

Renin–Angiotensin–Aldosterone System Inhibitor Prescription Patterns in Hemodialysis Patients: Results From the International Dialysis Outcomes and Practice Patterns Study (DOPPS)

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Introduction

- Renin–angiotensin–aldosterone system inhibitors (RAASi) are often prescribed to manage chronic kidney disease (CKD); including patients with diabetes mellitus (DM), hypertension, and class-specific indications including heart failure and ischemic heart disease¹
- Patients receiving hemodialysis (HD) have an increased risk of cardiovascular disease; thus, current clinical practice guidelines indicate that use of RAASi therapy may be beneficial^{2,3}
- Hyperkalemia can occur without RAASi use, but RAASi use may increase the likelihood of hyperkalemia leading to changes in RAASi treatment patterns to control hyperkalemia
- Here, real-world variations in RAASi prescription patterns by geographic region, time period, serum potassium (K⁺) levels, and comorbidities were evaluated among patients with kidney failure undergoing in-center HD using data from the Dialysis Outcomes and Practice Patterns Study (DOPPS)

Methods

- DOPPS is a large, international, prospective, observational cohort study of patients receiving HD currently ongoing in North America (US and Canada), Europe (Belgium, France, Germany, Italy, Spain, Sweden, and the UK), Australia, New Zealand, Russia, Turkey, countries in the Gulf Cooperation Council, and Asia (China and Japan)
- RAASi prescriptions (including angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blocker [ARBs], renin inhibitors, or aldosterone antagonists) were analyzed in a cross-section of patients undergoing HD enrolled in DOPPS phases 2–5 (phase 2, 2002–2004; phase 3, 2005–2008; phase 4, 2009–2011; phase 5, 2012–2015) in countries with available data
- Patients were stratified based on the following baseline parameters:
 - Length of time on HD at DOPPS entry: short-term (ST) HD (≤120 days [predialysis]) and long-term (LT) HD (>120 days); 120 days was chosen as a cut-off as it may be a reflection of predialysis medical care
 - Geographic region: North America (US and Canada), Europe/Australia/New Zealand, and Japan
 - DOPPS phase
 - Comorbidities: DM, congestive heart failure (CHF), and hypertension
 - Serum K⁺ concentration: ≤5.0, >5.0–≤5.5, >5.5–≤6.0, and >6.0 mEq/L
- Statistical analyses
 - Proportions of patients with different types of RAASi therapy by region and DOPPS phase or comorbidity

Results

- DOPPS phases 2–5 (2002–2015) included 11,710 and 37,852 patients receiving ST and LT HD, respectively
- Baseline characteristics (Table 1) were largely similar among regions and ST and LT HD groups
 - However, the use of other non-RAASi medications that may affect serum K⁺ levels, including K⁺-binding resins, β-blockers, and diuretics, varied among regions
- All patients had dialysis-dependent CKD, and most had comorbid hypertension (ST HD, 86.3%; LT HD, 82.5%), nearly one-half had DM (ST HD, 48.8%; LT HD, 41.5%), and nearly one-third had CHF (ST HD, 29.9%; LT HD, 29.7%)

Table 1. Baseline Patient Characteristics by RAASi Use, Region, and Length of Time on HD

