SP598

Salt intake and all-cause mortality in Japanese hemodialysis patients from the JSDT registry.

T. Ikenoue[1], K. Koike[2], S. Fukuma[3], S. Ogata[4], Y. Tsubakihara[4], K. Iseki[4], S. Fukuhara[3];

1. Fujiidera Keijinkai Clinic, Fujiidera, JAPAN,
2. Division of Nephrology, Department of Medicine, Kurume University School of Medicine, Kurume, JAPAN,
3. Department of Healthcare Epidemiology, School of Public Health, Kyoto University Faculty of Medicine, Kyoto, JAPAN,
4. Committee of the Renal Data Registry, The Japanese Society for Dialysis Therapy, Tokyo, JAPAN.

Aim

To clarify the association between salt intake and all-cause mortality in Japanese HD patients.

Conclusion

Low salt intake was associated with all-cause and CV death in HD patients. These findings do not support clinical guidelines recommending restricted salt intake to <6 g/day in this population.

Variable	Overall (n=88,115)		<2 (n=3,794)		2-3.99 (n=12,031)		4-5.99 (n=22,833)		6-7.99 (n=24,349)		8-9.99 (n=15,305)		10-11.99 (n=6,479)		12< (n=2,948)	
			Salt Intake, g/day													
Salt intake, g/day	6.50	(2.78)	1.25	(0.53)	3.16	(0.55)	5.06	(0.57)	6.97	(0.57)	8.88	(0.57)	10.83	(0.56)	12.94	(0.67)
nPCR, g/kg/day	1.16	(0.17)	1.08	(0.15)	1.12	(0.18)	1.15	(0.20)	1.17	(0.15)	1.18	(0.14)	1.19	(0.13)	1.20	(0.12)
Age, years old	65.09	(12.24)	68.99	(12.40)	68.74	(12.13)	67.24	(12.02)	65.09	(11.62)	62.30	(11.55)	59.24	(11.38)	56.01	(11.51)
Vintage HD, years	9.07	(6.62)	8.09	(6.38)	8.88	(6.81)	9.27	(6.79)	9.23	(6.67)	9.10	(6.45)	8.92	(6.22)	8.74	(6.11)
Gender (Male)	53,445	(60.9)	2,033	(53.6)	6,205	(51.6)	12,121	(53.1)	14,465	(59.4)	10,775	(70.4)	5,211	(80.4)	2,635	(89.4)
Cause of hemodialysis																
CGN	38,827	(44.5)	1,451	(39.0)	4,939	(41.1)	10,271	(45.0)	11,161	(45.8)	6,935	(45.3)	2,957	(45.6)	1,113	(44.5)
DMN	27,342	(31.4)	1,308	(35.1)	3,794	(31.5)	6,847	(30.0)	7,448	(30.6)	4,949	(32.3)	2,140	(33.0)	856	(34.2)
