**Abstract:**
Electrolyte disturbances are common in patients with cystic fibrosis (CF). Current guidelines on monitoring sodium status are based on research in a small group of infants and require blood sampling. The aim of this study was to evaluate urinary salt parameters as a surrogate for sodium-status in different age-groups.

Blood and urine samples for electrolytes were collected from 222 patients followed at the Ghent University Hospital CF-center. Fractional sodium excretion (FENa) and several urinary parameters were calculated. Clinical characteristics did not differ according to sodium status, defined as FENa <0.5%. ROC analysis demonstrated that sodium/creatinine ratio (UNa/Creat) predicted the sodium status most accurately with high sensitivity and specificity (97 and 91% respectively). The UNa/Creat cut-off predicting a FENa <0.5% differed significantly according to age.

The UNa/Creat is an excellent marker for the sodium status defined as a FENa <0.5%. However, different cut-offs according to age category should be applied.
**Funding and conflict of interest**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

None of the authors have a conflict of interest
Cover Letter

1. Has the work been seen and approved by all co-authors?

Yes

2. How is the work clinically relevant, and how does it add to existing research?

The diagnosis of sodium deficiency is cumbersome. Patients with CF are at risk for sodium deficiency due to high sweat losses. Therefore, sodium supplementation is necessary. Evidence lacks on supplementation dosage for children and adults. Having a proper method to screen for deficiencies can help us titrating sodium supplementation.

• Have papers closely related to the submitted manuscript been published or submitted for publication elsewhere? If so please provide details.

No
Responses to the reviewer

Reviewer #1

would suggest 1. include a statement on the statistical power of study based on sample size as the study makes recommendations with strong implications and number of subjects in each age subgroup does not appear to be large.

Thank your for the suggestion to perform a power analysis. We decided to perform a post hoc power analysis with G*Power software. The results showed a power > 95% with the current number of patients included per age group. This high power is a result of the strong correlation between UNa/Creat and FENa. This strong correlation was also seen in the study of Coates et al.

2. suggest making recommendation that studies with larger number of patients need to replicate similar results to make it a general standard of practice / guideline.

Based on the above results, we didn’t have to make a statement to repeat this study in a large population.
URINARY SODIUM/CREATININE RATIO IS A PREDICTOR FOR FRACTIONAL SODIUM EXCRETION AND RELATED TO AGE IN PATIENTS WITH CYSTIC FIBROSIS

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Abstract

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Abbreviations

CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane regulator
FE: fractional excretion
UNa/Creat: Urinary sodium/ urinary creatinine ratio
FVC: forced vital capacity
FEV1: forced expiratory volume in 1 second
PI: pancreatic insufficient
CFRD: CF related diabetes
CFLD: CF liver disease
Introduction

As result of the cystic fibrosis transmembrane regulator (CFTR) dysfunction, patients with cystic fibrosis (CF) lose 2-4 times more salt in their sweat (1). Siegentahler et al. demonstrated that CF patients, in contrast to healthy controls, were unable to decrease salt losses in sweat when confronted with salt deprivation (2). Hyponatremic, hypochloremic alkalosis with or without hypokalemia, also known as pseudo-Bartter syndrome, can be observed in patients with CF confronted with situations leading to inadequate salt and fluid intake or increased losses through the gastro-intestinal tract or sweating. Depending on the climate, up to 95% of all new CF diagnoses, present with hyponatremia (3). Despite the advised salt supplementation, this entity was also described during follow-up in up to 54% of infants living in an arid climate (3) and 57% of patients with end-stage disease (4).

The renin-angiotensin-aldosterone system has been demonstrated to react adequately in patients with CF in response to salt depletion and dehydration (5). Also, there is a normal osmoregulation after water deprivation and water load (6). However, the thirst drive in CF is lower, leading to insufficient compensation of their losses (7) and CF mice display a decreased renal pendrin activity (8). This Chloride/Bicarbonate exchanger plays an important role in vascular volume homeostasis precipitating the development of metabolic alkalosis in case of volume depletion (8).

Guidelines advise to regularly check the sodium status of CF patients using a urinary sodium/creatinine ratio, corresponding to the fractional excretion of sodium (9). The fractional sodium excretion (FENa) is influenced by glomerular filtration rate, tubular function and sodium intake (10, 11). It can be used as marker for sodium status in case of normal kidney function. Repeated calculation of the FENa to evaluate the sodium status is, however, difficult to perform as it necessitates a combined blood and urine
Surrogate urinary markers are useful as they allow repeated controls without the burden of repeated blood draws. Coates et al. determined the cut-offs of urinary sodium/creatinine ratio (UNa/Creat) on a spot urine sample in 10 infants to predict a FENa ≥0.5% (12).

