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On the Correlation between Hydration of the Stratum Corneum and the Nutritional Status of Dialysis Patients

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Abstract

Stratum corneum (SC) prevents evaporation of internal moisture and maintains dermal flexibility and fluidity. Malnutrition is known to decrease SC hydration, but involvement of nutritional status in SC hydration of dialysis patients is unclear. In this study, we examined the association between SC hydration and nutritional status on dialysis patients. We studied 16 control subjects and 81 dialysis patients to examine SC hydration of the neck, upper arm and lower leg. In the 81 patients, we measured serum albumin (Alb), transferrin, geriatric nutritional risk index (GNRI) and normalized protein catabolic rate (nPCR). We then classified the dialysis patients into a 21-patients group, with both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day, and a 60-patients group with either Alb ＜3.6 g/dl or nPCR ＜0.9 g/kg/day. SC hydration in the lower leg and the Alb value in the 81 patients were significantly lower than those in the control subjects. SC hydration in the upper arm and lower leg and the values of transferrin and GNRI in the 60-patients group were significantly lower than those in the 21-patients group. This study demonstrates for the first time that nutritional status is correlated with maintenance of SC hydration on dialysis patients.

キーワード：stratum corneum (SC), SC hydration, dialysis, serum albumin (Alb), normalized protein catabolic rate (nPCR)

Introduction

Stratum corneum (SC) which consists of skin defends the whole body against exogenous pathogens and toxic substances. SC also prevents evaporation of internal moisture and maintains dermal flexibility and fluidity [1]. SC hydration is decreased by various factors such

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as nutritional status and dialysis [2-5]. The decrease in SC hydration induces dry skin, resulting in developing cutaneous pruritus or curettage [5], which causes additional damage of SC by scrabbling the skin. The pruritus not only induces insufficient sleep and depression but also significantly effects survival rate for dialysis patients [6]. Dialysis patients often become malnourished from deficient energy and protein, leading to increased mortality risk [7, 8]. In addition, malnutrition is known to decrease SC hydration in children and the elderly [3, 4]. However, involvement of nutritional status in the SC hydration of dialysis patients is unclear.

In 1980, there were 158,000 dialysis patients worldwide; that number exceeded 2 million in 2010 [9]. Dialysis patients in Japan exceeded 320,000 people in 2015 [10]. Maintenance of SC hydration plays a crucial role in quality of life of dialysis patients. In the present study, we examined the association between SC hydration and nutritional status on dialysis patients.

Method

Study design: The present study was conducted in Miki Sanyo Hospital from August to December 2015. We studied 97 Japanese participants aged 55 years or older who included 16 control subjects and 81 stable dialysis patients. All participants did not have skin diseases, renal dysfunction, hepatic disorder or diabetes. We complied with the tenets of Helsinki Declaration and present study protocol was approved by the guidelines of Yasuda Women's University (Hiroshima, Japan) and Miki Sanyo Hospital (Miki, Japan). Informed consent was obtained from all participants.

Data collection: We evaluated demographic characteristics, body function, SC hydration, nutritional status, dialytic efficiency and blood tests as described below. Demographic characteristics such as sex, age, height, weight, underlying diseases and the dialysis period were collected from medical charts. The body function of dialysis patients was judged by reference to the section of body function in the malnutrition inflammation score [1].

Measurement of SC hydration: The values of SC hydration were measured using the Mobile Moisture HP10-N (Courage + Khazaka, Cologne, Germany) [12].

