Estimated dietary sodium intake in peritoneal dialysis patients using food frequency questionnaires and total urinary and peritoneal sodium losses and assessment of extracellular volumes

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# <u>Abstract</u>

## Background

Peritoneal dialysis (PD) patients are advised to restrict sodium intake. For best use of resources, rapid screening tools are required for dietary assessments to allow for targeting of patients. We wished to evaluate the usefulness of food frequency questionnaires (FFQ) for estimating dietary sodium.

#### Methods

Sodium intake was estimated using the Derby Salt Questionnaire (DSQ), and Royal Free Sodium Questionnaire (RFSQ). Body composition was determined by bioimpedance.

### Results

90 peritoneal dialysis patients, 52 men (57.8%), mean age 62±15.8 years, were asked to complete the DSQ and RFSQ questionnaires. 88 completed one or more questionnaire, with 87 completing the DSQ and 86 the RFSQ. The median estimated dietary sodium intake 104 (72-145) mmol/day (2.39 (1.64-3.34) g sodium/day) DSQ, and 92 (60-114) mmol/day (2.11 (1.38-2.62) g sodium/day) RFSQ. Younger patients, aged ≤ 52 years had greater dietary sodium intake compared to those ≥76 years (RFSQ 105.4 (73-129) vs 96 (71-116) mmol/day), p<0.05. Extracellular water to total body water (ECW/TBW) was greater in those with higher DSQ estimated dietary sodium intake (0.39±0.01 vs 0.40±0.01, p<0.05). A multivariable model showed that increased dietary sodium intake was independently associated with increased skeletal muscle mass (SMM) (DSQ odds ratio (OR) 1.17 (95% confidence limits 1.05-1.32, RFSQ OR 1.15 (1.04-1.27, p<0.05) and raised ECW/TBW (DSQ OR 1.88 (1.22-2.92) p=0.004, and ECW/height (RFSQ OR 1.42 (1.02-1.98) p=0.04.

### Conclusions

Both questionnaires were acceptable to patients, and the majority were found to be consuming more dietary sodium than recommended. Dietary sodium estimation was associated with SMM and increased ECW.

## Introduction

Patients with chronic kidney disease are at increased risk of sodium retention, as declining renal function leads to reduced urinary sodium excretion. Increased sodium retention potentially leads to expansion of the extracellular space, peripheral oedema and hypertension. The majority of adult dialysis patients have hypertension or a history of hypertension

Sodium retention is driven by excess dietary sodium intake, and dietary sodium intake plays a role in determining thirst. Trials of reduced dietary sodium intake have been shown to reduce blood pressure in the short term [1]. After peritonitis, failure to control extracellular volume is a common cause of peritoneal dialysis technique failure [1,2]. Studies in haemodialysis patients have shown that interventions designed to reduce dietary sodium and fluid intake can reduce blood pressure and weight gains between dialysis sessions [4,5]. The amount of salt in the modern Western-type diet has been estimated to be up to 12g/d (4.6 g or 200 mmol of sodium) [6]. There is consensus from clinical guideline committees from both North America and Europe that kidney dialysis patients should limit their dietary salt intake to 5 g per day (2.0 g or 85 mmol of sodium) [7,8,9]. As there is a physiological requirement for sodium, eliminating sodium from the diet is equally not advised either.

Although twenty-four-hour urine collections are the standard method for assessing dietary sodium intake in stable patients, patients with kidney failure may be oliguric or anuric. As such, other methods are required to assess dietary sodium intake. A number of dietary assessments are available ranging from detailed reports of weighing individual foods to three-day dietary histories and more recently the development of food frequency questionnaires (FFQs), designed to allow rapid screening of patients [9-11]. These have been validated in patients with chronic kidney disease by determining urinary sodium excretion, but there are few reports of using FFQs in dialysis patients [9-11]. Most haemodialysis patients are oligo-anuric and there are potential errors in collecting and estimating dialysate sodium losses [12], we chose to study

peritoneal dialysis patients as 24-hour urine and dialysate effluent collections are collected as part of routine clinical practice in the management of peritoneal dialysis patients. A previous study in peritoneal dialysis patients reported that a reduction in dietary sodium resulted in a reduction in total body water and blood pressure in normotensive patients [13], we wished to evaluate the usefulness of FFQs in clinical practice. We used 2 FFQs developed for use in the UK; the "Derby Salt Questionnaire" (DSQ) and the "Royal Free Salt Questionnaire (RFSQ) to estimate dietary sodium intake and to determine whether there was any association between DSQ and RFSQ scores and blood pressure, and the amount of extracellular water in peritoneal dialysis patients [10,14].