Nephrosclerosis	5,147	(5.9)	248	(6.7)	845	(7.0)	1,465	(6.4)	1,367	(5.6)	806	(5.3)	304	(4.7)	112	(4.5)
Others	15,907	(18.2)	717	(19.3)	2,453	(20.4)	4,250	(18.6)	4,373	(18.0)	2,615	(17.1)	1,078	(16.6)	421	(16.8)
Previous Medical history																
Myocardial Infarction	5,190	(6.8)	248	(7.6)	722	(6.9)	1,360	(6.9)	1,488	(7.0)	901	(6.8)	350	(6.2)	121	(5.5)
Cerebral Infarction	10,815	(14.2)	670	(20.5)	1,933	(18.4)	3,189	(16.0)	2,777	(13.1)	1,525	(11.4)	556	(9.8)	165	(7.5)
Cerebral Bleeding	3,635	(4.8)	242	(7.4)	696	(6.7)	1,029	(5.2)	927	(4.4)	482	(3.6)	189	(3.3)	70	(3.2)
Leg Amputation	1,997	(2.6)	112	(3.4)	319	(3.0)	517	(2.6)	534	(2.5)	306	(2.3)	167	(2.9)	42	(1.9)
Femoral neck Fracture	1,830	(2.4)	166	(5.1)	389	(3.7)	588	(3.0)	412	(2.0)	204	(1.5)	57	(1.0)	14	(0.6)
BMI	21.18	(3.70)	19.93	(3.30)	20.11	(3.14)	20.56	(3.20)	21.18	(3.65)	21.99	(3.88)	22.88	(4.13)	23.97	(4.29)
Serum Potassium, mEq/L	5.04	(0.79)	4.65	(0.85)	4.83	(0.8)	4.98	(0.78)	5.10	(0.76)	5.19	(0.75)	5.26	(0.74)	5.25	(0.74)
Serum Calcium-phosphorus product, mg^2/dl^2	48.33	(13.80)	42.60	(13.62)	44.79	(13.31)	46.91	(13.07)	48.90	(13.32)	50.62	(13.78)	52.96	(14.38)	54.58	(15.07)
CRP, mg/dL	0.48	(1.43)	0.93	(2.71)	0.64	(1.76)	0.48	(1.32)	0.41	(1.17)	0.38	(1.20)	0.39	(1.11)	0.37	(0.98)
Kt/V	1.19	(0.24)	1.21	(0.27)	1.23	(0.26)	1.22	(0.25)	1.20	(0.24)	1.16	(0.22)	1.11	(0.21)	1.08	(0.20)
Dialysis time, hours	3.99	(0.48)	3.81	(0.54)	3.86	(0.51)	3.94	(0.47)	4.01	(0.44)	4.08	(0.43)	4.14	(0.47)	4.21	(0.47)
Purification of dialysis	21,732	(28.8)	936	(29.1)	2,884	(27.7)	5,682	(28.8)	5,977	(28.3)	3,964	(29.9)	1,620	(28.8)	669	(30.3)
Vascular access																
Arteriovenous Fistula	62,854	(90.0)	2,561	(85.5)	8,338	(87.6)	16,131	(89.2)	17,683	(90.5)	11,384	(92.0)	4,850	(92.5)	1,907	(93.9)
Arteriovenous Graft	5,347	(7.7)	316	(10.5)	884	(9.3)	1,510	(8.4)	1,453	(7.4)	788	(6.4)	297	(5.7)	99	(4.9)
Others	1,608	(2.3)	120	(4.0)	301	(3.2)	450	(2.5)	406	(2.1)	209	(1.7)	97	(1.9)	25	(1.2)