Urinary creatinine excretion varies with muscle mass and is therefore different across age categories and body composition ([Heymsfield, 1983 #338]13). This resulted in the hypothesis that the UNa/Creat cut-offs corresponding to the FENa ≥0.5% would differ across age categories in patients with CF.

The aim of this study was to evaluate urinary salt parameters as a surrogate for the FENa in a large group of children and adults with CF in order to facilitate future follow-up of the sodium status using a spot urine sample. The previously reported association between the sodium-status and clinical parameters is also investigated (14).

**Methods**

All patients followed at the CF center of the Ghent University Hospital receive an annual check-up including a blood sample and urine sample for electrolytes. Data of patients delivering a simultaneous blood and urine sample between Jan 2019 and Dec 2020, were prospectively collected in a pseudonymized database. Collected data were age, gender, pulmonary function, weight, height, CF related complications as diabetes or liver disease and treatments as CFTR modulators and tube feeding. Patients on diuretics were excluded.

Height and BMI were converted into z-scores based on the Flemish growth charts (15). The FENa was calculated as well as several urinary surrogate parameters for sodium status: urinary sodium/urinary potassium ratio (UNa/K), urinary sodium/(urinary sodium + urinary potassium) ratio (UNa/(Na+K)) and the UNa/Creat expressed in mmol/mmol. Forced vital capacity (FVC) and forced expiratory volume in 1 second
(FEV1) were expressed as percentage of normal (pp) (16). Patients were categorized according to age: <6 years, 6-<12 years, 12-<18 years, ≥18 years. Patients were diagnosed as sodium-deficient if their FENa was <0.5% (11, 17, 18).

The statistics were done with IBM® SPSS® Statistics version 27 (IBM Corporation, 2020), using non-parametric tests for continuous variables and Chi-square for categorical variables and applying a Bonferroni correction for multiple testing if necessary. Single regression analysis was used to study Una/Creat as a predictor for FENa over different age categories. A receiver operating characteristic (ROC) analysis was used to determine sensitivity and specificity of the surrogate markers for sodium status. A post hoc power analysis for each age group was performed with G*Power software (ver. 3.1.9.6; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) (19). For each analysis standard deviation of both variables, correlation coefficient and total sample size was used. Results are reported as median (interquartile range (IQR)). The study was approved by the ethics committee and registered in clinicaltrials.gov (NCT04556162).

Results

The collected data of 222 patients (114 males) with a median age of 12.4 [7-19] years were analyzed. A hyponatremia (Na⁺ <135 mmol/L) was documented in the medical history of 53 patients (24%). An overview of patients’ characteristics, UNa/Creat and FENa stratified by age are presented in table 1.

