The correlation between age and sweat chloride levels in sweat tests

Dear Editor,

Although the sweat test (ST) is considered the gold standard for the diagnosis of cystic fibrosis (CF), it still remains the center of great interest as well as debate over its execution and interpretation.[1]

We read carefully the important article by Traeger and colleagues.[2] The study showed that in 13,775 ST [313 (2.3%) patients with CF], sweat chloride concentrations decrease in the first year of life, increase in the second year until the age of 18, and decrease slowly after age 18.

We assessed 5196 ST [671 (12.91%) patients with CF] in our university referral center. Unlike the study conducted by Traeger and colleagues, we assessed chloride levels by age, considering the reference values for the ST[3,4] (Fig. 1).

The sweat was collected following Gibson and Cooke's traditional method (1959) and the sweat chloride concentration was determined by chloridometry and the sweat sodium concentration by flame photometry. The sweat chloride levels were used to group the samples according to the CF diagnosis: (i) chloride < 30 mEq/L; (ii) chloride ≥ 30 mEq/L to <40 mEq/L; (iii) chloride ≥ 40 mEq/L to <60 mEq/L; (iv) chloride ≥ 60 mEq/L (group of patients with CF). The ST data was obtained from the medical records of the Pediatric Gastroenterology Laboratory and the Gastroenterology Center at the University Hospital.

The patients were divided into three age groups: (i) from birth to <six months; (ii) ≥six months to <18 years; (iii) ≥18 years.

Statistical analysis was carried out with linear regression test and Spearman's rank correlation test by the MedCalc software version 16.4.3. Significance level was set at 0.05 for all analyses. The power of the sample was greater than 80%.

The study was approved by the Ethics Committee of the University of Campinas (#474326).

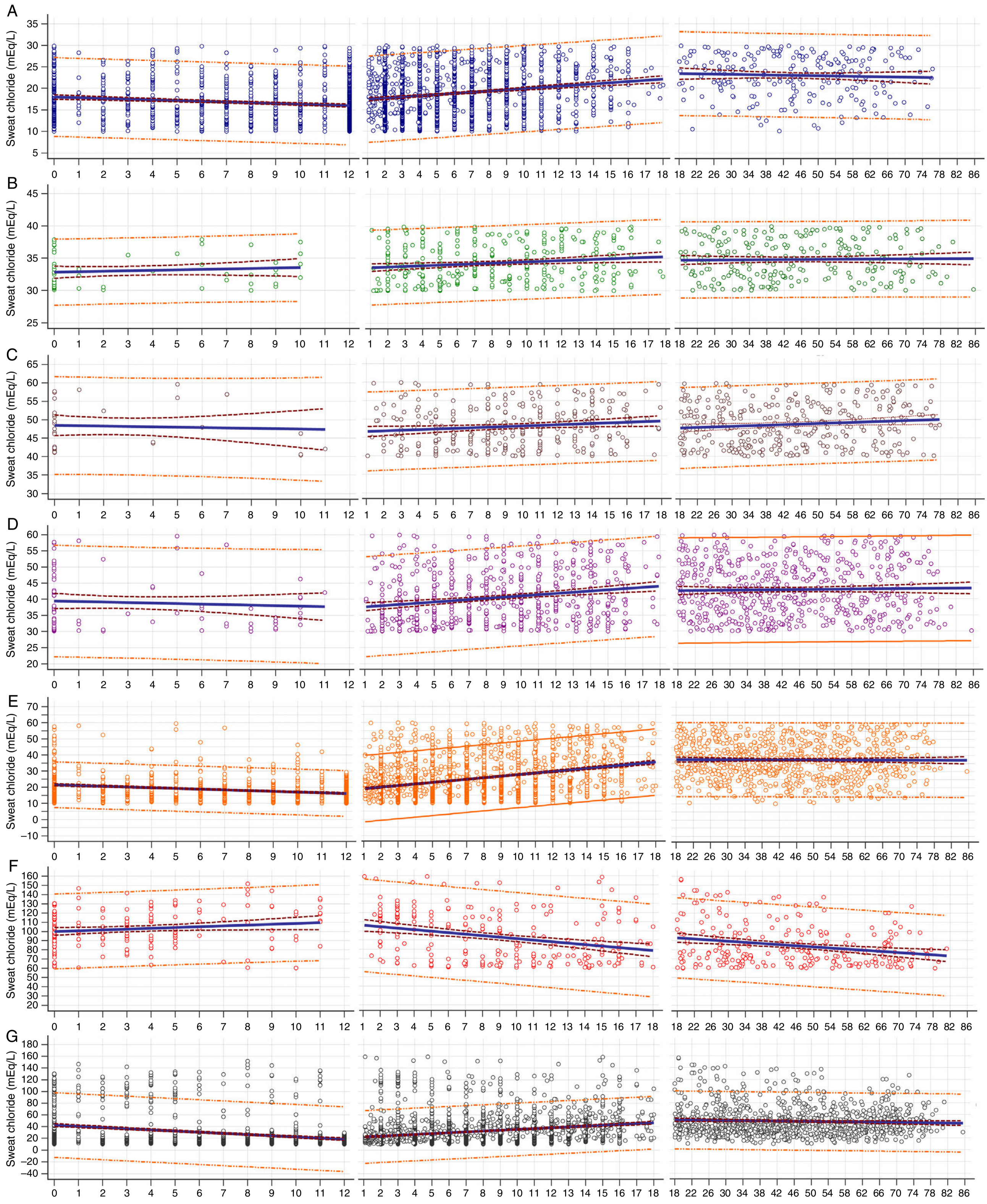
As observed in Fig. 1G, the results from our total population agree with those reported by Traeguer and colleagues.[2] The same correlation was observed for the groups of sweat chloride levels in mEq/L: (i) chloride < 30 mEq/L; (ii) chloride ≥ 30 mEq/L to <40 mEq/L; (iii) chloride ≥ 40 mEq/L to <60 mEq/L; (iv) chloride ≥ 30 mEq/L to <60 mEq/L; (v) chloride < 60 mEq/L (Fig. 1A–E).

