared to home HD.

Our study should be noted for a number of strengths. It is the first comparison of mortality for elderly home HD patients and KTx recipients from the United States. Secondly, our study used a PS-matched approach to balance measured confounders and to address potential confounding by indication and selection bias. We additionally performed sensitivity analyses with an alternate censoring method by continuing to follow patients after home HD therapy ended and also performed competing risk regression analyses to take into account so-called informative censoring, or the selective earlier censoring of healthier transplant eligible home HD patients. We also confirmed our primary result in sensitivity analyses performed in the entire cohort. Finally, we also examined associations across different subgroups of patients to test for potential effect modification by donor and recipient characteristics. Our results were consistent and robust across subgroups and in sensitivity analyses.

The results of our study should be interpreted in light of some potential limitations. First, we acknowledge that our sample size and event numbers in elderly home HD patients are small. However, to the best of our knowledge ours is the largest cohort of elderly home HD patients assembled to date and compares outcomes to a large cohort of elderly KTx recipients. Second, home HD data were derived from facilities operated by a single dialysis provider. However, patients from this provider constitute almost one-third of all patients undergoing maintenance dialysis in the United States. Third, the median follow-up time in home HD patients was relatively short. The main reason for this was that our home HD patients were transferred to other dialysis modalities after a relative short period of time. Further studies are needed to identify the cause of this observed phenomenon. Fourth, due to unavailable data, we were not able to analyze potential differences between hospitalization rate or quality of life outcomes in these patients. Furthermore, we did not have data regarding the home HD patients' wait-list status, and consequently we were not able to perform subgroup analysis in this subcohort. Fifth, our result may not be applicable to populations outside the US, as the nocturnal home hemodialysis practice is significantly different in Australia, Canada or Europe. Moreover, the dialysis and transplant outcomes are inferior in the US compared to Europe. Lastly, despite the fact that we were able to PS match our cohorts for many confounding factors, our study results may still have been subjected to residual confounding due to unmeasured or unknown confounders.

Conclusion

In conclusion, KTx is associated with a better chance of survival compared to home HD in elderly patients with ESRD. Further studies are needed to assess whether KTx also provides