Evaluation of nutritional status, dialytic efficiency and blood test: Blood samples were obtained from dialysis patients before and after dialysis. Nutritional status was evaluated by body mass index (BMI), and the values of serum albumin (Alb) and transferrin (Tf) which have a half-life of 21 and 7 days, respectively [13]. Current height and weight were used to calculate BMI. Dialytic efficiency was calculated by Daugirdas et al's equation [14]. The values of blood tests before and after dialysis were collected from the medical charts. The values of serum phosphorus (P), calcium (Ca), total cholesterol (T-ch), iron (Fe) and Tf before dialysis, and those of serum Alb, creatinine (Cr) and potassium (K) before and after dialysis were collected. Geriatric nutritional risk index (GNRI), a specific index of nutritional status for dialysis

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patients, was calculated by Yamada et al.'s equation [15]. Malnutrition was determined by the GNRI value less than 92 [16]. The value of normalized protein catabolic rate (nPCR), an index of protein intake [17], was calculated by Hara's equation using blood urea nitrogen (BUN) before and after dialysis [18].

Statistical analysis

All data are presented as means ± standard deviations (SDs). Comparisons of age, weight, BMI, SC hydration, nutritional status and blood tests between each group were performed using Student's unpaired t-test and those of the ratio of subject between each group using chi-square test.

Results and Discussion

SC hydration in control subjects and dialysis patients

We examined SC hydration in the neck, upper arm and lower leg of 16 control subjects and 81 dialysis patients. Age, weight, BMI and SC hydration in the neck and upper arm showed no significant differences between each group (Table 1). However, SC hydration in the lower leg of the dialysis patients (26.6 ± 13.6) was significantly lower than that of the control subjects (34.5 ± 14.1, Table 1). These results were consistent with those of the previous studies that SC hydration of dialysis patients was less than that of control subjects [5]. In addition, the value of serum Alb in the dialysis patients (3.5 ± 0.3 g/dl) was significantly lower than that in the control subjects (4.1 ± 0.4 g/dl, Table 1). The Alb value less than 3.5 g/dl (Alb < 3.5 g/dl) is known to physiologically show a decrease in internal protein, and is epidemiologically

Table 1 The demographic characteristics and SC hydration between control subjects and dialysis patients.

Parameters	control (n = 16)	dialysis (n = 81)	*P*-value
Age (y)	70.7 ± 7.5	72.1 ± 8.9	N.S.
Weight (kg)	58.0 ± 11.9	54.8 ± 10.5	N.S.
BMI (kg/m²)	22.5 ± 3.1	21.3 ± 3.1	N.S.
Neck	66.8 ± 16.5	64.1 ± 12.1	N.S.
Upper arm	48.3 ± 11.5	41.8 ± 10.0	N.S.
Lower leg	34.5 ± 14.1	26.6 ± 13.6	< 0.05
Alb (g/dl)	4.1 ± 0.4	3.5 ± 0.3	< 0.005

All values are means ± standard deviations (SDs). Weight in the dialysis patients shows dry weight. BMI; Body Mass Index, Alb; albumin.

considered as the risk factor of mortality rate and the prognosis-precipitating factor[19-22]. These results show that some of the dialysis patients had poor nutrition.

The association of Alb with nPCR on SC hydration in dialysis patients

In children with malnutrition and frail elderly with Alb < 3.5 g/dl, dry skin was visually observed[3, 4]. Based on these previous studies, we then examined the association between SC hydration and serum Alb.

We classified the 81 dialysis patients into a 28-patients group (21 males and 7 females), with Alb greater than or equal to 3.6 g/dl (Alb ≥ 3.6 g/dl), and a 53-patients group (35 males and 18 females) with Alb < 3.6 g/dl. Age, weight, BMI and SC hydration in the neck and lower leg showed no significant differences between each group (Table 2). There were also no significant differences in the body function between each group (data not shown, x2 = 4.82, p = 0.19). However, SC hydration in the upper arm of the 53-patients group (39.9 ± 9.1) was significantly lower than that of the 28-patients group (45.5 ± 10.8, Table 2). Dialytic period and efficiency, indexes of renal function (Cr and BUN), electrolytes (P, Ca and K), a dyslipidemia marker like T-ch and indexes of anemia (Fe and Fe/TIBC) showed no significant differences between each group (Table 3).