## <u>Methods</u>

We audited the usefulness of two sodium FFQs developed for the UK diet between May-July 2017 in a cohort of adult peritoneal dialysis patients attending for routine assessment of peritoneal membrane function [15]. Patients with previous peritonitis or an acute hospital admission in the preceding 3 months were excluded. Prior to starting dialysis patients were reviewed by specialist renal dietitians and given advice to restrict dietary salt intake to less than 5 g/day (85 mmol/day) (appendix). All patients attending for assessment of peritoneal membrane function were asked to complete the FFQs.

Details of patient demographics and routine blood tests were obtained from the hospital computerised renal database. Anthropometric measurements of height and weight were recorded (Marsden, Rotherham, UK). To assess body composition and extracellular water (ECW) and total body water (TBW), multisegmental bioimpedance measurements were obtained in a standardised manner after the patient had emptied their bladder and drained out peritoneal dialysate (InBody 720, Seoul, South Korea) [16,17]. Protein nitrogen appearance was calculated using standard methods [15]. Daily sodium balance was estimated from the amount of sodium instilled in fresh peritoneal dialysate from the volume of peritoneal dialysate and sodium concentration of the dialysate and the

amount of sodium in the 24-hour drained peritoneal effluent dialysate and the 24-hour urine sodium [18].

## Statistical methods

Statistical analysis was by standard parametric or non-parametric testing, and ANOVA or Kruskal Wallis with appropriate post hoc testing. Correlation with the FFQ scores was by Pearson or Spearman correlation (Prism 7.0, Graph Pad, San Diego, USA). The FFQs are designed to detect patients with an increased diertay sodium intake. As such we performed multi-variable logistic analysis, firstly analysing variables which would be considered as predictors of increased dietary sodium, and then secondly variables which would be considered a consequence of increased dietary sodium intake. All variables with a p<0.1 value on univariate analysis were entered into the multi-variable model, along with variables thought to be clinically relevant and analysed with SPSS (SPSS 24, IBM Corporation, Armonk, New York, USA) using a step backward approach eliminating variables which were not significant (p>0.05) in the model, unless they improved model fit. Non-parametric variables were log transformed as required to improve variable distribution. Models were checked for collinearity and variable inflation factor. We compared the two FFQ scores by Bland Altman analysis (Analyse It v 4.0, Leeds, UK). Data are reported as mean ± standard deviation, median, and range or interquartile range or percentage.

### Ethics

Our audit complied with the UK National Health Service (NHS) guidelines for clinical audit and service development, with all patient data anonymised and complied with UK National Institute for Clinical Excellence (NICE) best practices, www.nice.org.uk/media/796/23/bestpracticeclinicalaudit.pdf.

## Results

Ninety peritoneal dialysis patients attending their routine outpatient clinic appointments at a university hospital between April and July 2017, were asked to complete the DSQ and RFSQ questionnaires. Eighty eight patients were able to complete one or both questionnaires, with 87 completing the DSQ and 86 the RFSQ. The cohort comprised 52 men (57.8%), mean age 62±15.8 years, 33 (36.7%) diabetic, median duration of treatment with peritoneal dialysis was 11.5 [3 - 27] months. Forty-eight patients were prescribed 2 or more anti-hypertensives, and 22 a single anti-hypertensive agent.

The median estimated dietary sodium intake using the DSQ was 104 (72-145) mmol/day (2.39 (1.64-3.34) g sodium/day), and 92 (60-114) mmol/day (2.11 (1.38-2.62) g sodium/day) with the RFSQ. The correlation between the scores was r=0.64, p;<0.001. On Bland Altman analysis the estimated dietary sodium was higher using the DSQ compared to the RFSQ for those patients with higher dietary sodium intakes (Figure 1). The DSQ is a shorter questionnaire and patients took a median of 3 (1-12) minutes to complete this FFQ compared to 6 (2-16) minutes for the RFSQ, p<0.001. 38 and 33%, respectively reported, that completing the DSQ and RFSQ questionnaires was very easy, with 33 and 36% as easy and only 3 and 4% thought that the questionnaires were difficult to complete. 55.8% of patients had a dietary sodium of > 85 mmol/day using the RFSQ and 60.9% with the DSQ.

