Validation study of the Tanaka and Kawasaki equations to estimate the daily sodium excretion by a spot urine sample

Estudo de validação das equações de Tanaka e de Kawasaki para estimar a excreção diária de sódio através da coleta da urina casual

José Geraldo MillI, Sérgio Lamêgo RodriguesI, Marcelo Perim BaldoI, Deborah Carvalho MaltaII, Celia Landmann SzwarcwaldIII

ABSTRACT: Objective: To validate Tanaka and Kawasaki’s formulas to calculate the salt intake by the sodium/creatinine ratio in spot of urine. Methods: Two hundred and seventy two adults (20 – 69 years old; 52.6% women) with 24 h urine collection and two urinary spots collected on the same day (while fasting – spot 1 – or not fasting – spot 2). Anthropometry, blood pressure and fasting blood were measured on the same day. The analysis of agreement between salt consumption measured in the 24 h urine test and urinary spots were determined by the Pearson’s correlation (r) and the Bland & Altman method. Results: The mean salt consumption measured by the 24 h sodium excretion was 10.4 ± 5.3 g/day. The correlation between the measured 24 h sodium excretion and the estimation based on spots 1 and 2, respectively, was only moderated according to Tanaka (r = 0.51 and r = 0.55; p < 0.001) and to Kawasaki (r = 0.52 and r = 0.54; p < 0.001). We observed an increasing underestimation of salt consumption by Tanaka to increasing salt consumption and conversely, an overestimation of consumption by the Kawasaki formula. The estimation of salt consumption (difference between measured and calculated salt consumption lower than 1 g/day) was adequate only when the consumption was between 9 – 12 g/day (Tanaka) and 12 – 18 g/day (Kawasaki). Conclusion: Spot urine sampling is adequate to estimate salt consumption only among individuals with an actual consumption near the population mean.

Keywords: Sodium Chloride. Sodium. Urine. Sodium Chloride, Dietary.
INTRODUCTION

The prevalence of arterial hypertension (AH) in Brazil is high, around 25% among adults. Population studies show that the mean pressure level and the prevalence of AH are strongly influenced by the consumption of sodium. AH has been recognized as the factor that most contributes to cardiovascular morbidity and mortality around the world. As a consequence, the reduction in sodium consumption has been encouraged both to decrease cardiovascular morbidity and mortality and also to facilitate the treatment for AH. However, the control of sodium intake in the population is still precarious, because of the low reliability of some methods constantly used to estimate the sodium consumption through questionnaires and also the difficult of using the measurements of 24-hour urinary sodium excretion (NaUr-24h). To overcome these issues, some protocols have been made, such as urine collection in shorter periods and the estimation of sodium intake by measuring the sodium/creatinine ratio in casual urine. For that, equations were developed to estimate the 24-hour sodium excretion, and, consequently, the salt consumption. The accuracy of such an estimation depends on a precisely measurement of the 24-hour creatinine excretion based on weight and height. However, the daily creatinine excretion also depends on other variables, such as muscle mass and diet. So, studies to validate the equations in populations other than those in which they were developed are necessary. Therefore, the objective of this study was to assess the accuracy of the salt consumption estimation by applying the equations proposed by Tanaka et al. and Kawazaki et al. to parameters measured in a casual urine sample of adults collected in fasting and non fasting conditions.
METHODS

Three-hundred ninety six volunteers (living in Vitória, ES) were recruited from a random sample of households, raffled from 20 census sectors of the city. The households were visited for the inclusion of one volunteer (20 – 69 years old). The selection was based on quotas, with the goal of 50% for each gender and 20% per age decade. Individuals with acute diseases, in bed, with low mobility or difficulties of communication as well as pregnant or breast-feeding women were excluded. The project was approved by the Research Ethics Committee of the Center of Health Sciences at Universidade Federal do Espírito Santo (UFES, Protocol 201.110), and all participants signed the informed consent form.