Only the UNa/Creat is significantly different across age categories (p = 0.004). The other parameters did not differ significantly between age groups. Additional classification according to gender, FENa, modulator use and genotype is available in electronic supplementary data (table A). There was no significant difference of
genotype, clinical characteristics or modulator treatment in patients with low sodium status. At time of the annual visit 47% of the patients had a FENa <0.5% (table 1).
Table 1: An overview of patients’ characteristics and UNa/Creat and FENa result stratified for age at time of the annual review visit. Results are reported as median (IQR) unless otherwise stated. BMI: body mass index, FEV1: forced expiratory volume in 1 second, FVC, forced vital capacity, PI: pancreatic insufficiency, CFRD: cystic fibrosis related diabetes, CFLD: CF liver disease, TF: tube feeding, FENa: fractional sodium excretion, UNa/Creat: urinary sodium/urinary creatinine concentration (mmol/mmol).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (N= 222)</th>
<th>&lt; 6 yrs (N = 41)</th>
<th>6 - &lt; 12 yrs (N= 66)</th>
<th>12 - &lt;18 yrs (N= 53)</th>
<th>≥ 18 yrs (N= 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.6 (7-19.1)</td>
<td>2.9 (1.0-4.2)</td>
<td>8.2 (7.1-10.0)</td>
<td>15.4 (14.1-17.0)</td>
<td>28.4 (21.6-35.2)</td>
</tr>
<tr>
<td>Male (n(%))</td>
<td>114 (51.4%)</td>
<td>20 (48.8%)</td>
<td>36 (54.5%)</td>
<td>22 (41.5%)</td>
<td>36 (58.1%)</td>
</tr>
<tr>
<td>BMI (z-score)</td>
<td>-0.4 (-1.1 – 0.3)</td>
<td>-0.5 (-1.2 – 0.2)</td>
<td>-0.6 (-1.2 – 0.1)</td>
<td>-0.3 (-1.2 – 0.5)</td>
<td>-0.2 (-1.0 – 0.5)</td>
</tr>
<tr>
<td>Height (z-score)</td>
<td>-0.6 (-1.3 – 0.2)</td>
<td>-0.2 (-1.2 – 0.3)</td>
<td>-0.6 (-1.3 – 0.6)</td>
<td>-0.7 (-1.1 – 0.1)</td>
<td>-1.0 (-1.6 – 0.2)</td>
</tr>
<tr>
<td>FEV1pp</td>
<td>86.3 (68.3-96.9)</td>
<td>92.7 (75.5-103.0)</td>
<td>88.2 (77.1-94.9)</td>
<td>89.5 (77.0-95.7)</td>
<td>96.9 (81.1-100.9)</td>
</tr>
<tr>
<td>FVCpp</td>
<td>94.7 (82.9-103)</td>
<td>100.8 (91.5-109.1)</td>
<td>95.1 (84.1-98.5)</td>
<td>89.0 (77.0-95.7)</td>
<td>96.9 (81.1-100.9)</td>
</tr>
<tr>
<td>PI (n(%))</td>
<td>184 (82.9%)</td>
<td>37 (90.2%)</td>
<td>58 (87.9%)</td>
<td>39 (73.6%)</td>
<td>50 (80.6%)</td>
</tr>
<tr>
<td>CFRD (n(%))</td>
<td>30 (13.5%)</td>
<td>1 (2.4%)</td>
<td>6 (9.1%)</td>
<td>5 (9.4%)</td>
<td>18 (29.0%)</td>
</tr>
<tr>
<td>CFLD (n(%))</td>
<td>29 (13%)</td>
<td>0</td>
<td>12 (18.2%)</td>
<td>8 (15.1%)</td>
<td>9 (14.5%)</td>
</tr>
<tr>
<td>TF (n(%))</td>
<td>10 (4.5%)</td>
<td>2 (4.8%)</td>
<td>3 (4.5%)</td>
<td>2 (3.8%)</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>Modulator (n(%))</td>
<td>35 (15.7%)</td>
<td>2 (4.8%)</td>
<td>5 (7.6%)</td>
<td>9 (17.0%)</td>
<td>19 (30.6%)</td>
</tr>
<tr>
<td>FENa</td>
<td>0.5 (0.3-0.8)</td>
<td>0.4 (0.3-0.7)</td>
<td>0.6 (0.3-0.9)</td>
<td>0.4 (0.3-0.6)</td>
<td>0.6 (0.4-0.8)</td>
</tr>
<tr>
<td>UNa/Creat</td>
<td>13.3 (7.5-20.5)</td>
<td>14.6 (8.9-27.0)</td>
<td>17.2 (7.4-25.4)</td>
<td>9.1 (7.1-15.0)</td>
<td>12.7 (7.3-17.2)</td>
</tr>
<tr>
<td>FENa &lt;0.5% (n(%))</td>
<td>105 (47.3%)</td>
<td>24 (48.5%)</td>
<td>26 (39.4%)</td>
<td>31 (58.5%)</td>
<td>24 (38.7%)</td>
</tr>
</tbody>
</table>
The ROC curve analysis (figure 1) demonstrates the superiority of the UNa/Creat ratio compared to UNa, UNa/K and UNa/Na+K, although all parameters predicted a FENa <0.5%.

**Figure 1:** ROC curve of different urinary parameters predicting a fractional sodium excretion <0.5%.

Since there is a significant difference in UNa/Creat according to age without significant difference for FENa, the UNa/Creat cut-offs predicting a FENa of <0.5% is significant different according to age (Figure 2). After regression analysis the UNa/Creat cut-off (mmol/mmol) 17.6, 14.8, 11.7 and 10.3 for patients <6 years, 6-<12 years, 12-<18 years and >18 years, respectively. Using these cut-offs to predict a FENa <0.5% the sensitivity is 97.1% and the specificity is 90.6%. There were 11 false positive results and only 3 false negatives. Sensitivity and specificity stratified by age is available as additional electronic information (table B).
Figure 2: Scatter dot plotting urinary sodium over urinary creatinine to the corresponding fractional sodium excretion. Patients are stratified according to age category with the cut-off corresponding to FENa of 0.5%.