There was no difference in the estimated dietary sodium intake between the genders (male RFSQ 95 (73-112), DSQ 105 (68-160) vs female RHSQ 86 (51-112), DSQ 103 (72-144) mmol sodium/day), or for those patients prescribed 2 or more antihypertensive drugs and those not prescribed medications (RFSQ 92 (58-109) vs 94 (75-115), DSQ 97 (66-152) vs 116 (91-182) mmol sodium/day. The youngest tertile of patients, aged < 52 years had greater dietary sodium intake using the RFSQ compared to those >76 years (105.4 (73-129) vs 96 (71-116) mmol sodium/day, (X2=6.98, p=0.03, but there was no difference using the DSQ (93 (67-173) vs 120 (85-164) mmol sodium/day. Dividing patients into those without diabetes and those diabetes (HbA1c 34.4 (31.9-38.8) vs 54.1

(43.2-60.7) mmol/mol, p<0.001; there was no difference in total sodium losses (nondiabetic 125 (90-169) vs 128 (83-176) diabetic mmol/day). Althoug on Chi square analysis fewer diabetic patienst had a greater dietary sodium intake (X2=6.1, p=0.013), but the absolute estimates of dietary sodium intake were not different (nondiabetic RFSQ 70 (98.5-116) vs diabetic 87 (60-94) mmol/day, and DSQ (nondiabetic 102 (62-161) vs diabetic 105 (76-128) mmol/day.

We divided patients according to the median estimated dietary sodium intake. There were no differences in blood pressure, or body composition (table 1). Patients with greater dietary sodium intake with the DSQ had a greater ECW/TBW ratio, and lower serum albumin (table 2). Using the SSQ, patients with greater estimated protein intake had greater dietary sodium intake.

There were no differences in peritoneal dialysis prescription, use of higher glucose dialysates or icodextrin, dialysis adequacy or residual renal function between groups (table 2). Glycated haemoglobin was lower in patients with a greater dietary sodium intake with the RFSQ. However, there were no differences in measured daily sodium losses between groups.

On univariate analysis there was a negative correlation between sodium intake estimated by both FFQs s and glycated haemoglobin mmol/day) (RFSQ; r = -0.37, p < 0.01, DSQ r = -0.24, p = 0.02). There were also negative correlations with the 4-hour D/P creatinine (RFSQ r = -0.30, p = 0.01) also the volume of 2.27% glucose dialysate used per day (RDSQ r = -0.23, p = 0.03).

We then performed multi-variable logistic regression to determine which factors were associated with an increased FFQ estimated high dietary sodium intake. These predictors included skeletal muscle mass (SMM) for both FFQs. (table 3). We then performed multi-variable logistic regression to determine which factors were associated with the consequence of an increased FFQ estimated high dietary sodium intake. For both FFQs there was no statistical association with blood pressure, anti-hypertensive prescription, or net daily sodium balance. However the DSQ was associated with ECW/TBW, odds ratio

1.88 (95% confidence limits 1.23-2.92), p=0.004, and the RFSQ ECW adjusted for height, odds ratio 1.42 (95% confidence limits 1.02-1.98), p=0.04.

### Discussion

As patients lose residual renal function then the ability to excrete sodium declines, and patients are at risk of retaining sodium, which can lead to expansion of the ECW and hypertension. As such one of the key objectives goals of peritoneal dialysis is to restore sodium homeostasis. For haemodialysis patients, restricting sodium intake and increasing sodium removal by the use of lower dialysate sodium concentrations leads to an improvement in blood pressure control [19-21]. Similarly, both dietary sodium restriction and lower sodium dialysates been reported to lower blood pressure in peritoneal dialysis patients in the short term [13,22].