In contrast, as shown in Fig. 1F, CF patients show increased sweat chloride levels in the first year of life. These levels gradually reduced after the second year or life. This was not evidenced by Traeguer and colleagues,[2] possibly due to the effect of sample dispersion of CF patients within the total sample.

It is important to note that sweat chloride levels tend to be lower among adults compared to children. Another important factor is the evidence that sweat chloride levels have intra- and inter-individual variability, even in patients with the same genotype in the Cystic Fibrosis Transmembrane Regulator (*CFTR*) gene.[5]

Such alterations should be further studied by measuring amounts of sweat chloride in CF patients and healthy individuals on a long-term basis.

One hypothesis that may explain decreased amounts of sweat chloride in sweat with increasing age is related to changes in the stability of the CFTR protein in healthy individuals and CF patients with borderline sweat chloride levels. On the other hand, for all subjects, reduced sweat chloride levels after 18 years of age may be a consequence of the aging process. Aging is a natural response, which causes physiological changes, including alterations in other chloride regulating channels and the action of modifier genes.


A
B
C
D
E
F
G
Sweat chloride (mEq/L)
Months
Years
Years

Therefore, studies should also be made on the factors that interfere with sweat chloride levels in different ages among healthy individuals and CF patients.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of University of Campinas (#474326).

Authors' contributions

AGF, FALM, JDR made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; were involved in drafting the manuscript and revising it critically for important intellectual content; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work by ensuring that questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

AFR made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data.

Conflicts of interest

All the authors declare that they have no conflicts of interest.