However, the Tf values in both patients groups were less than the reference value (190 mg/ml), indicating that the dialysis patients with Alb < 3.6 g/dl always had poor nutrition. In addition, the GNRI value in the 53-patients group (90 ± 7) was significantly lower than that in the 28-patients group (96 ± 7, Table 3), which was reasonable because GNRI is dependent on serum Alb. Furthermore, the nPCR value, an index of protein intake, in the 53-patients group (0.8 ± 0.2 g/kg/day) showed less than the reference value (0.9 g/kg/day), and was significantly lower than that in the 28-patients group (0.9 ± 0.1 g/kg/day, Table 3). These results suggest

Table 2 The demographic characteristics and SC hydration between dialysis patients with Alb ≥ 3.6 g/dl and those with Alb < 3.6 g/dl.

Parameters	Alb ≥ 3.6 g/dl (n = 28)	Alb < 3.6 g/dl (n = 53)	*P*-value
Age (y)	71.0 ± 8.8	72.7 ± 9.1	N.S.
Weight (kg)	53.9 ± 12.5	55.3 ± 9.3	N.S.
BMI (kg/m²)	20.6 ± 3.6	21.7 ± 2.7	N.S.
Neck	66.1 ± 13.9	63.0 ± 11.0	N.S.
Upper arm	45.5 ± 10.8	39.9 ± 9.1	< 0.05
Lower leg	29.6 ± 11.9	25.0 ± 14.2	N.S.

All values are means ± SDs. Weight between patients groups shows dry weight.

Table 3 The values of blood tests between dialysis patients with Alb ≥ 3.6 g/dl and those with Alb < 3.6 g/dl.

Parameters	Criteria (dialysis patient)	Alb ≥ 3.6 g/dl (n = 28)	Alb < 3.6 g/dl (n = 53)	*P*-value
Alb (BD, g/dl)	≥ 4.0	3.8 ± 0.2	3.3 ± 0.2	< 0.001
Alb (AD, g/dl)	-	4.2 ± 0.4	3.8 ± 0.4	< 0.001
Dialytic periods (y)	-	6.9 ± 5.2	4.9 ± 4.0	N.S.
Dialytic efficiency (Kt/V)	1.2-1.4	1.2 ± 0.2	1.1 ± 0.2	N.S.
Cr (BD, mg/dl)	-	10.1 ± 2.5	9.4 ± 2.6	N.S.
Cr (AD, mg/dl)	-	3.7 ± 1.1	3.7 ± 1.2	N.S.
BUN (BD, mg/dl)	70-90	65 ± 12	59 ± 15	N.S.
BUN (AD, mg/dl)	-	19 ± 5	19 ± 7	N.S.
P (BD, mg/dl)	3.5-6.0	5.6 ± 1.5	5.2 ± 1.3	N.S.
Ca (BD, mg/dl)	8.4-10.8	9.1 ± 0.6	8.8 ± 1.4	N.S.
K (BD, mEq/l)	3.5-5.5	5.1 ± 0.7	4.8 ± 0.8	N.S.
K (AD, mEq/l)	-	3.5 ± 0.4	3.5 ± 0.4	N.S.
T-Ch (BD, mg/dl)	140-199	157 ± 49	147 ± 35	N.S.
Fe (BD, μg/dl)	-	82 ± 32	72 ± 32	N.S.
Fe/TIBC (%)	> 20	37 ± 17	36 ± 18	N.S.
Tf (BD, mg/dl)	190-320	170 ± 39	154 ± 39	N.S.
GNRI	≥ 92	96 ± 7	90 ± 7	< 0.001
nPCR (g/kg/day)	0.9-1.2	0.9 ± 0.1	0.8 ± 0.2	< 0.05

AD: After dialysis, BD: before dialysis, Cr: creatinine, BUN; blood urea nitrogen, P; phosphorus, Ca: calcium, K; potassium, T-ch; total cholesterol, Fe; iron, TIBC; total iron-binding capacity, Tf; transferrin, GNRI; geriatric nutritional risk index, nPCR; normalized protein catabolic cate.