better quality of life or lower hospitalization rates compared to home HD in elderly patients with ESRD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Flow chart of patients' selection
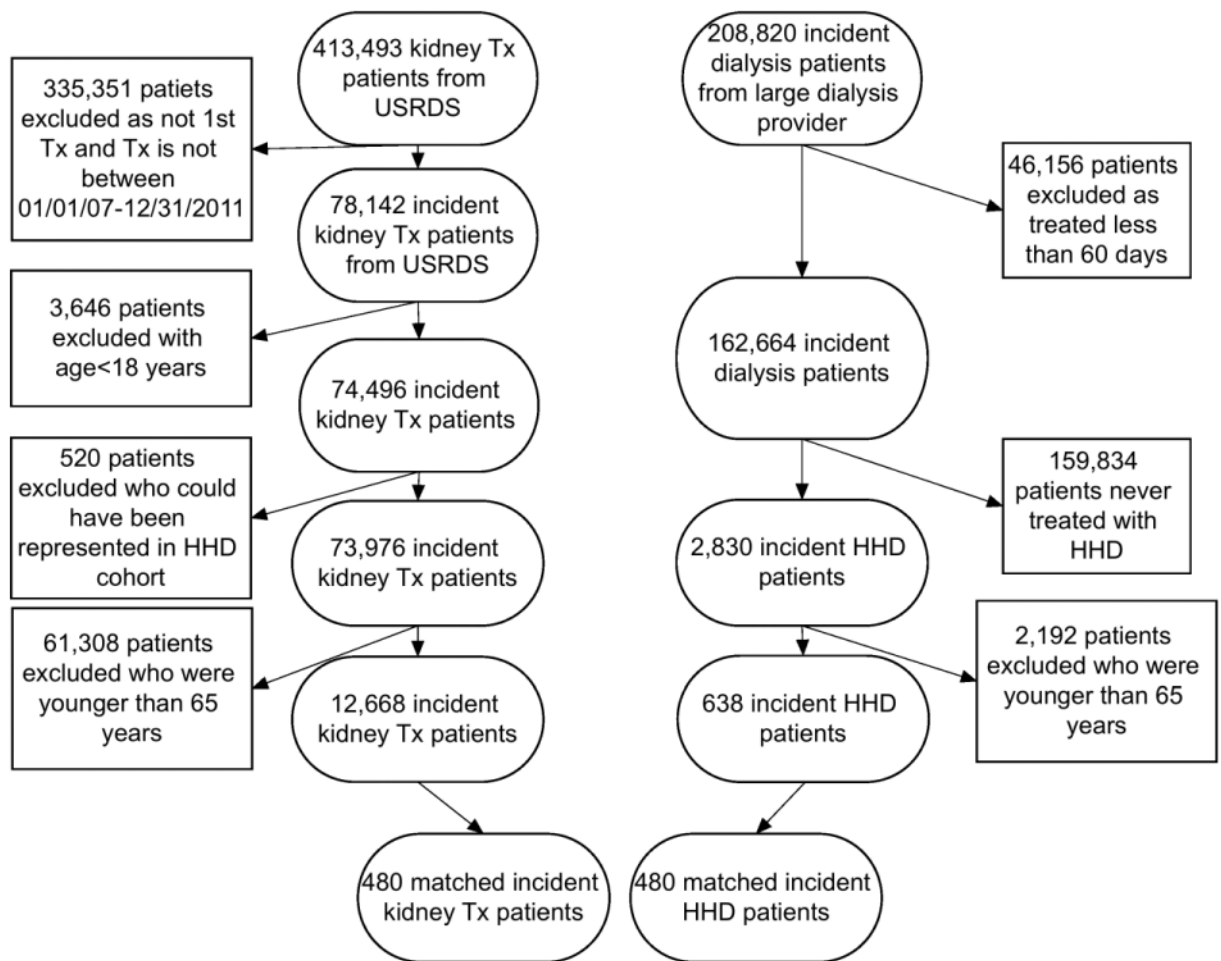Abbreviations: HHD: Home Hemodialysis; Tx: Kidney Transplant; USRDS: United States
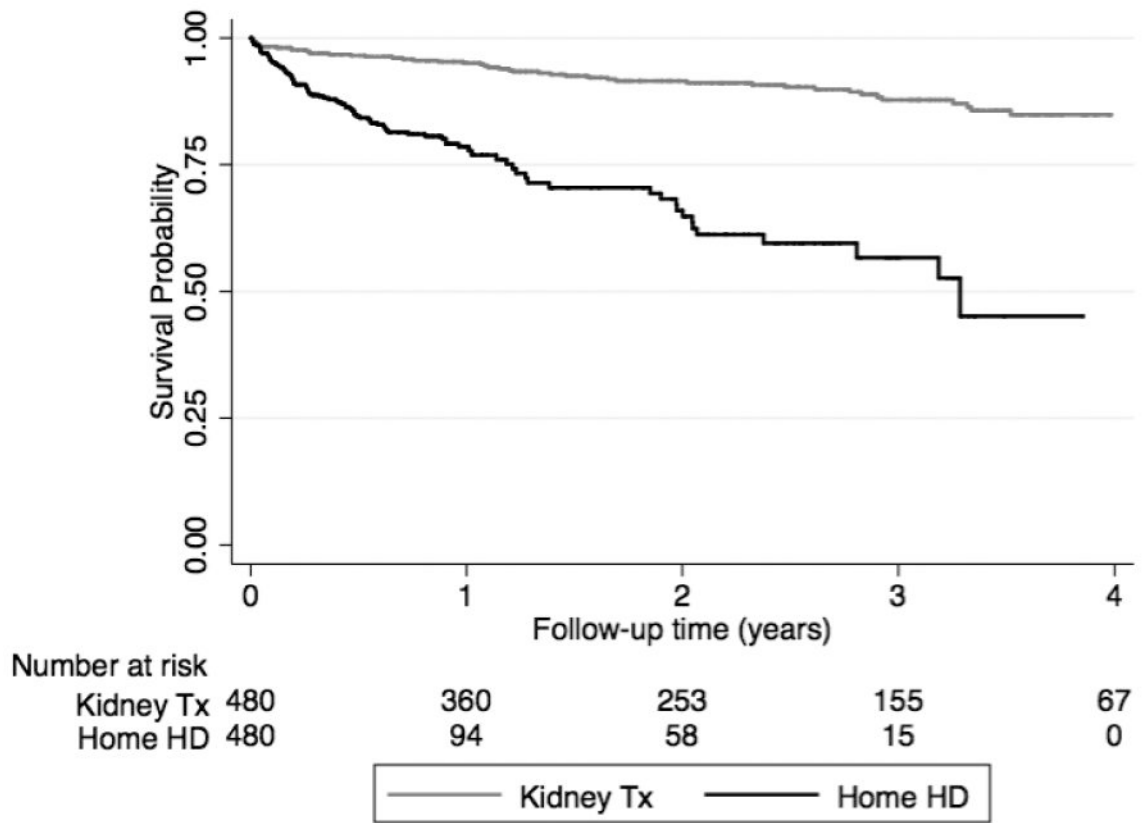Renal Data System