Research assistants collected sociodemographic data in the household (sex, self-reported race/ethnicity, monthly income and schooling), practice of physical activities, use of medicines and life habits (smoking), and scheduled the day for urine collection. On the same day, clinical and laboratory examinations were programmed in the Clinical of Cardiovascular Investigation (CIC), at the University Hospital of UFES. The participants were advised not to interrupt the use of medications and to keep up with their dietary habits until the conclusion of the tests. The day before collection, they should fast after 8 p.m., not consume alcohol and not perform vigorous physical activities, as well as on the day of the collection. On this day, they should empty their bladder in the morning, when they woke up, and write down the time on the form, starting the 24-hour urine collection. Still fasting, they should go to CIC to undergo examinations and draw a blood sample.

CLINICAL AND LABORATORY EXAMINATIONS

When they arrived at CIC, the time of morning vesical emptying was checked, and participants were given a sterile bottle for the first collection in the 24-hour period. After that, the anthropometric (weight and height) and blood pressure (oscillometric method, Onrom 765CP, Japan) measurements were obtained. Tetrapolar bioimpedance (InBody 320, Korea) was also performed to obtain lean mass and body fat. Three blood pressure and heart rate measurements were taken (one minute interval between measurements), in the seated position and after a five-minute rest. Still fasting, blood sample was drawn to establish biochemical parameters.

24-HOUR URINE COLLECTION

After urination, participants were advised to collect urine, initially, in a plastic cup (0.7 L), and then transfer the content to the storage bottle (2 L), and keep it in the refrigerator. From the first collection taken while fasting, a 5 mL aliquot was obtained (casual urine 1). Each participant was taught how to continue collecting urine, always using the same procedure, and to make
the last collection on the next day, 24 hours after the vesical emptying from the morning before. A second 5 mL sample was required to be collected in the afternoon (casual urine 2), using the same procedure of the previous casual collection. For that, they received the necessary material (cup, disposable Pasteur pipette and Falcon tube, previously labeled). The training for sample aliquoting with water was carried out at CIC by an instructor. The time of the last collection should be written down on the form, and the 24-hour urine and the tube containing the casual urine 2 were collected in the household by a research assistant, after checking for possible losses. Valid 24-hour collections were those with no report of urine loss and with collection time between 23 and 25 hours. Volume was measured in beaker (precision of 10 mL) and adjusted for 24 hours. 24-hour and casual 1 and 2 urine aliquots were stored at -80°C until they were sent to a central laboratory to determine sodium and potassium (selective electrode) and creatinine concentrations (Jaffé method). Urinary volumes < 500 mL in 24 hours were not considered, as well as those presenting creatinine excretion corrected for body weight outside the intervals of 14.4 – 33.6 mg/kg for men and 10.8 – 25.2 mg/kg for women. Out of the 396 individuals recruited from the households, 330 underwent the 24-hour collection and 272 had a validated collection. The non-validation occurred for report of loss (n = 8), volume < 500 mL (n = 4), collection > 25 h (n = 2) or creatinine outside the established interval (n = 44).

PREDICTIVE EQUATIONS FOR 24-HOUR CREATININE AND SODIUM EXCRETION

Tanaka et al. estimated the 24-hour creatinine excretion (CrPr-24h) based on age, weight and height, using the same equation for both genders. Kawasaki et al. developed gender-specific equations. After establishing the CrPr-24h and the sodium/creatinine ratio in casual urine (Na/CrUr), it is possible to estimate the total sodium content in the 24-hour urine (Na-24h).

TANAKA METHOD

\[
\text{CrPr}_{24h} \text{ (mg)} = [(14.89 \times \text{weight, kg}) + (16.14 \times \text{height, cm}) (2.04 \times \text{age, years})] – 2,244.45
\]

\[
\text{NaUr} \text{ (mEq)} = \left[\frac{\text{Na casual urine, mEq/L} \times (\text{Cr casual urine, mg/dL} \times 10)}{10}\right] \times \text{CrPr}_{24h} \text{ (mg)}
\]

Estimation of Na_{24h} (mEq) excretion = 21.98 x NaUr^{0.392}

KAWASAKI METHOD

Men

\[
\text{CrPr}_{24h} \text{ (mg)} = [(15.12 \times \text{weight, kg}) + (7.39 \times \text{height, cm}) (12.63 \times \text{age, years})] – 79.9
\]
Women

CrPr24h (mg) = [(8.58 x weight, kg) + (5.09 x height, cm) (4.72 x age, years) – 74.95

NaUr (mEq) = [Na casual urine (mEq/L)/(Cr casual urine mg/dL X 10)] x CrPr24h (mg)

Estimation of Na24h (mEq) excretion = 16.3 X (√[(NaUr) x (CrPr24h)]

The daily intake of salt was calculated from the sodium excretion in 24-uring, considering that the sodium came from only NaCl intake.