A post hoc power analysis resulted for each age group in a power > 95%. Suggesting that the number of patients included per age group are adequate to support our
findings. This high power is a result of the strong correlation between UNa/Creat and FENa.

**Discussion**

Due to the CFTR dysfunction, people with CF are prone to electrolyte disturbances especially in situations with increased salt wasting through increased sweating or gastro-intestinal loss and/or decreased salt and fluid intake (1). None of the patients had a hyponatremia at the time of the annual check-up, but 24% had a documented hyponatremia in their medical history. The presence of electrolyte abnormalities in CF is not well documented. Guimaraes et al. describe the presence of hyponatremia in 95% (19/20) of all new CF diagnoses at a Brazilian CF center, with a median age of 45 months (3). Scurati-Manzoni et al. summarized all papers describing electrolyte disturbances in patients with CF (n=262), a documented hyponatremia was present in 94% of them (206/218) (14). Due to the selection bias this reported frequency cannot be a measure for actual prevalence. On the other hand, the moderate maritime Belgian climate might also play a role in the lower prevalence.

In case of normal kidney function, a FENa between 0.5 and 1.5% reflects a normal sodium status (10, 11, 18). Patients in our center are regularly advised to take supplementary salt in case of warm weather and sport activities, but the amount could not be calculated as data on sodium supplementation were not accurately recorded in patient’s medical record. The FENa was above 0.5% in 52.7% (117/222) of which 1 exceeded 1.5%. This is in keeping with the Iranian study describing a FENa between 0.5 and 1.5% in 47.5% (19/40) of patients with CF using a sodium supplement of 2-4 mEq/kg (20). However, in this cohort one out of 4 patients took too much salt (10/40) resulting in a FENa > 1.5% (20). In contrast, the study of Knepper et al. describes a
normal FENa in only 25.7% (9/35) of patients and 1 had a FENa exceeding 1.5% (21).
They did not elaborate on their policy on salt supplementation. Coates et al. studied 50 consecutive paired samples in 10 infants with a variable sodium supplement between 1-4 mmol/kg. They describe a normal FENa in 46% (23/50) and an increased FENa in 12% (6/50) (12). Since both over and under supplementation is present according to these studies, follow-up of the supplementation is necessary as advised in the guidelines (9).
Knepper et al. suggested an association between normonatremic sodium depletion and poor growth and weight gain (21). This was not observed in our total and pediatric cohort using a single FENa measurement but patients were regularly advised to adapt salt supplements in case of expected increased losses. Despite the theoretical influence of CFTR modulators on the sodium status, this could not be confirmed probably due to the small numbers of CFTR modulator treated patients (8%, 18/222) (22).
Since both too much and too little sodium supplementation might have a clinical impact, guidelines indicate the necessity to monitor the sodium status (9). However, the use of FENa is cumbersome as it involves paired blood and urine samples. As serum sodium and creatinine concentration are fairly stable in case of normal kidney function, the UNa/Creat ratio was the best urinary surrogate marker with an excellent specificity and sensitivity. Coates et al. described in infants a UNa/Creat cut-off of 17 mmol/mmol to predict a FENa of 0.5% (12). This study confirms a comparable cut-off of 17.6 mmol/mmol for children <6 years of age. However, as muscle mass increases with age we discovered age specific cut-offs for older patients corresponding to a FENa of 0.5%: 14.8 for the 6-<12 years, 11.7 for the 12-<18 years and 10.3 for the adults.
As muscle mass influences urinary creatinine excretion, an over estimation of the
sodium status can be made in patients with muscle mass depletion when using the 
UNa/Creat ratio (23). Due to the absence of body composition data this could not be 
evaluated in this study.

With the introduction of CFTR-targeting drugs follow up of sodium status will remain 
important as some have the capacity to almost normalize the sweat salt losses (22). 
Therefore, if salt-intake is not adapted to the decreased losses, the patients might be 
prone to develop hypertension (24).

Although normal FENa excretion (0.5-1.5%) is a well-established parameter in 
nephrology, the lack of an age-matched healthy control group is a weakness. Further 
on, information on salt intake and body composition could improve interpretation of the 
results.