Figure 2. Association between renal replacement type (home hemodialysis (Home HD) versus kidney transplantation (Kidney Tx)) and mortality using Kaplan-Meiers curves in the propensity score matched cohort
Abbreviations: Home HD: Home Hemodialysis; Kidney Tx: Kidney Transplant
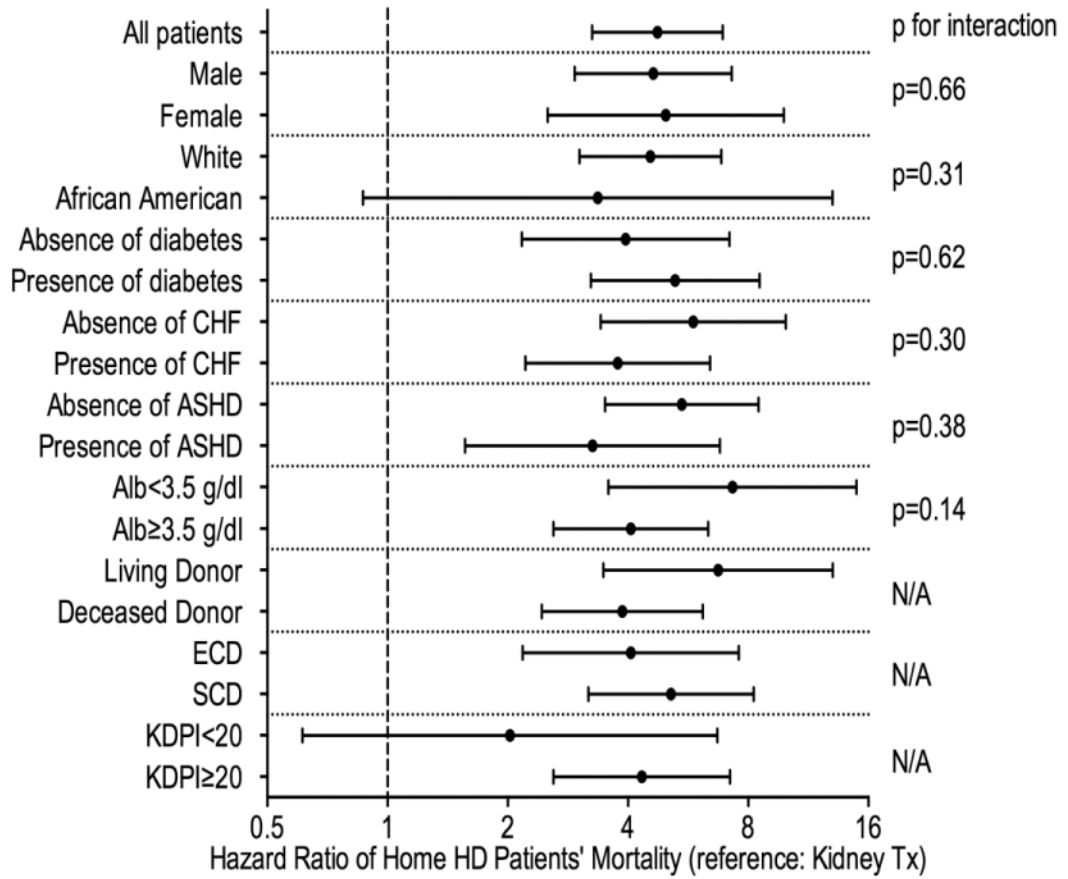
Figure 3. Mortality risk of home hemodialysis patients compared to kidney transplant recipients in groups of patients with different recipient and donor characteristics using the propensity score matched cohort