Table 1. Back ground characteristic at baseline.
Data are the mean (standard deviation) or percentage. Abbreviations: nPCR, protein catabolic rate normalized to body weight; HD, hemodialysis; CGN, chronic glomerulonephritis; DMN, diabetes mellitus nephropathy; BMI, body mass index.

Salt intake (g/day)		-2	2-4	4-6	6-8	8-10	10-12	12-
nPCR (g/kg/day)	>1.2	1.51 (0.87-2.61) n=531	1.43 (1.04-1.96) n=2803	1.57 (1.22-2.01) n=7376	reference n=9557	0.99 (0.73-1.36) n=6537	1.01 (0.64-1.58) n=2918	1.21 (0.65-2.25) n=1448
	1.2-1.0	2.14 (1.68-2.73) n=2710	1.56 (1.28-1.90) n=7633	1.32 (1.10-1.58) n=13553	reference n=13442	1.01 (0.80-1.29) n=8106	1.27 (0.90-1.79) n=3299	1.04 (0.55-1.95) n=1379
	<1.0	1.86 (1.19-2.91) n=914	1.63 (1.08-2.46) n=1551	1.47 (0.98-2.20) n=1809	reference n=1282	0.50 (0.22-1.13) n=629	1.30 (0.49-3.44) n=249	1.33 (0.27-6.44) n=117
Albumin (g/dl)	>3.8	1.58 (0.88-2.86) n=1257	1.33 (0.89-2.01) n=3875	1.29 (0.93-1.79) n=8196	reference n=9439	0.99 (0.66-1.47) n=6318	1.1 (0.62-1.94) n=2825	1.11 (0.49-2.53) n=1427
	<3.8	2.4 (1.91-3.03) n=2790	1.79 (1.48-2.16) n=7752	1.54 (1.30-1.82) n=13899	reference n=14145	0.92 (0.73-1.17) n=8504	1.08 (0.77-1.51) n=3433	0.91 (0.51-1.63) n=1423
BMI	>23	1.81 (0.98-3.33) n=675	1.52 (0.95-2.43) n=1962	1.67 (1.15-2.43) n=4436	reference n=6007	0.96 (0.62-1.50) n=5043	1.58 (0.96-2.62) n=2743	1.34 (0.67-2.68) n=1593
	<23	2.27 (1.80-2.85) n=3495	1.79 (1.49-2.15) n=10069	1.49 (1.26-1.76) n=18397	reference n=18342	0.90 (0.72-1.13) n=10262	0.78 (0.54-1.12) n=3736	0.59 (0.30-1.17) n=1355
Albumin>3.8 & BMI>23		0 (0.00--------) n=237	2.04 (0.78-5.34) n=699	1.72 (0.79-3.72) n=1652	reference n=2418	0.88 (0.37-2.12) n=2144	1.31 (0.49-3.47) n=1235	1.67 (0.54-5.19) n=807

Table 2. Stratified analysis between salt intake and all cause death.
BMI, body mass index; HD, hemodialysis; nPCR, protein catabolic rate normalized to body weight
Adjusted for age, gender, BMI, HD vintage, dialysis time, Kt/V, nPCR, comorbid conditions, type of vascular access, serum potassium, phosphate, calcium, CRP level, and endotoxin level in dialysate in multivariable model.