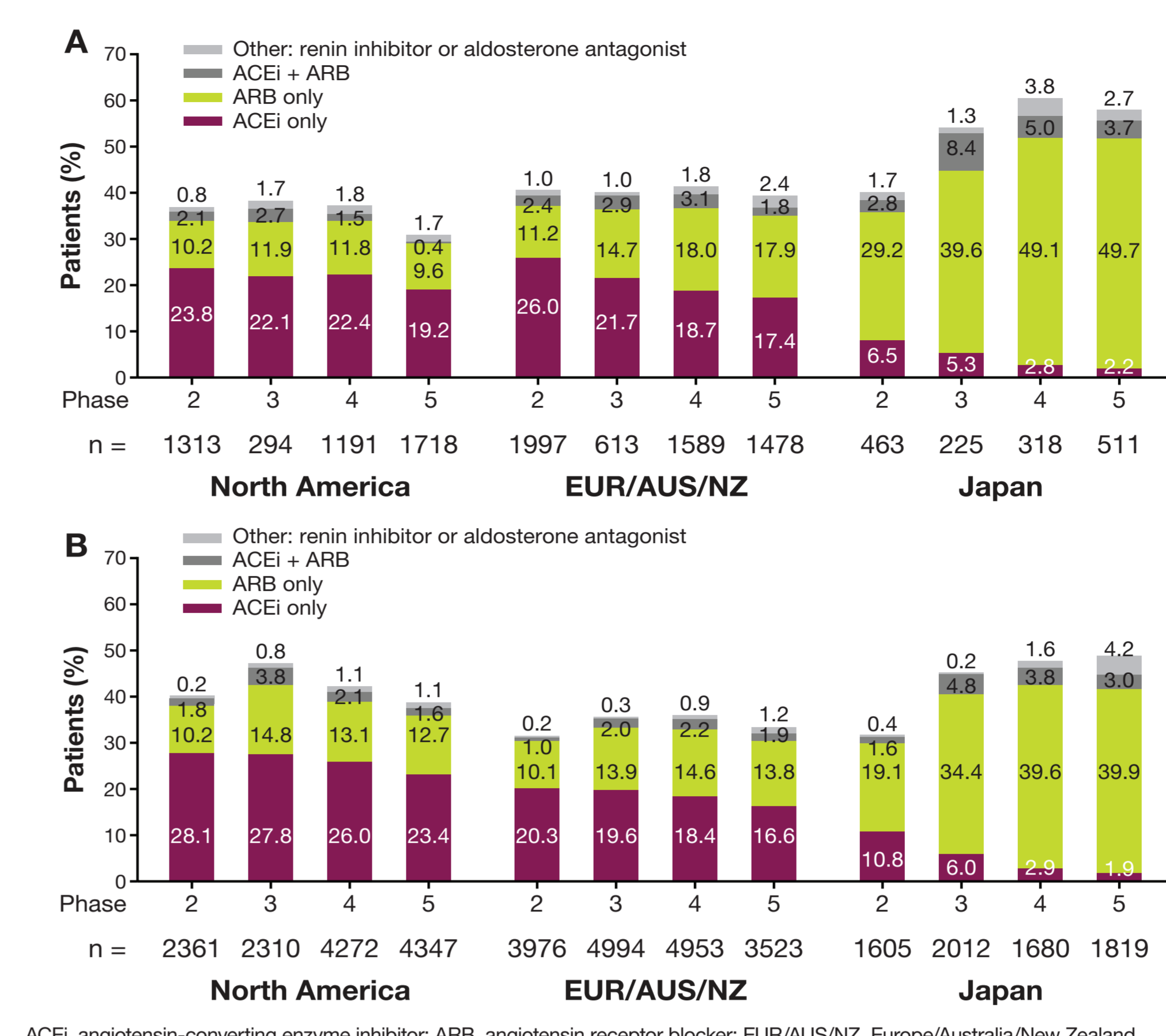
	Short-Term HD					
	North America		Europe/Australia/New Zealand		Japan	
	No RAASi (n = 2942)	RAASi (n = 1574)	No RAASi (n = 3378)	RAASi (n = 2299)	No RAASi (n = 1717)	RAASi (n = 800)
Patient characteristics						
Age, years, mean (SD)	64.3 (15.0)	61.0 (15.2)	66.9 (14.2)	62.7 (14.8)	66.4 (13.1)	63.9 (13.0)
Male, %	58	58	63	63	69	67
Black, %	20	25	2	2	0	0
Duration on HD, days, median (IQR)	51 (16–85)	49 (12–82)	41 (5–80)	40 (4–78)	37 (9–77)	49 (17–85)
HD-related characteristics						
Central venous catheter use, %	70	66	48	42	11	7
Single pool Kt/V, mean (SD)	1.4 (0.4)	1.4 (0.4)	1.3 (0.4)	1.3 (0.3)	1.0 (0.3)	1.0 (0.3)
Treatment time, minutes, mean (SD)	218 (34)	218 (33)	219 (38)	224 (41)	207 (39)	208 (36)
Dialysate K ⁺ , mEq/L, mean (SD)	2.5 (0.6)	2.4 (0.6)	2.3 (0.7)	2.4 (0.8)	2.0 (0.1)	2.0 (0.1)
Laboratory and biometric measurements, mean (SD)						
Body mass index, kg/m ²	28.1 (7.0)	28.0 (6.8)	25.9 (5.3)	26.8 (5.6)	21.7 (3.7)	22.0 (3.4)
Predialysis SBP, mm Hg	143 (23)	150 (23)	141 (22)	145 (22)	147 (22)	153 (21)
Hemoglobin, g/dL	10.8 (1.5)	10.9 (1.6)	10.5 (1.6)	10.6 (1.6)	9.5 (1.7)	9.7 (1.5)
Serum creatinine, mg/dL	6.2 (2.7)	6.5 (3.0)	6.7 (2.4)	6.7 (2.6)	7.8 (2.8)	8.0 (2.7)
Serum albumin, g/dL	3.5 (0.6)	3.5 (0.6)	3.5 (0.6)	3.5 (0.6)	3.5 (0.6)	3.4 (0.6)
Serum bicarbonate, mEq/L	23.4 (3.8)	23.3 (3.8)	22.9 (3.7)	22.9 (3.8)	20.6 (4.1)	22.0 (3.8)
Serum calcium, mg/dL	8.7 (0.8)	8.7 (0.8)	8.8 (1.0)	8.8 (0.9)	8.2 (0.9)	8.2 (0.8)
Serum phosphorus, mg/dL	5.0 (1.6)	5.2 (1.8)	5.1 (1.8)	5.3 (1.8)	5.2 (1.6)	5.3 (1.4)
Serum K ⁺ , mEq/L	4.4 (0.7)	4.5 (0.7)	4.7 (0.8)	4.8 (0.8)	4.4 (0.7)	4.5 (0.8)
Medications, %						
K ⁺ -binding resin	1	1	6	10	5	7
β-blocker	58	66	43	51	17	25
Diuretic	31	41	47	64	52	61
Comorbid conditions, %						
Coronary artery disease	43	45	37	40	27	24
Cancer (non-skin)	15	10	19	14	12	9
Cerebrovascular disease	13	14	14	16	15	11
Heart failure	37	36	28	25	31	27
Diabetes	57	66	35	44	44	57
Hypertension	85	91	82	91	80	89
Peripheral vascular disease	24	24	25	28	13	11
Other cardiovascular disease	26	22	30	29	24	21