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Figure 1 Correlation between levels of sweat chloride and age of subjects undertaking sweat tests, considering possibilities of groups by chloride concentrations. (A) Chloride < 30 mEq/L: (age: $\leq$12 months) $N = 1178$; Spearman's coefficient rank correlation (rho) = -0.159, 95%CI = -0.214 to -0.103; $p < 0.001$. Coefficient of determination $R^2 = 0.025$; $y = 17.9905 + (-)0.1643x$; $p < 0.001$. (Age: >1 year to $\leq$18 years) $N = 1827$; rho = 0.192, 95%CI = 0.148–0.236; $p < 0.001$. $R^2 = 0.039$; $y = 17.1432 + 0.2749x$; $p < 0.001$. (Age: >18 years) $N = 230$; rho = -0.048, 95%CI = -0.176 to 0.082; $p = 0.469$. $R^2 = 0.002$; $y = 23.7087 + (-)0.01622x$; $p = 0.538$. (B) Chloride $\geq$ 30 mEq/L to <40 mEq/L: (age: $\leq$12 months) $N = 52$; rho = 0.097, 95%CI = -0.181 to 0.360; $p = 0.495$. $R^2 = 0.013$; $y = 32.8243 + 0.07205x$; $p = 0.427$. (Age: >1 year to $\leq$18 years) $N = 340$; rho = 0.151, 95%CI = 0.045–0.253; $p = 0.005$. $R^2 = 0.021$; $y = 33.4949 + 0.09905x$; $p = 0.007$. (Age: >18 years) $N = 244$; rho = 0.026, 95%CI = -0.100 to 0.151; $p = 0.692$. $R^2 < 0.001$; $y = 34.6330 + 0.003532x$; $p = 0.758$. (C) Chloride $\geq$ 40 mEq/L to <60 mEq/L: (Age: $\leq$12 months) $N = 33$; rho = 0.025, 95%CI = -0.321 to 0.365; $p = 0.892$. $R^2 < 0.001$; $y = 48.4653 + (-)0.09778x$; $p = 0.748$. (Age: >1 year to $\leq$18 years) $N = 278$; rho = 0.134, 95%CI = 0.016–0.248; $p = 0.026$. $R^2 = 0.018$; $y = 46.4328 + 0.1699x$; $p = 0.026$. (Age: >18 years) $N = 343$; rho = 0.117, 95%CI = 0.011–0.220; $p = 0.031$. $R^2 = 0.014$; $y = 46.9588 + 0.03910x$; $p = 0.031$. (D) Chloride $\geq$ 30 mEq/L to <60 mEq/L: (Age: $\leq$12 months) $N = 85$; rho = -0.049, 95%CI = -0.259 to 0.166; $p = 0.656$. $R^2 = 0.005$; $y = 39.4291 + (-)0.1577x$; $p = 0.5224$. (Age: >1 year to $\leq$18 years) $N = 618$; rho = 0.210, 95%CI = 0.134–0.285; $p < 0.001$. $R^2 = 0.042$; $y = 37.2303 + 0.3772x$; $p < 0.001$. (Age: >18 years) $N = 587$; rho = 0.017, 95%CI = -0.064 to 0.098; $p = 0.678$. $R^2 < 0.001$; $y = 42.3785 + 0.01182x$; $p = 0.565$. (E) Chloride < 60 mEq/L: (Age: $\leq$12 months) $N = 1263$; rho = -0.246, 95%CI = -0.297 to -0.193; $p < 0.001$. $R^2 = 0.078$; $y = 21.5579 + (-)0.4503x$; $p < 0.001$. (Age: >1 year to $\leq$18 years) $N = 2445$; rho = 0.336, 95%CI = 0.300–0.370; $p < 0.001$. $R^2 = 0.127$; $y = 17.9823 + 0.968.9x$; $p < 0.001$. (Age: >18 years) $N = 817$; rho = -0.01, 95%CI = -0.078 to 0.0586; $p = 0.775$. $R^2 < 0.001$; $y = 37.6153 + (-)0.007263x$; $p = 0.776$. (F) Chloride $\geq$ 60 mEq/L: (Age: $\leq$12 months) $N = 179$; rho = 0.134, 95%CI = -0.013 to 0.275; $p = 0.073$. $R^2 = 0.021$; $y = 99.9960 + 0.8686x$; $p = 0.058$. (Age: >1 year to $\leq$18 years) $N = 238$; rho = -0.287, 95%CI = -0.400 to -0.166; $p < 0.001$. $R^2 = 0.085$; $y = 107.6871 + (-)1.6094x$; $p < 0.001$. (Age: >18 years) $N = 254$; rho = -0.190, 95%CI = -0.306 to -0.068; $p = 0.002$. $R^2 = 0.056$; $y = 98.6663 + (-)0.3083x$; $p < 0.001$. (G) All samples: (Age: $\leq$12 months) $N = 1442$; rho = -0.352, 95%CI = -0.396 to -0.306; $p < 0.001$. $R^2 = 0.1032$; $y = 42.6550 + (-)2.0145x$; $p < 0.001$. (Age: >1 year to $\leq$18 years) $N = 2683$; rho = 0.348, 95%CI = 0.315–0.381; $p < 0.001$. $R^2 = 0.066$; $y = 20.8087 + 1.4323x$; $p < 0.001$. (Age: >18 years) $N = 1071$; rho = -0.052, 95%CI = -0.111 to 0.008; $p = 0.09$. $R^2 = 0.003$; $y = 52.1251 + (-)0.07962x$; $p = 0.090$. $\alpha = 0.05$. Statistical analysis was made with linear regression test and Spearman's rank correlation test.