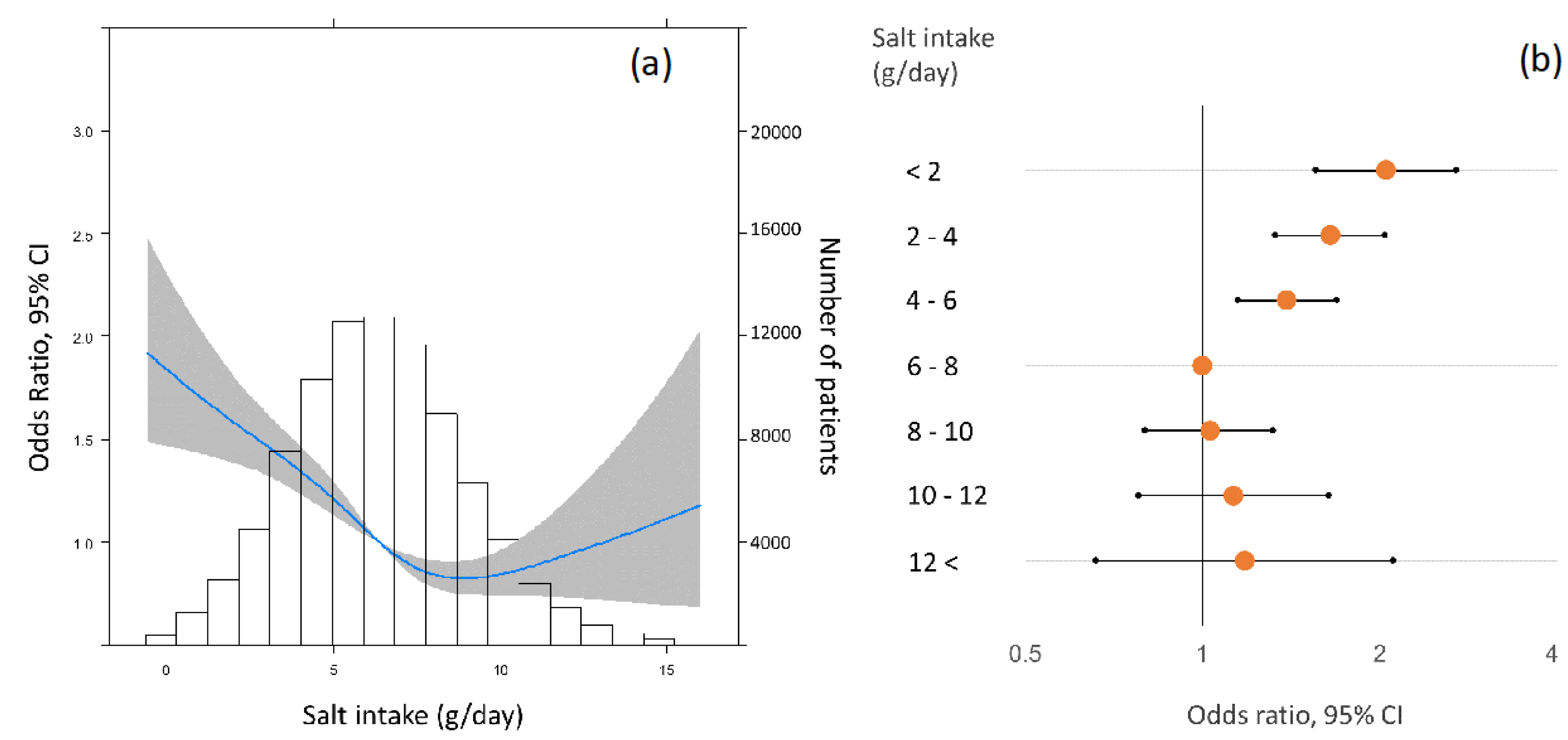

Figure 1. Association between estimated salt intake and all cause death.
Figure 1(a) shows cubic splines between estimated salt intake and all-cause death. The reference was the median estimated salt intake (6.4 g/day). Figure 1(b) shows the association between estimated salt intake and all-cause death categorized by estimated salt intake. The reference was 6-8 g/day. 95% CI, 95% confidence interval.