STATISTICAL ANALYSIS

The data are described as mean, standard deviation (SD) and median for continuous variables or as proportions and percentages. The adjustment to normal distribution was assessed by the Kolmogorov-Smirnov test. The comparison of two means was made with the Student’s t-test (normal data) or by the Mann-Whitney test (asymmetric distributions). Proportions were compared by χ². The comparison of creatinine medians excreted in 24-hour urine and that predicted by the equations was analyzed by one-way ANOVA with the post-hoc Tukey. The associations between sodium, salt and creatinine excretions measured and estimated by the formulas were determined by Pearson or Spearman correlation coefficient, when necessary. The analysis of agreement between 24-hour urine sodium and the value estimated by the formulas applied to casual urine 1 and 2 was assessed by the Bland and Altman method. The percentage of error in the estimation of salt excretion was calculated using the formula: Error (%) = 1.96 x [(SD (24h measured Na – estimated Na) / mean of 24-hour measured Na)] X 100. Accuracy was considered to be acceptable when the difference between the measured and estimated salt consumption was lower than 1 g/day. The statistical analysis was made with SPSS 13.0 (Chicago, IL, USA), and statistical significance was established in p < 0.05.

RESULTS

Data from 272 adults (129 men), with mean age of 44 ± 14 years old, with no difference (p > 0.05) between genders and balance between age groups were analyzed. In the sample, there was 23.5% of obese (BMI ≥ 30 kg/m²), 31.2% of hypertensive and 7.0% of diabetic participants. The creatinine excreted in 24 hours was higher (p < 0.05) among men (1,617 ± 343 mg versus 1,094 ± 267 mg). The Tanaka and Kawasaki formulas tend to overestimate the creatinine excretion, especially when the Kawasaki formula is used in men. In women, the Kawasaki formula showed more accuracy.
Table 1 shows the sodium excretion measured in the 24 h urine and that estimated by the formulas. The Kawasaki formula overestimates sodium excretion and salt consumption in men and women when using casual urine 1 and 2. The Tanaka formula underestimates the consumption among men and establishes a small overestimation among women. The errors between the measured and estimated values tend to be higher with data from casual urine 2, except for men using the Tanaka formula.

Figure 1 shows the correlation between the creatinine excreted in the 24 hours and that predicted by both formulas. It is possible to observe (upper panels) good correlation ($r \geq$...
0.70) with both formulas. The correlation, however, was strongly influenced by the inclusion of men and women on the same plot, which is questionable due to the lower muscle mass in women. Bland and Altman diagrams (lower panels) indicate agreement in the acceptance limits (95 and 95% of individuals within limits ± 1.96 SD; respectively). The Tanaka formula, however, is slightly more accurate due to the difference between means is lower (measured and estimated), and fewer individuals were outside the agreement limits. It is important to observe that most individuals outside the agreement limits are men. Besides, it is also possible to see the occurrence of estimation bias regarding the creatinine predicted for women in the Kawasaki formula.

Figure 2 presents the correlation plots between the sodium measured in the 24-hour urine and that estimated by casual urine 1 and 2. Correlations were moderate (r between 0.51 and 0.55). The Tanaka formula underestimates the sodium in individuals with higher excretion within 24 hours, regardless of casual urine. On the other hand, the Kawasaki

![Figure A](image1.png)  
**Figure 1.** Analysis of correlation (A and B) and agreement (C and D) between creatinine excreted in 24-hour urine and predicted by the Tanaka and Kawasaki formulas. The regression lines were calculated by the least squares method.

r: Pearson’s correlation coefficient; SD: standard deviation
formula tends to overestimate the sodium regarding urine with lower sodium excretion in both collected samples. Figure 3 presents the Bland and Altman diagrams to assess the agreement between the methods estimating the sodium excretion. It is possible to observe that, even though the Tanaka formula has a lower difference between means, especially in casual urine 2, there is estimation bias, with increasing underestimation of excretion values when the intake of this nutrient increases. The Kawasaki formula has the higher difference between means, and the value estimated by the formula is about 50 mEq/day higher than the measured value (corresponding to an estimation error of about 3 g of salt a day).