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Survival analysis of patients with non-small cell lung cancer treated by surgery with curative intent

Dear Editor,

Lung cancer is the leading cause of cancer deaths in the entire world, representing 19.4%–27% of all deaths from cancer.[1] Surgical resection is considered the treatment standard for early stage disease (stage I and II) and for some cases in IIIA stage.[1] Accordingly to the TNM system, 5-years survival for IA, IB, IIA, IIB, IIIA, IIIB and IV stage disease, is about 73%, 58%, 46%, 36%, 24%, 9% and 13% respectively.[2]

The purpose of this study is to describe a population of patients submitted to curative intent surgery for lung cancer and analyze the survival.

Data was collected retrospectively from the clinical process of patients with NSCLC who had indergone pulmonary resection surgery with curative intent who were being followed at the Pneumological Oncology Service of a University Hospital. Patients who had not had lymphadenectomy were excluded.

After initial treatment was completed, patients were followed every 3 months with a complete physical examination, blood analyses and chest X-ray for 5 years, every 6 months with computed tomography (CT) for 2 years and then annually.

A descriptive analysis of the variables of 102 patients undergoing pulmonary resection surgery was carried out. This included patients who were operated on between 1 January 2008 and 31 December 2012 and were followed until 31 December 2015.

The comparison of the distribution of variables was made using adjustment tests (Binomial and Chi-square). Kaplan–Meier survival analysis was used to determine mean survival time and mortality rate according to the disease stage and comparison of these by log-rank test. The association between pathologic stage and survival was assessed using Fisher's exact test. The analysis was performed in the SPSS, version 23, and the statistical tests analyzed at the significance level of 5%.

The study was conducted with a group of 102 patients with an average age of 63.69 ± 9.31; 68.6% were men. The distribution of tumor location is preferentially peripheral (72.5%), appearing in the lobar bronchus (15.7%) or main bronchus (11.8%) with less frequency ($p < 0.001$). Most of the patients had Adenocarcinomas (61.8%) or squamous tumors (26.5%). Most of the surgeries performed were lobectomies (81.4%), followed by pneumonectomy (14.7%), wedge excision (2.9%) and segmentectomy (1%). 26.5% cases were in pathological stage IA, 24.5% in IB, 21.6% in IIA, 9.8% in IIB and 17.6% in IIIA ($p = 0.064$).

Of the 102 cases analyzed, 41 died during the study period (40.2%). The estimated mortality rate in the population should be between 30.7% and 47.7%. The median overall survival time was 65.61 ± 3.56 months and the 5-year survival (60 months) was 46.20 ± 1.93 months. There was a statistically significant difference in mean survival time depending on the disease stage ($p < 0.001$) [Fig. 1]. The tendency is that patients with stage IA have a better prognosis, with a statistically significant difference between this and any of the other stages. Table 1 presents the mean survival time observed at the 5-year follow-up, and the respective estimated mean survival time in the population, in relation to the disease stage. In the legend, the *p*-values adjusted for multiple comparisons of the survival time between pairs of stages evaluated are presented.