that the dialysis patients with Alb ≥ 3.6 g/dl intake an appropriate protein amount compared with those with Alb < 3.6 g/dl, but some of the dialysis patients with Alb ≥ 3.6 g/dl have poor nutrition. Protein is a component of the natural moisturizing factor, which forms a hydrogen bond to water molecules, resulting in maintaining SC hydration [1]. It has been reported that a decrease in amino acid is an etiology of xeroderma [1] and that children associated with kwashiorkor caused by protein insufficiency markedly have dry skin [3]. These previous studies indicate that protein insufficiency leads to dry skin. Previous studies and our results suggest a possibility that SC hydration is correlated with not only serum Alb but also nPCR.

The association of both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day on SC hydration in dialysis patients

In Japan, the ideal value of nPCR in dialysis patients is defined as 0.9-1.2 g/kg/day, and the nPCR value less than 0.9 g/kg/day (nPCR < 0.9 g/kg/day) is known to increase the mortality rate [17]. We further classified the same 81 dialysis patients into a 21-patients group (15 males and 6 females), with both Alb ≥ 3.6 g/dl and nPCR greater than or equal to 0.9 g/kg/day

(nPCR ≥ 0.9 g/kg/day), and a 60-patients group (41 males and 19 females) with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day. Age, weight and SC hydration in the neck showed no significant differences between each group (Table 4). There were also no significant differences in body function between each group (data not shown, x2 = 0.767, p = 1.14). Intriguingly, the values of SC hydration in the upper arm (39.9 ± 9.2) and lower leg (24.8 ± 13.6) of the 60-patients group were significantly lower than those in the upper arm (47.2 ± 10.7) and lower leg (31.9 ± 12.4) of the 21-patients group, respectively (Table 4). Meanwhile, the values of SC hydration in the neck, upper arm and lower leg showed no significant differences between the 16 control subjects and the 21-patients group (Table 5). These results and Table 2 suggest that maintenance of SC hydration needs to keep both serum Alb and nPCR greater than or equal

Table 4 The demographic characteristics and SC hydration between dialysis patients, with both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day, and those with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day.

Parameters	Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day (n = 21)	Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day (n = 60)	*P*-value
Age (y)	70.7 ± 8.7	72.6 ± 9.0	N.S.
Weight (kg)	51.3 ± 11.2	56.1 ± 10.0	N.S.
BMI (kg/m²)	20 ± 3	22 ± 3	< 0.05
Neck	65.4 ± 13.0	63.6 ± 11.8	N.S.
Upper arm	47.2 ± 10.7	39.9 ± 9.2	< 0.005
Lower leg	31.9 ± 12.4	24.8 ± 13.6	< 0.05

All values are means ± SDs. Weight between patients groups shows dry weight.

Table 5 The SC hydration between control subjects and dialysis patients with both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day.

Parameters	control (n = 16)	Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day (n = 21)	*P*-value
Neck	66.8 ± 16.5	65.4 ± 13.0	N.S.
Upper arm	48.3 ± 11.5	47.2 ± 10.7	N.S.
Lower leg	34.5 ± 14.1	31.9 ± 12.4	N.S.

All values are means ± SDs.

Table 6 The value of blood tests between dialysis patients, with both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day, and those with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day.