Conclusion

The urinary sodium over urinary creatinine ratio is an excellent surrogate marker for 
the fractional sodium excretion in our cohort. The cut-offs predicting a FENa <0.5% 
differ according to age.

Author Contributions

SVB and DD contributed to the concept and the design of the study, the acquisition, 
the analysis and interpretation of the data. LP and MG contributed to the data 
analysis and interpretation. SVB and DD drafted the article. YW, HS, EVB, ES and 
SVd revised it critically for important intellectual content. All authors gave approval of 
version to be published.

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The statistics were done with IBM® SPSS® Statistics version 27 (IBM Corporation, 2020), using non-parametric tests for continuous variables and Chi-square for categorical variables and applying a Bonferroni correction for multiple testing if necessary. Single regression analysis was used to study Una/Creat as a predictor for FENa over different age categories. A receiver operating characteristic (ROC) analysis was used to determine sensitivity and specificity of the surrogate markers for sodium status. A post hoc power analysis for each age group was performed with G*Power software (ver. 3.1.9.6; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) (19). For each analysis standard deviation of both variables, correlation coefficient and total sample size was used. Results are reported as median (interquartile range (IQR)). The study was approved by the ethics committee and registered in clinicaltrials.gov (NCT04556162).

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The collected data of 222 patients (114 males) with a median age of 12.4 [7-19] years were analyzed. A hyponatremia (Na+ <135 mmol/L) was documented in the medical history of 53 patients (24%). An overview of patients’ characteristics, UNa/Creat and FENa stratified by age are presented in table 1.

Only the UNa/Creat is significantly different across age categories (p = 0.004). The other parameters did not differ significantly between age groups. Additional classification according to gender, FENa, modulator use and genotype is available in electronic supplementary data (table A). There was no significant difference of
genotype, clinical characteristics or modulator treatment in patients with low sodium status. At time of the annual visit 47% of the patients had a FENa $<0.5\%$ (table 1).
Table 1: An overview of patients’ characteristics and UNa/Creat and FENa result stratified for age at time of the annual review visit. Results are reported as median (IQR) unless otherwise stated. BMI: body mass index, FEV1: forced expiratory volume in 1 second, FVC, forced vital capacity, PI: pancreatic insufficiency, CFRD: cystic fibrosis related diabetes, CFLD: CF liver disease, TF: tube feeding, FENa: fractional sodium excretion, UNa/Creat: urinary sodium/urinary creatinine concentration (mmol/mmol).

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The ROC curve analysis (figure 1) demonstrates the superiority of the UNa/Creat ratio compared to UNa, UNa/K and UNa/Na+K, although all parameters predicted a FENa <0.5%.

Figure 1: ROC curve of different urinary parameters predicting a fractional sodium excretion <0.5%

Since there is a significant difference in UNa/Creat according to age without significant difference for FENa, the UNa/Creat cut-offs predicting a FENa of <0.5% is significant different according to age (Figure 2). After regression analysis the UNa/Creat cut-off (mmol/mmol) 17.6, 14.8, 11.7 and 10.3 for patients <6 years, 6-<12 years, 12-<18 years and >18 years, respectively. Using these cut-offs to predict a FENa <0.5% the sensitivity is 97.1% and the specificity is 90.6%. There were 11 false positive results and only 3 false negatives. Sensitivity and specificity stratified by age is available as additional electronic information (table B).
Figure 2: Scatter dot plotting urinary sodium over urinary creatinine to the corresponding fractional sodium excretion. Patients are stratified according to age category with the cut-off corresponding to FENa of 0.5%.

A post hoc power analysis resulted for each age group in a power > 95%. Suggesting that the number of patients included per age group are adequate to support our
findings. This high power is a result of the strong correlation between UNa/Creat and FENa.

Discussion

Due to the CFTR dysfunction, people with CF are prone to electrolyte disturbances especially in situations with increased salt wasting through increased sweating or gastro-intestinal loss and/or decreased salt and fluid intake (1). None of the patients had a hyponatremia at the time of the annual check-up, but 24% had a documented hyponatremia in their medical history. The presence of electrolyte abnormalities in CF is not well documented. Guimaraes et al. describe the presence of hyponatremia in 95% (19/20) of all new CF diagnoses at a Brazilian CF center, with a median age of 45 months (3). Scurati-Manzoni et al. summarized all papers describing electrolyte disturbances in patients with CF (n=262), a documented hyponatremia was present in 94% of them (206/218) (14). Due to the selection bias this reported frequency cannot be a measure for actual prevalence. On the other hand, the moderate maritime Belgian climate might also play a role in the lower prevalence.

