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Beta-blocker practice patterns in chronic kidney disease patients with atrial fibrillation transitioning to hemodialysis

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To the Editor:

The transition from chronic kidney disease (CKD) to end-stage renal disease requiring maintenance dialysis is a period associated with high rates of morbidity and mortality.[1] Cardiovascular events account for a large proportion of death during this period.[2] Patients with atrial fibrillation are particularly vulnerable, with double the risk of death compared to those without.[3] Central to the management of atrial fibrillation is achieving adequate heart rate control. Guidelines recommend use of beta-blockers for rate control in patients with atrial fibrillation[4] as beta-blocker therapy has been associated with a reduction in all-cause mortality.[5] Beta-blockers represent a heterogenous group of medications with varying pharmacological properties. Some beta-blockers such as atenolol, metoprolol, and nadolol are effectively removed from the circulation by hemodialysis and are considered dialyzable. Others, including carvedilol, nebivolol, and propranolol, are not effectively removed as a result of dialysis and are characterized as nondialyzable. The varying dialyzability of beta-blockers may influence their effectiveness as the plasma concentrations of the medications would differ.[6,7] There is no clear consensus regarding adjustment of beta-blocker therapy when a patient is started on hemodialysis. Our study was designed to understand practice patterns of beta-blocker use in patients with atrial fibrillation transitioning from CKD to hemodialysis.

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In this United States Renal Data System (USRDS) special center study, we performed a retrospective cohort study examining CKD patients with concomitant atrial fibrillation transitioning to hemodialysis within the Kaiser Permanente Southern California health system between January 1, 2007 and June 30, 2016. A total of 9629 patients transitioned to hemodialysis during this period. Using pharmacy dispensing records, we identified 4811 patients who were treated with a beta-blocker at the date of transition to hemodialysis (as defined as dispense date plus supply days covering the transition date). Within this group, 547 patients had a prevalent diagnosis of atrial fibrillation (ascertained using *International Classification of Diseases-9/10* codes within 1 year prior to transition). Bisoprolol was categorized as dialyzable based on recent findings showing intermediate dialytic clearance.[8] This study was approved by the Kaiser Permanente Southern California Institutional Review Board and exempted from informed consent (IRB #10591).

Prior to initiation of hemodialysis, 389 (71.1%) patients were treated with dialyzable beta-blockers and 158 (28.9%) were on nondialyzable beta-blockers (Table 1). The groups were well balanced with respect to age, sex, and race/ethnicity. There was a higher prevalence of coronary artery disease and congestive heart failure in the nondialyzable beta-blocker group. Mean heart rate was 74 ± 13 beats per minute (bpm) in the dialyzable beta-blocker group, and 73 ± 13 bpm in the nondialyzable beta-blocker group. Concomitant use of calcium channel blockers, alpha agonist, or alpha-blockers were less common in the nondialyzable beta-blocker group (Table 1).

Within 120 days after transition to hemodialysis, 315 (57.6%) continued on the same type of beta-blockers and 33 (6.0%) patients switched beta-blocker types. There were 20 (5.1%) patients who switched from a dialyzable beta-blocker to a nondialyzable beta-blocker, and 13 (8.2%) who switched from a nondialyzable beta-blocker to a dialyzable beta-blocker. Adequate heart rate control was achieved regardless of beta-blocker types used. Mean heart rates were well below 110 bpm, the target recommended by national guidelines, in all beta-blocker groups.[4] Overall, 131 (23.9%) patients discontinued beta-blockers after transition to hemodialysis. A similar posthemodialysis transition decline (11% per quarter) in beta-blocker use was also described among a low-income USRDS subpopulation with Medicare Part D who newly initiated dialysis.[9] Sixty-four (11.7%) died within 120 days (Figure 1). Among patients who discontinued beta-blockers, 39 (29.8%) died between 121 and 485 days. Patients who discontinued beta-blockers had a higher mortality rate compared to those who took beta-blockers (29.8% vs. 22.4%).