Parameters	Criteria (dialysis patient)	Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day (n = 21)	Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day (n = 60)	*P*-value
Alb (BD, g/dl)	≥ 4.0	3.8 ± 0.2	3.4 ± 0.3	< 0.001
Alb (AD, g/dl)	-	4.2 ± 0.4	3.8 ± 0.4	< 0.001
nPCR (g/kg/day)	0.9-1.2	1.0 ± 0.1	0.8 ± 0.2	< 0.001
Tf (BD, mg/dl)	190-320	174 ± 43	154 ± 37	< 0.05
GNRI	≥ 92	93 ± 6	89 ± 6	< 0.05
Dialytic period (y)	-	7.3 ± 5.7	5.0 ± 3.9	< 0.05
Dialytic efficiency (Kt/V)	1.2-1.4	1.3 ± 0.2	1.1 ± 0.2	< 0.05
Cr (BD, mg/dl)	-	10.0 ± 2.6	9.5 ± 2.5	N.S.
Cr (AD, mg/dl)	-	3.6 ± 1.2	3.7 ± 1.1	N.S.
BUN (BD, mg/dl)	70-90	69 ± 10	56 ± 14	< 0.001
BUN (AD, mg/dl)	-	20 ± 5	19 ± 7	N.S.
P (BD, mg/dl)	3.5-6.0	5.9 ± 1.4	5.1 ± 1.3	< 0.05
Ca (BD, mg/dl)	8.4-10.8	9.2 ± 0.5	8.8 ± 1.3	N.S.
K (BD, mEq/l)	3.5-5.5	5.1 ± 0.8	4.9 ± 0.8	N.S.
K (AD, mEq/l)	-	3.5 ± 0.4	3.5 ± 0.4	N.S.
T-Ch (BD, mg/dl)	140-199	162 ± 49	146 ± 36	N.S.
Fe (BD, μg/dl)	-	86 ± 36	72 ± 30	N.S.
Fe/TIBC (%)	> 20	37.8 ± 19.0	35.2 ± 16.6	N.S.

All values are means ± SDs.

to the reference values. Unexpectedly, BMI in the 60-patients group (22 ± 3) was significantly higher than that in the 21-patients group (20 ± 3, Table 4). However, the Alb value in the 60-patients group (3.4 ± 0.3 g/dl) was significantly lower than that in the 21-patients group (3.8 ± 0.2 g/dl, Table 6). These results suggest that edema formed by a decrease in serum Alb causes an increase in body weight, resulting in increased BMI in the dialysis patients with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day. Cr, BUN after dialysis, Ca, K, T-Ch, Fe and Fe/TIBC showed no significant differences between each group (Table 6). However, the values of nPCR, BUN before dialysis and P in the 60-patients group were significantly lower than those in the 21-patients group (Table 6).

These results suggest that the dialysis patients with either Alb < 3.6 g/dl or nPCR < 0.9 g/kg/day have poor nutrition compared with those with both Alb ≥ 3.6 g/dl and nPCR ≥ 0.9 g/kg/day, because BUN, which nPCR is calculated by using before and after dialysis [18], and P correlate with dietary intake of protein [23]. Meanwhile, hyperphosphatemia is associated with the progression of vascular lesion and prognosis [24]. Thus, nutrition education about dietary intake of energy and protein against the dialysis patients should be noted.

In conclusion, we demonstrate for the first time that nutritional status is correlated with

maintenance of SC hydration on dialysis patients and that the maintenance needs to keep not only serum Alb but also nPCR greater than or equal to the reference values. Improvement of nutritional status for dialysis patients maintains SC hydration, which leads to the prevention of cutaneous pruritus by drying, insufficient sleep and depression. Measurement of SC hydration to improve malnutrition may help improve quality of life for dialysis patients.