Dietary sodium intake stimulates thirst, and so dialysis patients are advised to restrict dietary sodium to reduce ultrafiltration requirements [23]. However, due to various reasons dialysis patients may not always follow dietary advice [24]. Not all centres can provide patients with ready access to dietitians. As such, food frequency questionnaires have been developed to act as a screening tool to detect patients who may benefit from targeted nutritional or other educational intervention. Sodium FFQs are generally country specific and validated by comparing dietary estimates of sodium intake with urinary excretion in stable patients with chronic kidney disease [10,11,25]. We used two FFQs developed for UK patients, and depending upon the FFQ, then 55.8-60.9% of patients had a dietary sodium greater than the 85 mmol/day recommendation for dialysis patients [7]. There was no systematic bias between the two scores, although the DSQ gave higher estimates of sodium intake for those patients with greater dietary sodium intake. Only two patients (2.2%) were unable to complete either FFQ, due to their inability to read English. Patients found the questionnaires generally easy to complete and within a short time.

Previous studies in non-dialysis patients and those treated by haemodialysis and peritoneal dialysis have reported that male patients have a higher dietary sodium intake [10,11,15,26]. Although we did not find a specific effect of gender, we noted that patients with greater skeletal muscle mass, as measured by bioimpedance, had greater estimated dietary sodium intakes, and men had greater muscle mass. This is in keeping with earlier studies reporting an association between muscle mass, determined by creatinine kinetics and dietary sodium intake [27-30]. In addition we noted that with the RFSQ patients with higher haemoglobin also had greater sodium intake, suggesting that more physically active patients would be more likely to have a greater dietary sodium intake.

Younger patients have been reported to have greater dietary sodium intake [25], and although we did note that with the RFSQ, the youngest and oldest tertiles had greater estimated dietary sodium intake compared to the middle tertile, but on multi-variable analysis older patients were more likely to have greater estimated dietary sodium intake. This may reflect more older patients not being able to shop and cook their own food and now relying on ready-made meals, or living in nursing homes being fed meals with greater sodium content.

As sodium intake can stimulate thirst, we had anticipated that patients with the highest dietary sodium intake would have increased ECW and using the DSQ then patients with greater dietary sodium intake had an increased ECW/TBW ratio, supporting this contention. On multivariable analysis, ECW/TBW remained an independent factor associated with dietary sodium intake with the DSQ, and similarly higher estimated dietary sodium using the RFSQ was associated with greater ECW/height. Our finding supports a previous report of increased ECW in peritoneal dialysis patients with a high dietary sodium intake [27].

Previous studies have reported that diabetic patients are more likely to have higher inter-dialytic weight gains and ECW expansion [31,32]. However, we

found no differences between our diabetic and non-diabetic patients. Compared to other studies we measured glycated haemoglobin in all patients, and not just those with diabetes, and as such the mean glycated haemoglobin for all patients studied was within the normal reference range. Contrary to what we had expected patients with higher glycated haemoglobin concentrations had a lower estimated dietary sodium intake. We suspect that our diabetic patients would have received more advice from dietitians both when attending diabetic and nephrology clinics to avoid sodium-rich foodstuffs, prior to initiating dialysis.

We did not find any association between estimated dietary sodium intake and blood pressure, or pulse pressure or prescription of anti-hypertensive medications. This may reflect clinical practice of controlling blood pressure to target ranges and is in keeping with other studies finding no effect of dietary sodium restriction on blood pressure [13]. Neither did we find any association between the daily sodium balance (the difference between the sodium content of the fresh PD dialysate and that recovered from the spent dialysate and urine), as if in neutral balance one may have expected that those with the greater sodium daily losses would have the higher dietary sodium intake. This may have been due to the FFQs estimating an average daily sodium intake, which may have differed from that consumed in the previous 24 hours, accuracy of patient self-reports, and errors in measuring sodium in PD effluent due to the effects of glucose on sodium measurements [18]. In addition, it is now also realised that the body has tissue sodium stores, and magnetic resonance studies have reported greater muscle and skin sodium stores in hypertensive patients and those on dialysis [33]. We were unable to measure whether these tissue stores, so sodium may have been taken up in these tissue stores, or conversely released

There has been debate as to whether sodium removal by peritoneal dialysis is a marker of volume excess, or simply reflects greater sodium intake [31]. As one hand volume overload is associated with increased mortality and technical or membrane failure [34], whereas on the other it may be associated

with greater food intake along with increased sodium intake, and increased patient survival [25,35]. In our study on multivariable analysis then dietary sodium intake was associate with greater muscle mass, supporting the latter.