	Long-Term HD					
	North America		Europe/Australia/New Zealand		Japan	
	No RAASi (n = 7754)	RAASi (n = 5536)	No RAASi (n = 11,429)	RAASi (n = 6017)	No RAASi (n = 3994)	RAASi (n = 3122)
Patient characteristics						
Age, years, mean (SD)	62.6 (15.2)	60.8 (14.9)	65.0 (14.7)	62.6 (15.1)	63.2 (12.7)	62.6 (12.2)
Male, %	59	58	59	62	60	66
Black, %	28	30	2	2	0	0
Duration on HD, years, median (IQR)	2.7 (1.2–5.4)	2.8 (1.2–5.3)	3.0 (1.2–6.4)	2.7 (1.1–5.7)	5.9 (2.3–12.3)	4.6 (1.7–9.1)
HD-related characteristics						
Central venous catheter use, %	26	24	22	21	1	1
Single pool Kt/V, mean (SD)	1.6 (0.3)	1.6 (0.3)	1.5 (0.3)	1.5 (0.3)	1.4 (0.3)	1.4 (0.3)
Treatment time, minutes, mean (SD)	220 (35)	221 (33)	242 (38)	246 (38)	239 (31)	236 (29)
Dialysate K ⁺ , mEq/L, mean (SD)	2.2 (0.6)	2.1 (0.5)	2.1 (0.6)	2.1 (0.7)	2.0 (0.1)	2.0 (0.1)
Laboratory and biometric measurements, mean (SD)						
Body mass index, kg/m ²	28.3 (7.0)	27.5 (6.7)	25.7 (5.4)	25.4 (5.4)	21.0 (3.2)	21.1 (3.4)
Predialysis SBP, mm Hg	144 (23)	154 (23)	136 (23)	145 (22)	145 (23)	155 (20)
Hemoglobin, g/dL	11.4 (1.3)	11.4 (1.3)	11.6 (1.5)	11.5 (1.4)	10.4 (1.3)	10.3 (1.2)
Serum creatinine, mg/dL	8.3 (3.1)	8.5 (3.0)	8.3 (2.7)	8.3 (2.7)	10.8 (2.9)	10.7 (2.9)
Serum albumin, g/dL	3.8 (0.5)	3.8 (0.4)	3.7 (0.5)	3.8 (0.5)	3.8 (0.4)	3.8 (0.4)
Serum bicarbonate, mEq/L	23.4 (3.5)	23.4 (3.4)	22.7 (3.2)	22.7 (3.2)	20.2 (3.1)	20.5 (3.0)
Serum calcium, mg/dL	9.1 (0.8)	9.1 (0.8)	9.2 (0.8)	9.1 (0.9)	9.0 (0.9)	9.0 (0.9)
Serum phosphorus, mg/dL	5.3 (1.6)	5.5 (1.7)	5.1 (1.7)	5.4 (1.8)	5.5 (1.5)	5.5 (1.4)
Serum K ⁺ , mEq/L	4.7 (0.7)	4.8 (0.7)	5.1 (0.8)	5.2 (0.8)	4.9 (0.8)	5.0 (0.8)
Medications, %						
K ⁺ -binding resin	2	3	17	19	11	13
β-blocker	52	68	34	50	13	25
Diuretic	17	22	26	40	21	31
Comorbid conditions, %						
Coronary artery disease	45	49	41	46	32	31
Cancer (non-skin)	13	10	16	13	10	10
Cerebrovascular disease	15	15	17	19	14	14
Heart failure	38	40	26	31	19	20
Diabetes	54	61	30	40	29	42
Hypertension	85	90	78	91	64	66
Peripheral vascular disease	25	26	30	33	16	16
Other cardiovascular disease	28	26	37	36	32	27