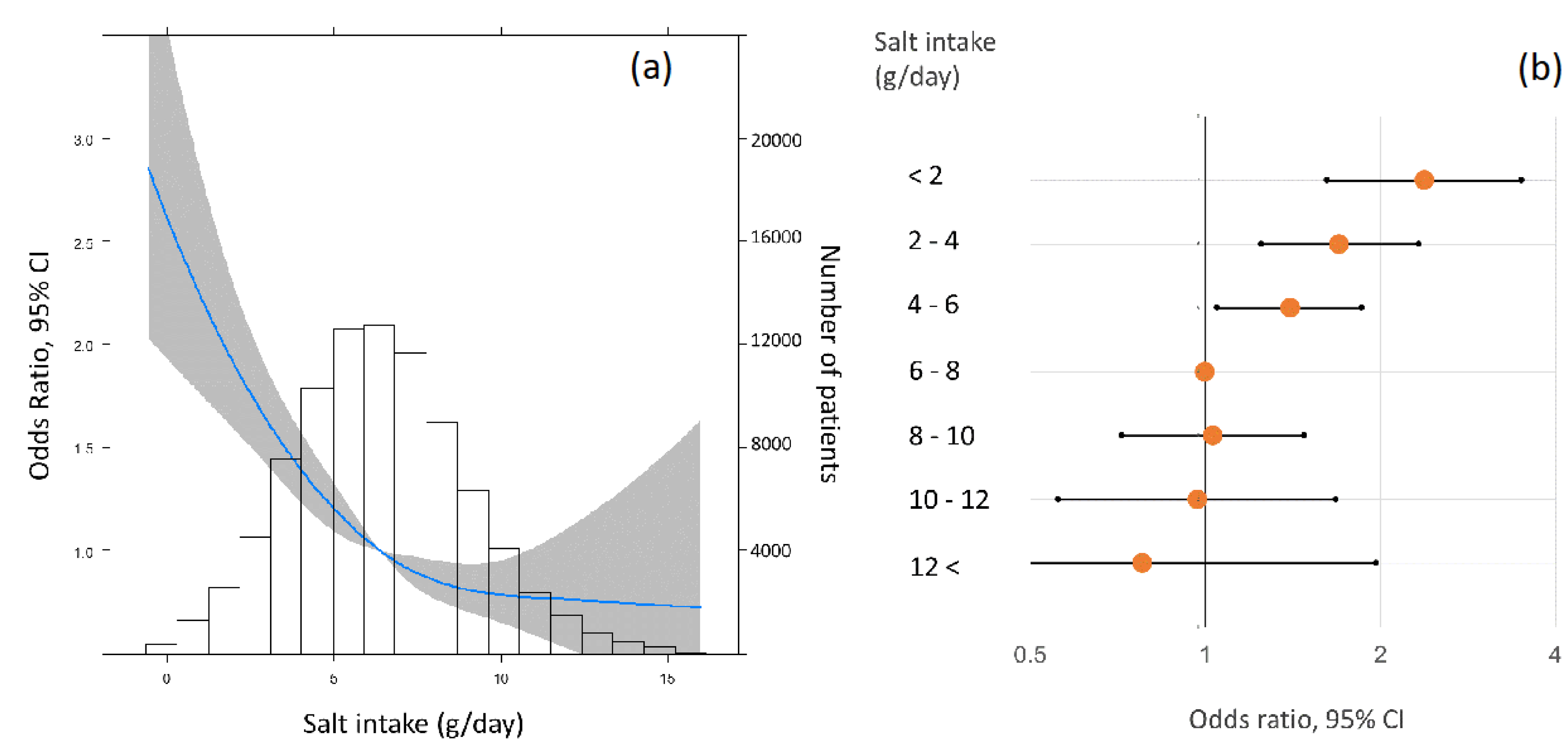

Figure 2. Association between estimated salt intake and cardiovascular death.
Figure 2(a) shows cubic splines between estimated salt intake and cardiovascular death. The reference was the median estimated salt intake (6.4 g/day). Figure 2(b) shows the association between estimated salt intake and cardiovascular death dealing categorized by estimated salt intake. The reference was 6-8 g/day. 95% CI, 95% confidence interval.

Introduction

While salt restriction has been recommended for hemodialysis (HD) patients,[1,2] few studies have examined the association between salt intake and clinical outcomes in this patient population. On the other hand, low dietary salt intake independently predicts high overall and cardiovascular mortality in peritoneal dialysis patients.[3] Compared with baseline sodium excretion of 4 to 5.9 g/day (10.2 to 15.2 g/day in salt), a sodium excretion of less than 3 g/day (7.6 g/day in salt) has been associated with increased risk of CV mortality in non-ESRD patients.[4]

Methods

Study design

Retrospective cohort study

Patients

We included patients enrolled in the Japanese Society for Dialysis Therapy (JSDT) registry (2008) who had been receiving HD for at least two years and whom we regarded as anuric. Because of improper estimation of salt intake, we excluded patients whose interdialytic weight gain (IWG) was under 0 kg, who were not receiving HD thrice weekly, and who received HD with peritoneal dialysis.

Exposure/comparison and outcomes

The main predictor was estimated salt intake, which calculated from IWG and serum sodium level before and after dialysis. This method was validated by G. Kimura and G. Ramdeen.[5,6] Given that intra-dialysis weight loss (IWL) correlates strongly with preceding IWG, IWL was used in place of IWG.[7]

The main outcome was all-cause death during one year, and the secondary outcome was cardiovascular (CV) death. Cardiovascular death included sudden death; death from heart failure, myocardial infarction, or stroke; and death from other vascular disease.