Peritoneal dialysis patients are advised to restrict dietary sodium intake, and we found that the majority of our patients were not following current guideline restrictions. Our study would suggest that FFQs designed to assess sodium intake can be used as screening tools to rapidly identify those patients who would most benefit from targeted education.

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Figure 1. Bland Altman plot of the daily dietary sodium intake estimated using the Royal Free Sodium Questionnaire (RF-SQ) and the Derby Salt Questionnaire (DSQ), and the difference between the DSQ and RF-SQ. Solid black line – mean bias, dotted lines 95% limits of agreement.

Table 1. Patient demographics in all patients and then above and below the median dietary sodium intake using the Royal Free Sodium Questionnaire (RFSQ) (92 mmol/day) and Derby Salt Questionnaire (DSQ) score (104 mmol/day). Body mass index (BMI), Appendicular lean mass (ALM), Body mass index (BMI), Extracellular water (ECW), Intracellular water (ICW), pulse pressure (PP), protein nitrogen appearance (PNA), total body water (TBW), systolic blood pressure (SBP), Weight (Wt). Data expressed as mean  $\pm$ SD or median and range. \* p<0.05 vs lower dietary sodium intake

		RF	<b>SQ</b>	DSQ		
Variable	All	Lower	Higher	Lower	Higher	
		Intake	Intake	Intake	Intake	
Wt kg	73.6 ± 16.3	72.1 ± 15.4	75.0 ± 17.1	71.9 ± 17.4	75.2 ± 15.1	
BMI kg/m²	27.0 ± 4.9	26.9 ± 4.9	27.1 ± 4.9	26.8 ± 5.6	27.2 ± 4.0	
PNA g/day	64.8±17.4	61.1±14.6	68.8±19.5*	65.6±18.4	64.0±16.6	
ALM kg	20.6 ± 5.7	20.7 ± 5.5	20.4 ± 6.0	21.3 ± 6.0	19.9 ± 5.3	
ECW L	14.5 ± 3.3	14.6 ± 3.2	14.4 ± 3.5	15.0 ± 3.5	14.1 ± 3.1	
ICW L	22.0 ± 5.1	22.2 ± 5.0	21.9 ± 5.2	22.5 ± 5.4	21.6 ± 4.7	
TBW L	36.6 ± 8.3	36.8 ± 8.2	36.3 ± 8.6	37.5 ± 8.9	35.7 ± 7.8	
ECW/TB W	0.39 ± 0.01	0.39 ± 0.01	0.39 ± 0.01	0.39 ± 0.01	0.40 ± 0.01*	
SBP	141.1±22.1	142.6 ±	137.5 ±	141.6 ± 19.7	140.7 ± 24.5	
mmHg		16.4	22.7			
PP mmHg	58 [49-70]	61 [50-72]	56 [48-70]	58 [50-72]	58 [48-69]	

Table 2. Peritoneal dialysis adequacy and sodium excretion, and biochemistry in patients above and below the median dietary sodium intake using the Royal Free Sodium Questionnaire (RFSQ) (92 mmol/day) and Derby Salt Questionnaire (DSQ) score (104 mmol/day). N terminal proBrain Natriuretic Peptide (NTproBNP), C - Reactive Protein (CRP), Glycosylated Haemoglobin (HbA1C), Haemoglobin (Hb), Protein Nitrogen Appearance (PNA). Data expressed as mean  $\pm$ SD or median and interquartile range. \* p<0.05, \*\*p<0.01 vs lower dietary sodium intake.