HD, hemodialysis; IQR, interquartile range; K⁺, potassium; Kt/V, clearance of urea multiplied by dialysis time (ie, the volume of plasma cleared of urea) divided by the distribution volume of urea; RAASi, renin–angiotensin–aldosterone system inhibitor; SBP, systolic blood pressure; SD, standard deviation.

- Total RAASi prescriptions were more common among patients receiving ST HD in Japan than in Europe/Australia/New Zealand and North America during DOPPS phases 3–5 (Figure 1A)
- A similar trend was observed over the same time period among patients receiving LT HD; however, the overall proportions of patients with RAASi prescriptions in Japan were lower for patients undergoing LT versus ST HD (Figure 1B)
- The type of RAASi therapy prescribed varied by geographic region (Figure 1)
 - ACE inhibitors were prescribed as a single therapy more often in North America and Europe/Australia/New Zealand compared with Japan
 - ARBs were more frequently prescribed as a single therapy in Japan versus other regions, and their use increased over time
 - Within each region, RAASi prescription patterns were similar among patients undergoing ST or LT HD

Figure 1. RAASi Prescriptions by DOPPS Phase and Region in (A) ST HD and (B) LT HD Populations



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; EUR/AUS/NZ, Europe/Australia/New Zealand.

- In North America, RAASi prescriptions were most common among patients with serum K⁺ >6.0 mEq/L undergoing ST or LT HD; however, sample size was limited (n = 71), and this pattern was not observed in other regions (Table 2)
- In all populations examined, RAASi use was greater among patients with serum K⁺ >5.0 mEq/L versus ≤5.0 mEq/L