Abbreviations: Alb: Serum Albumin; ASHD: Arthero-Sclerotic Heart Disease; CHF: Congestive Heart Failure; ECD: Extended Criteria Donor; Home HD: home hemodialysis; KDPI: Kidney Donor Profile Index; Kidney Tx: Kidney Transplant; N/A: Not Applicable; SCD: Standard Criteria Donor

Table 1

Baseline characteristics of the unmatched and the 1:1 propensity score-matched cohort

	Unmatched			Matched		
	Home HD	Kidney Tx	Std. Diff.	Home HD	Kidney Tx	Std. Diff.
	(n =638)	(n = 12,668)		(n=480)	(n=480)	
Age (years)	72 ± 6	69 ± 4	0.547	71 ± 6	71 ± 5	0.052
Female (%)	30	37	-0.141	31	31	0.005
Race/Ethnicity (%)						
Whites	84	62	0.262	81	79	0.054
African-American	9	19	-0.315	11	12	-0.039
Asian	4	11	-0.244	4	4	-0.068
Hispanic	1	6	-0.282	2	3	-0.010
Other	2	2	0.045	2	2	0
Primary insurance (%)						
Medicare	71	65	0.496	71	70	0.027
Medicaid	1	8	-0.312	1	1	-0.024
Other	28	27	0.197	28	29	-0.023
Comorbid States (%)						
Diabetes mellitus	66	44	0.450	61	59	0.025
Alcohol abuse	0	0.4	-0.089	0	0	0
History of cancer	7	4	0.111	7	8	-0.048
Hypertension	70	64	0.139	74	74	0.005
Cerebrovascular disease	2	3	-0.071	3	2	0.043
Artherosclerotic Heart Disease	32	11	0.539	27	29	-0.037
Congestive heart failure	51	10	1.000	40	43	-0.072
Other cardiovascular disease	28	9	0.514	23	24	-0.046
Chronic Obstructive Pulmonary Disease	9	2	0.294	7	8	-0.020
Access Type at time of Home HD initiation/time of KTx (%)						
AV Fistula	51	16	0.815	47	48	-0.017
AV Graft	9	2	0.302	7	10	-0.106

	Unmatched				Matched		
	Home HD	Kidney Tx	Std. Diff.		Home HD	Kidney Tx	Std. Diff.
	(n =638)	(n = 12,668)			(n=480)	(n=480)	
Central Venous Catheter	22	28	-0.148		25	21	0.079
Other/unknown	18	54	-0.809		21	21	0
Cause of ESRD (%)							
Diabetes	40	36	0.089		40	38	0.034
Hypertension	27	27	0.010		27	27	0.005
Glomerulonephritis	12	13	-0.036		12	13	-0.044
Cystic kidney disease	3	8	-0.199		3	4	-0.046
Other reason	18	16	0.078		18	18	0.011
Laboratory Tests at time of Home HD initiation/time of KTx							
Serum albumin (g/dL)	3.8 ± 0.4	3.5 ± 0.6	0.473		3.7 ± 0.4	3.7 ± 0.5	0.018
Blood hemoglobin (g/dL)	11.0 ± 1.2	10.5 ± 1.6	0.405		10.9 ± 1.2	10.9 ± 1.5	-0.014
Other							
Total ESRD time before modality initiation (days)	332 ± 330	975 ± 936	-0.916		465 ± 354	383 ± 344	-0.054
Body Mass Index (kg/m^2)	29 ± 6	28 ± 6	0.061		29 ± 6	28 ± 6	0.032

Abbreviations: AV: Arterio-Venosus; ESRD: End Stage Renal Disease; Home HD: home hemodialysis; Kidney Tx: Kidney Transplant; Std Diff: Standardized Difference