Several potential limitations should be acknowledged. This was an observational study and may be subject to confounding by indication. Beta-blocker type use was not randomly allocated, with selections made by treating clinicians based on clinical judgment. Differences in evidence-based indications for the different types of the beta-blocker class may have influenced the distribution of the comorbidities between groups. The study population was relatively small and most likely underpowered to detect significance differences in outcomes between patients using different beta-blocker types. Misclassification bias from coding errors and other sources could have affected results. Last, the study design precluded differentiation of paroxysmal vs. chronic atrial fibrillation.

In conclusion, we found that while dialyzable and nondialyzable beta-blockers are both commonly used in atrial fibrillation patients transitioning to hemodialysis, only a small subset of patients switched beta-blocker types (similarly in both directions) after initiation of dialysis. This suggests that dialyzability may not have been an important factor in the consideration of beta-blocker choice.

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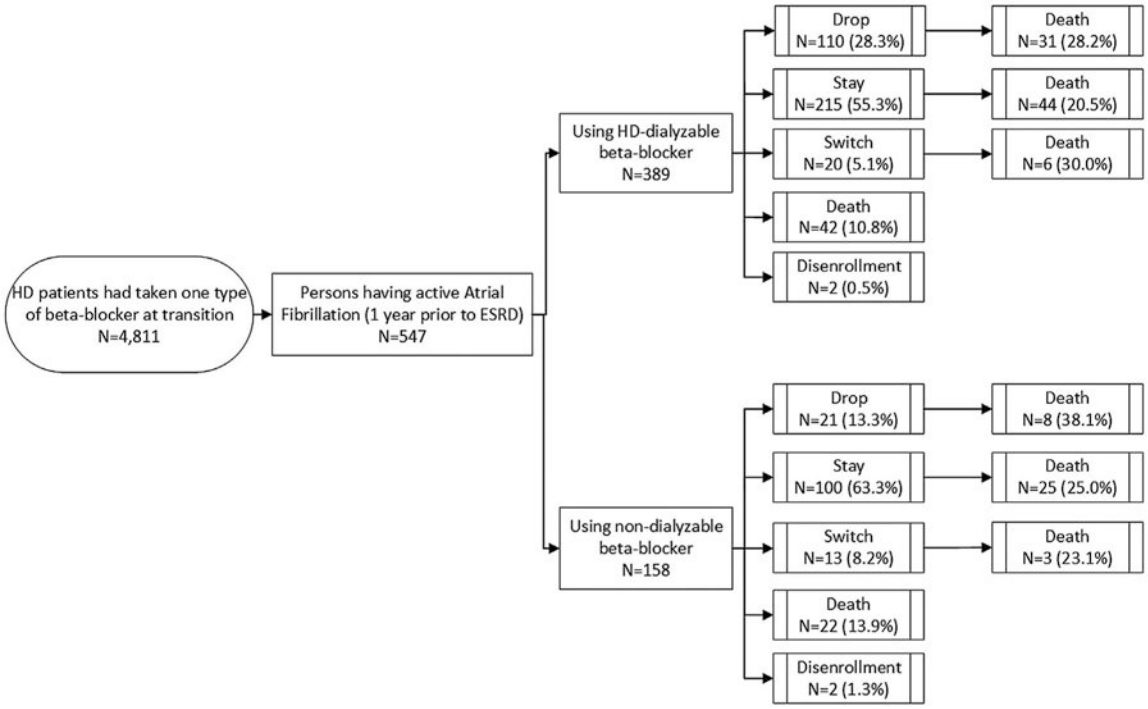

Figure 1.

Flowchart of study population. Medication changes are within 120 d after transition to hemodialysis. Last column of death reflect mortality 121 to 485 d after transition.