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References

[1] Tagami H. Electrical measurement of the hydration state of the skin surface in vivo. The British journal of dermatology. 2014; 171 Suppl 3:29-33.
[2] Liakou AI, Theodorakis MJ, Melnik BC, Pappas A, Zouboulis CC. Nutritional clinical studies in dermatology. Journal of drugs in dermatology : JDD. 2013; 12:1104-9.
[3] Heilskov S, Rytter MJ, Vestergaard C, Briend A, Babirekere E, Deleuran MS. Dermatosis in children with oedematous malnutrition (Kwashiorkor): a review of the literature. Journal of the European Academy of Dermatology and Venereology : JEADV. 2014; 28:995-1001.
[4] Ooura Y, Yuzawa, Y. The Association between Serum Albumin and Condition of the Skin in the Frail Elderly : Early Detection of Malnutrition from Skin Observation (in Japanese). journal of Japan Academy of Gerontological Nursing. 2007; 11:84-92.
[5] Suzuki C, Hiratani H, Okumoto K, Suzuki K, Kato K. rrelation between hydration of stratum corneum and pruritus in maintenance hemodialysis patients (in Japanese). Nihon Toseki Igakkai Zasshi. 2005; 38:1717-21.
[6] Manenti L, Tansinda P, Vaglio A. Uraemic pruritus: clinical characteristics, pathophysiology and treatment. Drugs. 2009; 69:251-263; Combs SA, Teixeira JP, Germain MJ Pruritus in Kidney Disease. Seminars in nephrology. 2015; 35:383-91.
[7] Kumagai H. Nutritional therapy for patients undergoing hemodialysis. Contributions to nephrology. 2007; 155:59-71.
[8] Sigrist MK, Levin A, Tejani AM. Systematic review of evidence for the use of intradialytic parenteral nutrition in malnourished hemodialysis patients. Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation. 2010; 20:1-7.
[9] Lysaght MJ. Maintenance dialysis population dynamics: current trends and long-term implications. Journal of the American Society of Nephrology : JASN. 2002; 13 Suppl 1:S37-40.
[10] The-Japanese-Society-for-Dialysis-Therapy. (2015). http://docs.jsdt.or.jp/overview/index.html
[11] Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2001; 38:1251-63.
[12] Iizaka S., Takehara K., Sanada H. Validation of a portable device for measuring stratum corneum hydration (in Japanese). Journal of Japanese Society of Wound, Ostomy and Continence Management 2015:33-9.
[13] Steinman TI. Serum albumin: its significance in patients with ESRD. Semin Dial,. 2000; 13:404-8.
[14] Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an

analysis of error. Journal of the American Society of Nephrology : JASN. 1993; 4:1205-13.
[15] Yamada K., Furuya R., Takita T. , Maruyama Y, Yamaguchi Y, Ohkawa S. et al. Simplified nutritional screening tools for patients on maintenance hemodialysis. The American journal of clinical nutrition. 2008; 87:106-13.
[16] Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. The American journal of clinical nutrition. 2005; 82:777-83.
[17] Fein PA, Weiss S, Avram MM, Ramos F, Singh P, See SY et al. Relationship of Normalized Protein Catabolic Rate with Nutrition Status and Long-Term Survival in Peritoneal Dialysis Patients. Advances in peritoneal dialysis Conference on Peritoneal Dialysis. 2015; 31:45-48.
[18] Hara M. Calculation of protein catabolic rate using pre- and postdialysis blood urea nitrogen concentration (in Japanese). Nihon Toseki Igakkai Zasshi. 2000; 33:347-52.
[19] Starker PM, Gump FE, Askanazi J, Elwyn DH, Kinney JM. Serum albumin levels as an index of nutritional support. Surgery. 1982; 91:194-99.
[20] Salive ME, Cornoni-Huntley J, Phillips CL et al. Serum albumin in older persons: relationship with age and health status. Journal of clinical epidemiology. 1992; 45:213-21.
[21] Corti MC, Guralnik JM, Salive ME, Sorkin JD. Serum albumin level and physical disability as predictors of mortality in older persons. Jama. 1994; 272:1036-42.
[22] Owen WF, Jr., Lew NL, Liu Y. Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. The New England journal of medicine. 1993; 329:1001-6.
[23] Japanese dialysis medical society academic committee guidelines making subcommittee Issue of nutrient examination working group. An Overview of Regular Dialysis Treatment in Japan (in Japanease). The Japanese Society for Dialysis Therapy. 2014; 47:287-291.
[24] Scialla JJ, Wolf M. Roles of phosphate and fibroblast growth factor 23 in cardiovascular disease. Nature reviews Nephrology. 2014; 10:268-278.