Variables	Lower	Higher	Lower Intake	Higher Intake	
Variables	Intake SSQ	Intake SSQ	DSQ	DSQ	
Total weekly	1.96 [1.56 -	2.10 [1.55 -	2.01 [1.64 -	2.01 [1.53 -	
Kt/Vurea	2.48]	2.55]	2.28]	2.72]	
Weekly urinary	0.54 [0.10 -	0.86 [0.23 -	0.66 [0.31 -	0.75 [0.16 -	
Kt/Vurea	1.14]	1.67]	1.31]	1.65]	
Weekly	1.20 [0.84 -	1.15 [0.89 -	1.15 [0.84 -	1.20 [0.93 -	
peritoneal	1.44]	1.51]	1.39]	1.53]	
Kt/Vurea					
Urine Output	667 [296 -	784 [162 -	667 [237.75 -	753 [270 -	
ml/day	1029]	1359]	1254.75]	1250]	
Urine Sodium	30 [11 - 78]	43 [4 - 82]	31 [7 - 83]	43 [6 - 8]	
mmol/day					
Total Sodium	129 [93-	123 [83 - 180]	125 [93 - 144]	134. [83 - 196]	
Loss mmol/day	165]				
4 hour D/P	0.78 ± 0.09	0.72 ± 0.09**	0.77 ± 0.09	0.73 ± 0.09	
Creatinine					

2.27% glucose	2.0 [0 - 4.8]	0 [0 - 4.7]	2 [0 - 7.0]	0 [0 - 4.0]	
dialysate L/day					
Icodextrin	1.3 [0 - 2.0]	1.5 [0 - 2.0]	1.3 [0 - 2.0]	1.3 [0 - 1.8]	
L/day	1.5 [0 2.0]	1.5 [0 2.0]	1.5 [0 2.0]	1.5 [0 1.5]	
,	100 / . 17 5	110 F . 10 2	100.7 . 17.0	110.4 . 17.0	
Hb g/L	109.6 ± 17.5	110.5 ± 18.3	109.7 ± 17.9	110.4 ± 17.9	
Serum Albumin	39.0 [36.0 -	38.0 [37.0 -	40.0 [37.0 -	38.0 [37.0 -	
gl/L	41.0]	41.0]	42.0]	40.0] *	
CRP mg/L	3.0 [1.0 -	3.0 [2.0 - 8.0]	3.0 [1.0 - 5.0]	4.0 [2.0 - 9.0]	
	8.0]				
NT proBNP	3474 [1001 -	3944 [1508 -	2996 [1181 -	3623 [1214 -	
pg/mL	8563]	10836]	13707]	9235]	
Cholesterol	4.4 [3.5 -	4.3 [3.5 - 5.6]	4.7 [3.6 - 6.2]	4.2 [3.5 - 5.0]	
mmol/L	5.9]				
Triglycerides	1.8 [1.1 -	1.7 [1.18 -	1.8 [1.1 - 2.8]	1.7 [1.2 - 2.8]	
mmol/L	2.8]	2.85]			
HbA1C	41.6 [36.3 -	34.4 [31.1 -	39.9 [34.4 -	35.5 [33.3 -	
mmol/mol	55.8]	39.9] **	53.6]	49.]	
Serum	4.5 ± 0.8	4.6 ± 0.6	4.5 ± 0.8	4.5 ± 0.7	
Potassium					
mmol/L					
Serum 1.7 [1.3 -		1.6 [1.3 - 1.89	1.6 [1.3 - 1.9]	1.7 [1.3 - 1.9]	
Phosphorus	1.9]				
mmol/L					
PNA g/day	58.4 [51.6 -	67.1 [52.8 -	62. [54.2 -	63.2 [50.9 -	
	68.5]	77.8]	75.6]	72.8]	

Table 3. Logistic step-backward model of variables associated with high dietary sodium intake estimated by the Derby Salt Questionnaire (DSQ) and Royal Free Hospital Salt Questionnaire (RFH-SQ) estimated dietary sodium intake. Skeletal muscle mass (SMM), glycated haemoglobin (HbA1c) mmol/mol, haemoglobin (Hb). Standard error of  $\beta$  (SE), odds ratio (ORR), 95% confidence limits (CL). DSQ Nagelkerke  $r^2$ =0.20, RFH-SQ  $r^2$ =0.26.

variable	β	StE ß	Wald	Odds ratio	95% CL	p value
DSQ						
Age year	0.05	0.02	8.0	1.06	1.02-1.09	0.005
SMM kg	0.12	0.60	4.4	1.13	1.01-1.27	0.040
RFH-SQ						
SMM kg	0.14	0.05	7.6	1.15	1.04-1.27	0.006
Log HbA1c	-7.03	2.6	7.4	0.01	0.01 -0.14	0.020
Hb g/L	0.34	0.17	4.2	1.41	1.02-1.95	0.041