Table 1

Characteristics of chronic kidney disease patients with atrial fibrillation who transitioned to hemodialysis

	Total population (n = 547)	Dialyzable beta-blocker pretransition (n = 389)	Nondialyzable beta-blocker pretransition (n = 158)	P value
Age, mean yrs ± SD	73.5 ± 9.3	73.9 ± 9.3	72.5 ± 9.3	0.10
Females, N (%)	199 (36.4)	143 (36.8)	56 (35.4)	0.80
Race/ethnicity, N (%)				0.90
White	258 (47.2)	184 (47.3)	74 (46.8)	
Black	69 (12.6)	48 (12.3)	21 (13.3)	
Hispanic	148 (27.1)	105 (27)	43 (27.2)	
Asian	61 (11.2)	43 (11.1)	18 (11.4)	
Other	11 (2.0)	9 (2.5)	2 (1.2)	
Comorbidities, N (%)				
Hypertension	539 (98.5)	384 (98.7)	155 (98.1)	0.30
Diabetes	459 (83.9)	323 (83)	136 (86.1)	0.40
Coronary heart disease	382 (69.8)	257 (66.1)	125 (79.1)	0.003
Congestive heart failure	494 (90.3)	341 (87.7)	153 (96.8)	0.001
Primary cause of end-stage renal disease, N (%)				0.30
Diabetes	315 (57.6)	223 (57.3)	92 (58.2)	
Primary glomerulonephritis	16 (2.9)	13 (3.3)	3 (1.9)	
Secondary glomerulonephritis/vasculitis	2 (0.4)	2 (0.5)	0 (0)	
Interstitial nephritis/pyelonephritis	9 (1.6)	6 (1.5)	3 (1.9)	
Hypertension/large vessel disease	137 (25)	98 (25.2)	39 (24.7)	
Cystic/hereditary/congenital disease	7 (1.3)	7 (1.8)	0 (0)	
Neoplasms/tumors	9 (1.6)	7 (1.8)	2 (1.3)	
Miscellaneous conditions	36 (6.6)	20 (5.1)	16 (10.1)	
Unknown	16 (2.9)	13 (3.3)	3 (1.9)	
Hemodynamics in 120 d pretransition				
Average heart rate < 60 bpm, N (%)	66 (12.1)	50 (12.9)	16 (10.1)	0.40
Average systolic blood pressure, mean mmHg ± SD	129.0 ± 18.9	131.1 ± 17	124.1 ± 20	<0.001
Beta-blocker type, N (%)				<0.001

	Total population (n = 547)	Dialyzable beta-blocker pretransition (n = 389)	Nondialyzable beta-blocker pretransition (n = 158)	P value
Atenolol	93 (17)	93 (23.9)	0 (0)	
Bisoprolol	20 (3.7)	20 (5.1)	0 (0)	
Carvedilol	148 (27.1)	0 (0)	148 (93.7)	
Metoprolol	266 (48.6)	266 (68.4)	0 (0)	
Other[a]	20 (3.7)	10 (2.6)	10 (6.3)	
Other common cardiac medications used at transition, N (%)				
Angiotensin converting enzyme inhibitors	146 (26.7)	100 (25.7)	46 (29.1)	0.40
Angiotensin receptor blockers	85 (15.5)	57 (14.7)	28 (17.7)	0.40
Aldosterone antagonist	40 (7.3)	27 (6.9)	13 (8.2)	0.60
Diuretics	414 (75.7)	287 (73.8)	127 (80.4)	0.10
Hydralazine	161 (29.4)	115 (29.6)	46 (29.1)	0.90
Nitrates	161 (29.4)	108 (27.8)	53 (33.5)	0.20
Calcium channel blocker	246 (45)	201 (51.7)	45 (28.5)	<0.001
Alpha agonist	53 (9.7)	46 (11.8)	7 (4.4)	0.008
Alpha blocker	146 (26.7)	117 (30.1)	29 (18.4)	0.005
Digoxin	69 (12.6)	45 (11.6)	24 (15.2)	0.20
Antiarrhythmic[b]	78 (14.3)	49 (12.6)	29 (18.4)	0.08
Other[c]	197 (36)	149 (38.3)	48 (30.4)	0.10

Values are mean ± SD or n (%).

[a]Other beta-blocker medication include labetalol, nadolol, propranolol, sotalol, and betaxolol.

[b]Antiarrhythmic medications include amiodarone, procainamide, flecainide, and quinidine.

[c]The other in other common cardiac medications used at transition include hydralazine and minoxidil.

bpm = beats per minute.

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