Figure 4 shows the difference between the measured salt (24-hour urine) and that estimated by the formulas applied to casual urine 1 and 2 as a function of the daily intake of salt measured in the 24-hour urine. It is observed that the Tanaka formula estimates, with accuracy of 1 g of salt/day, only those individuals with salt intake between 9 and 12 g/day. The Tanaka formula tends to overestimate categories with lower intake and to underestimate categories with higher intake.

Figure 2. Analysis of correlation between 24-hour measured urine sodium and that estimated by the Tanaka and Kawasaki formulas applied to the parameters measured in casual urine 1 and 2. The regression lines were calculated by the least squares method.
The Kawasaki formula properly estimates the salt intake between 12 and 18 g/day by casual 1, and tends to overestimate the intake in categories with low salt consumption.

DISCUSSION

The 24-hour urine collection has been used as gold-standard to estimate the sodium consumption among individuals and populations. However, it is difficult to conduct this procedure considering the need to collect outside the household, sometimes in work places. Therefore, there have been efforts to standardize more practical methods of collection. The accuracy of these methods, however, has been questioned, and that is why it is necessary to conduct validation studies in different populations than that they were developed. The accuracy of the estimation of sodium excretion in casual urine mostly depends on the estimated accuracy of the 24-hour creatinine excretion, based on gender, weight and height.

Figure 3. Analysis of agreement (Bland and Altman) between 24-hour measured urine sodium and that estimated with the Tanaka and Kawasaki formulas applied to the parameters measured in casual urine 1 and 2.

SD: standard deviation
Figure 4. Differences between the salt measured in 24 h and the salt estimated by the Tanaka and Kawasaki formulas based on data obtained in casual urine 1 and 2, related to the categories of salt consumption.

However, diet and lean mass also influence this parameter\textsuperscript{15,16}, so it is important to validate these formulas in our population.

The sample used can be considered to be representative of the adult population in Vitória based in other studies\textsuperscript{26-28}. The initial loss (n = 66) happened because the 24-hour urine collection was not conducted properly. Among those who collected the urine (n = 330), there was a rigorous verification of the time of beginning and end of collection, using strict criteria to consider the collection as “valid”. The criterion that led to most losses was creatinine excreted per kilo of body weight\textsuperscript{16,17}. Calculations were based on 272 adults, with distribution balanced by gender and age group. Despite being sufficient for agreement studies, it was insufficient to analyze subgroups. One differential of this study was to include two samples of casual urine to verify if the time of collection would influence the agreement and the accuracy.

One of the factors that mostly contribute with the inaccuracy of the formulas is the estimation of 24-hour creatinine excretion\textsuperscript{12,14}. We observed that, despite the strong correlation between the measured and estimated excretion, the analysis of agreement shows a mean difference between estimated and measurement values of almost 100 mg/24 h, that is, error close to 8%. Therefore, it is possible to expect such minimum error in the estimation of
sodium excretion and salt consumption. Based on this fact, we inferred it is not possible to estimate the sodium consumption using these formulas with errors lower than 10%, which would be equal to 1 g of salt a day. Another fact was the presence of systematic error when estimating creatinine excretion among women using the Kawasaki formula. Therefore, the data suggest that the Tanaka formula would have better performance to estimate the 24-hour creatinine excretion in our population. So, it would be important to create specific formulas for our population, possibly based on the lean mass, to reduce the bias resulting from obesity. The increasing mean BMI in the Brazilian population in the past decades is inaccurate in this area.