Statistical analysis

We used nonlinear logistic regression to determine the association of salt intake with mortalities, adjusting for age, gender, body mass index (BMI), HD vintage, dialysis time, Kt/V, protein catabolic rate normalized to body weight (nPCR), comorbid conditions, type of vascular access, serum potassium, phosphate, calcium, CRP level, and endotoxin level in dialysate. We plotted cubic splines, and the reference was the median of salt intake. In addition, we categorized salt intake by every 2 g/day and examined the association between these categories and mortality.

Stratified and subgroup analyses

To avoid any influence of malnutrition on findings, we performed stratified analysis. After dividing patients into groups by nPCR, serum albumin, and body mass index (BMI), we then determined the association of salt intake with mortality. We restricted examination to patients with serum albumin >3.8 g/dl and BMI >23, in accordance with the concept of protein-energy wasting.

Results

Patients

We enrolled 88,115 adult patients. At baseline, the median (25th-75th percentile) daily salt intake was 6.4 (4.6-8.3) g.

Distribution of all cause and cardiovascular death

After a year, all-cause death occurred in 1,845 (2.1%) patients, including 821 cardiovascular deaths. We found the association between low salt intake and clinical outcomes (all-cause death and CV death) (Figure 1 and 2). Mortality was highest in the low-salt-intake group. We noted no marked association between high salt intake and mortality. Associations were similar between salt intake and CV death, with death rates highest in the low-salt-intake group.

Stratified and subgroup analyses (Table 2)

Regardless of nPCR, serum albumin level, or BMI, associations between salt intake and all-cause death remained relatively unchanged from initial findings. Further, subgroup analysis of good nutrition group also failed to note any marked change in associations between salt intake and all-cause death, suggesting that this association was relatively resilient.

Discussions

Malnutrition was associated with death in HD patients.[8,9] To assess the influence of malnutrition, we examined a subgroup determined to have good nutrition based on the concept of protein-energy wasting and found similar associations between salt intake and all-cause death. However, we did not use the gold standard of nutrition in this study, and therefore further study will be required to clarify true association between salt intake and death without the effect of nutrition.

Estimation of salt intake included bias caused by sweat, feces, and residual renal function. The lack of concern about sweat, feces, and residual renal function might have led to over-estimation of salt intake but did not affect the association between low salt intake and all-cause mortality.

Limitations

- This was an observational study and did not evaluate the influence of intervention efforts to reduce salt intake (restricted salt diet or advice to reduce salt intake).
- Estimation of intake salt was based on single series of HD.
- We assumed IWG and IWL were the same in the present study; however, in clinical settings, IWG and IWL may differ.
- Models that predicted all-cause mortality for one year were used.
- Patients with HD history <2 years were excluded.

Reference

1. Sanaka T, Tsubakihara Y, et al. The Japanese journal of nephrology 2007;49: 871-8.
2. K/DOQI Workgroup. Am J Kidney Dis 2005;45(Suppl 3):S1-153.
3. Dong J, et al. Clin J Am Soc Nephrol. 5: 2010. 240-7.
4. O'Donnell MJ, et al. JAMA. 306: 2011. 2229-38.
5. Kimura G, et al. Int J Artif Organs. 11: 1988. 161-8.
6. Ramdeen G, et al. ASAIO J. 44: 1998. 812-7.
7. Hecking M, Karaboyas A, Saran R, et al. Clin J Am Soc Nephrol. 2012;7: 92-100.
8. Kalantar-Zadeh K, Block G, McAllister CJ, et al. Am J Clin Nutr 2004; 80: 299-307.
9. K/DOQI) NKFKDOQIN. Am J Kidney Dis 2000;35: S1-140

Acknowledgement

The authors wish to express the greatest appreciation to the Japanese Society for Dialysis Therapy, and the principal investigators of all prefectures and to all the personnel at the participating institutions involved in this Renal Data Registry of the Japanese Society for Dialysis Therapy. Without their tireless hard work, the compilation of data for this paper would not have been possible.

DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014