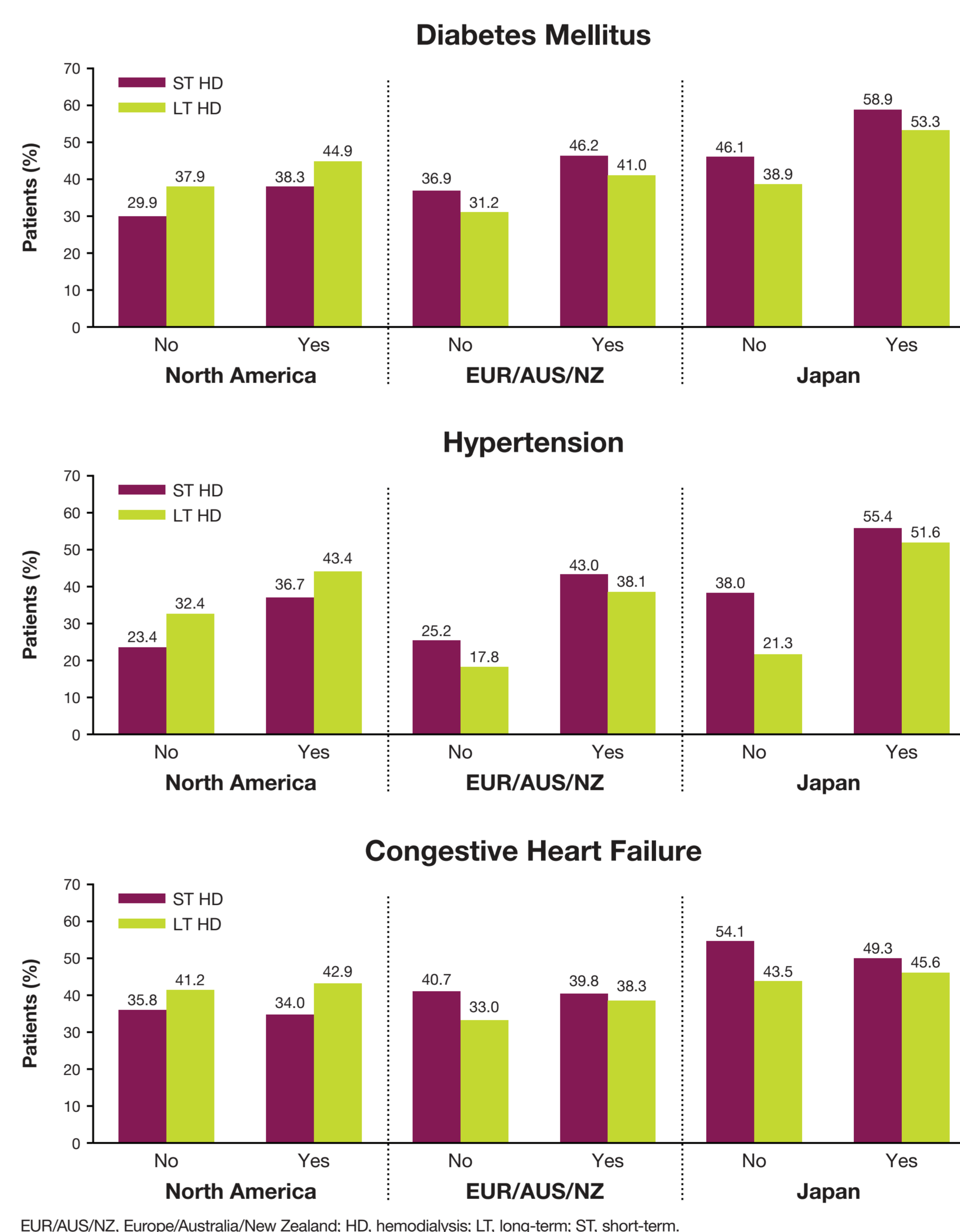
Table 2. RAASi Prescriptions by Serum K⁺ Strata in the ST and LT HD Populations

Serum K ⁺ , mEq/L	Patients on Any RAASi, %					
	Short-Term Hemodialysis			Long-Term Hemodialysis		
	North America	EUR/AUS/NZ	Japan	North America	EUR/AUS/NZ	Japan
≤5.0	34	38	50	40	32	41
>5.0–≤5.5	37	45	64	45	36	46
>5.5–≤6.0	37	46	63	47	38	51
>6.0	49	44	60	49	38	46

EUR/AUS/NZ, Europe/Australia/New Zealand; K⁺, potassium; RAASi, renin–angiotensin–aldosterone system inhibitor.

- In all regions presented, RAASi prescriptions were more common among patients with DM or hypertension versus patients without these comorbid conditions, but this pattern was not observed in patients with or without CHF (Figure 2)

Figure 2. RAASi Prescriptions Varied by Region, Comorbidity, and Length of Time on HD (2002–2015)



EUR/AUS/NZ, Europe/Australia/New Zealand; HD, hemodialysis; LT, long-term; ST, short-term.

Limitations

- Analysis was restricted to patients receiving in-center HD at participating centers and is therefore not representative of patients receiving home HD or those in other countries
- This is a cross-sectional analysis
- Only descriptive results are presented, and no statistical comparisons were made

Conclusions

- Data from DOPPS indicate that RAASi prescription patterns among patients undergoing HD vary by geographic region, both by overall use and type
- Overall, RAASi prescriptions were more common among patients with DM and hypertension versus patients without these conditions; however, patients with CHF were no more likely to receive RAASi prescriptions than those without CHF
- These data indicate that RAASi therapy may be underprescribed in patients with an indication for treatment, particularly patients with CHF

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