In case of normal kidney function, a FENa between 0.5 and 1.5% reflects a normal sodium status (10, 11, 18). Patients in our center are regularly advised to take supplementary salt in case of warm weather and sport activities, but the amount could not be calculated as data on sodium supplementation were not accurately recorded in patient’s medical record. The FENa was above 0.5% in 52.7% (117/222) of which 1 exceeded 1.5%. This is in keeping with the Iranian study describing a FENa between 0.5 and 1.5% in 47.5% (19/40) of patients with CF using a sodium supplement of 2-4 mEq/kg (20). However, in this cohort one out of 4 patients took too much salt (10/40) resulting in a FENa > 1.5% (20). In contrast, the study of Knepper et al. describes a
normal FENa in only 25.7% (9/35) of patients and 1 had a FENa exceeding 1.5% (21). They did not elaborate on their policy on salt supplementation. Coates et al. studied 50 consecutive paired samples in 10 infants with a variable sodium supplement between 1-4 mmol/kg. They describe a normal FENa in 46% (23/50) and an increased FENa in 12% (6/50) (12). Since both over and under supplementation is present according to these studies, follow-up of the supplementation is necessary as advised in the guidelines (9).

Knepper et al. suggested an association between normonatremic sodium depletion and poor growth and weight gain (21). This was not observed in our total and pediatric cohort using a single FENa measurement but patients were regularly advised to adapt salt supplements in case of expected increased losses. Despite the theoretical influence of CFTR modulators on the sodium status, this could not be confirmed probably due to the small numbers of CFTR modulator treated patients (8%, 18/222) (22).

Since both too much and too little sodium supplementation might have a clinical impact, guidelines indicate the necessity to monitor the sodium status (9). However, the use of FENa is cumbersome as it involves paired blood and urine samples. As serum sodium and creatinine concentration are fairly stable in case of normal kidney function, the UNa/Creat ratio was the best urinary surrogate marker with an excellent specificity and sensitivity. Coates et al. described in infants a UNa/Creat cut-off of 17 mmol/mmol to predict a FENa of 0.5% (12). This study confirms a comparable cut-off of 17.6 mmol/mmol for children <6 years of age. However, as muscle mass increases with age we discovered age specific cut-offs for older patients corresponding to a FENa of 0.5%: 14.8 for the 6-<12 years, 11.7 for the 12-<18 years and 10.3 for the adults. As muscle mass influences urinary creatinine excretion, an over estimation of the...
sodium status can be made in patients with muscle mass depletion when using the UNa/Creat ratio \((23)\). Due to the absence of body composition date this could not be evaluated in this study.

With the introduction of CFTR-targeting drugs follow up of sodium status will remain important as some have the capacity to almost normalize the sweat salt losses \((22)\). Therefore, if salt-intake is not adapted to the decreased losses, the patients might be prone to develop hypertension \((24)\).

Although normal FENa excretion \((0.5-1.5\%)\) is a well-established parameter in nephrology, the lack of an age-matched healthy control group is a weakness. Further on, information on salt intake and body composition could improve interpretation of the results.

**Conclusion**

The urinary sodium over urinary creatinine ratio is an excellent surrogate marker for the fractional sodium excretion in our cohort. The cut-offs predicting a FENa \(<0.5\%\) differ according to age.

**Author Contributions**

SVB and DD contributed to the concept and the design of the study, the acquisition, the analysis and interpretation of the data. LP and MG contributed to the data analysis and interpretation. SVB and DD drafted the article. YW, HS, EVB, ES and SVd revised it critically for important intellectual content. All authors gave approval of version to be published.

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This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

None of the authors have a conflict of interest.
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Highlights

- Patients with cystic fibrosis are prone to electrolyte disturbances.
- Guidelines state to monitor sodium status.
- Sodium/creatinine ratio is an excellent surrogate marker for fractional sodium excretion.
- Cut-offs for sodium/creatinine ratio are age related.
Credit Author Statement

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SVB and DD contributed to the concept and the design of the study, the acquisition, the analysis and interpretation of the data. LP and MG contributed to the data analysis and interpretation. SVB and DD drafted the article. YW, HS, EVB, ES and SVd revised it critically for important intellectual content. All authors gave approval of version to be published.