Our data showed that the salt consumption estimated by the gold-standard is higher in comparison to other populations, being higher than twice the current recommendation of 5 g of salt a day. The impact of salt consumption on blood pressure of the study participants was described in another publication. It is possible to observe that the current consumption seems to be decreasing in relation to previous studies conducted in the same population of Vitória. However, this finding should be carefully analyzed, because the method for urine collection was different in previous studies. It is worth to mention that the subgroups that mostly benefitted from the reduction in salt consumption, such as hypertensive people, still consume much more than the recommended amount.

Similarly to what was observed in other studies, we observed moderate correlation between the salt intake estimated by casual urine and the consumption measured in 24 hours. Many authors have accepted the use of such formulas just based on correlation analyses. However, high correlation coefficients can be obtained just by the existence of subgroups (clusters), aligned around a tendency, as it is clear when we analyze the correlation between the creatinine predicted and measured in Tanaka and Kawasaki formulas (Figure 1). The high correlations (r > 0.7) are owed to the fact that women excrete less creatinine than men, and that these two groups are aligned throughout a single tendency. If the correlation analysis was made separately, by gender, the coefficients would be much lower (r < 0.4), or, in a worse scenario, with different angles as observed by using Kawasaki formula (Figure 1B). So, the reliability of these formulas requires an analysis of agreement between both methods, which was obtained by the Bland and Altman method. This analysis showed limited validity of casual urine to estimate the 24-hour sodium excretion, once the agreement between methods and the percentage of error (about 70% between measured and estimated values in some individuals) is high. Both formulas, however, have good accuracy to determine the mean consumption of the sample. The errors found around the mean underestimated the intake of men (about 15%) and, in general, overestimate the intake of women (from 5 to 10%). Therefore, it is possible to see that the accuracy of the mean consumption of a population depends on the compensation of errors regarding estimations involving men and women. Our data show that the accuracy of the mean also depends on the balance between genders in the group, so the error is higher if we calculate the mean for a specific subgroup.
Another bias observed in our study results from the final formulas used in the calculation of total sodium excretion in 24 hours. The use of potency lower than 1 (0.392 in the Tanaka formula and 0.5 in the Kawasaki formula) reduces the consumption extremes, going towards the group average. The wanted effect is exactly that of improving the accuracy of the estimation regarding the mean consumption of the studied population. However, it makes it more difficult to conduct a subgroup analysis, and completely distorts the estimation of individual consumption, as observed in Figure 4. Since the mean salt intake was about 10 g/day, and given the great variability of this item in the diet, we considered the error of up to 1 g a day to be tolerable. If this parameter is used, the Tanaka formula would only be adequate to estimate the intake of salt in individuals consuming between 9 to 12 g/day. With the Kawasaki formula, the same accuracy will only be reached for individuals with intake ranging from 12 to 18 g/day. This conclusion is in agreement with recent reviews, but different from other studies that considered the estimations of salt consumption based on casual urine to be adequate for epidemiological analyses or for follow-up of individual consumption. The acceptance of methods, however, was based on analyses of agreement. The introduction of a potency that reduces consumption extremes was mentioned by Tanaka et al., in their initial study, highlighting the inadequacy of the method for estimations of individual consumption. High correlation coefficients are not sufficient to show the equivalence between methods.

Our study has strong aspects and limitations. The strong items are the data from the general population and the methodological rigor to determine the time of urine collection for 24 hours. Besides, it was possible to compare the performance of formulas in two casual urine collections. Finally, we used robust tests of validation. Our greatest limitation is that we have an insufficient sample to analyze subgroups, and the fact that it is not possible to assess sodium loss by swearing, which is an important factor in a tropical country.

CONCLUSION

Considering the data and the limitations, it is possible to conclude that the application of the Tanaka formula with parameters measured in the casual urine collected outside the fasting period would lead to lower error to estimate the daily sodium excretion and salt consumption in our population. The 1 g/day precision, however, is only reached for a narrow consumption group, around the population mean.

ACKNOWLEDGMENTS

We would like to thank all the participants in this research and Laboratório Tommasi, in charge of making the biochemical blood tests. The study was conducted with resources from the Department of Health Surveillance, Ministry of Health.
REFERENCES


