ally reported. In a recent systematic review of inhalers' critical errors, 11 out of 21 studies exploring the relationship between previous inhaler instructions and frequency of inhaler errors found a positive association between previous instructions and a better inhaler technique.[8] In the present study, some improvement in inhalation technique was achieved after a single education intervention in all types of IDs, with statistical significance in the group of inhalers with an easy feed-back to the patient that a significant amount of medication had been inhaled. It appears that these devices attributes, by improving patient confidence in their use, improve the maintenance of a correct inhaler technique. We found a significant positive association between symptoms and improvement of the inhaler technique. We hypothesized that more symptomatic patients can be more motivated to learn how to use inhalers properly. We also found that male patients who improve their inhalation technique seem to greater belief in need for medication than women. Probably men, but not women, have to believe in the need of medication to improve their learning of correct inhalation techniques. This information is new and needs to be confirmed by other studies.

Author contributions

Duarte-de-Araújo conceived and developed the study, carried out the collection of data and data interpretation, wrote the first draft and collaborated in the final text. Pedro Teixeira carried out the statistical analysis, contributed to the section on methods and results, and collaborated in the final writing. Venceslau Hespanhol reviewed the final draft. Jaime Correia-de-Sousa reviewed all the drafts and collaborated in the final writing. All the authors approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Should tobacco interventions be different in men and women?

Men and women differ in their smoking behaviour: women smoke fewer cigarettes per day, their consumption is more related to sensory effects, mood and negative emotions, they start smoking later with a lower cumulative consumption and tend to use cigarettes with lower nicotine content, show lower dependency scores than men, become dependent earlier and have greater difficulty quitting smoking experiencing more severe nicotine withdrawal symtoms.[1]

We conducted an observational, multicenter study of consecutive patients who attended several smoking clinics to stop smoking between October 2014 and October 2015. We wanted to know if there were differences between men and women in terms of tobacco consumption. To investigate this we included qualitative variables (questionnaires to measure motivation to quit and nicotine dependence) and quantitative variables (age, tobacco consumption, num-

Table 1 Mean values of the quantitative variables for the global series and by sex, and comparison between men and women.

Variable	Global series mean (SD)	Sex		p^a
		Males mean (SD)	Woman mean (SD)	
Age	51.3 (10.8)	51.8 (10.9)	50.9 (10.8)	0.227
Cigarettes per day	23.1 (10.5)	24.8 (11.4)	21.5 (9.3)	0.006
Number of years smoking	34.8 (10.8)	35.5 (11.1)	34.2 (10.6)	0.314
Packs-years	41.0 (24.3)	45.1 (26.4)	37.3 (21.7)	0.007
Number of previous quit attempts	1.7 (1.6)	1.7 (1.7)	1.7 (1.5)	0.897
Number of previous quit attempts in the last year	0.2 (0.6)	0.3 (0.7)	0.2 (0.5)	0.272
Richmond test	7.9 (1.6)	7.9 (1.6)	7.8 (1.6)	0.706
Henri Mondor Hospital motivacional test	13.1 (2.8)	13.2 (2.9)	13.0 (2.7)	0.589
Khimji–Watts test	11.3 (2.6)	11.4 (2.6)	11.3 (2.7)	0.836
Motivation visual analogue scale	7.9 (2.0)	8.0 (2.0)	7.8 (2.1)	0.22
Fagerström test	6.1 (2.1)	6.1 (2.3)	6.1 (2.1)	0.986

SD: standard deviation.
[a] *p*: degree of significance of the comparison of means between men and women.
The *t*-Student test or the Welch test for the comparison of mean values, or, if a normal distribution was not reached, the *U*-Mann–Whitney test was used. The assumption of homogeneity of the variances was proven by the Levene test. An $\alpha < 0.05$ value was considered as statistically significant.

Table 2 Frequency distribution of qualitative variables for the global series and by sex, and comparison between men and women.

Variable	Global series AV (%)	Sex		p^a
		Males AV (%)	Woman AV (%)	
Fagerström test				
Low dependence (≤3)	2 (0.6)	1 (0.7)	1 (0.6)	
Moderate dependence (4–7)	124 (39.7)	58 (38.4)	66 (41–0)	
High dependence (>7)	186 (59.6)	92 (60.9)	94 (58.4)	0.897
Richmond test				
Low motivation (≤4)	8 (2.6)	4 (2.6)	4 (2.5)	
Medium motivation (5–6)	50 (16.0)	20 (13.2)	30 (18.6)	
High motivation (≥7)	254 (81.4)	127 (84.1)	127 (78.9)	0.431
Henri Mondor Hospital motivacional test				
It's the moment? (≤6)	6 (2.1)	2 (1.4)	4 (2.6)	
Real opportunities but difficult to take into account (7–12)	105 (36)	52 (37.1)	53 (34.9)	
Enough possibilities (13–15)	121 (41.4)	50 (35.7)	71 (46.7)	
Many possibilities (≥16)	60 (20.5)	36 (25.7)	24 (15.8)	0.101
Khimji–Watts test				
Weak motivationl (3–6)	7 (2.2)	2 (1.3)	5 (3.1)	
Medium motivation (7–11)	178 (56.9)	86 (57)	92 (56.8)	
Strong motivation (12–15)	128 (40.9)	63 (41.7)	65 (40.1)	0.567

In the boxes of the column ''Global series'' the absolute value is indicated and between () the percentage. In the columns ''Males'' and ''Females'' it is indicated in this order: absolute value; () indicates the percentage within the sex, that is, read the table by columns.
[a] *p*: degree of significance of the comparison of means between men and women.
The *t*-Student test or the Welch test for the comparison of mean values, or, if a normal distribution was not reached, the *U*-Mann–Whitney test was used. The assumption of homogeneity of the variances was proven by the Levene test. An $\alpha < 0.05$ value was considered as statistically significant.

ber of years smoking, cumulative consumption, previous attempts to quit, number of attempts in the last year, and motivation to quit and nicotine dependence questionnaires). The statistical analysis was descriptive. A <0.05 value was considered as statistically significant. The study was authorized by the different ethics committees of the participating hospitals.

We included 314 patients [162 women, (51.59%)]. Table 1 shows the average values of the quantitative variables and Table 2 the percentage values of the qualitative variables. We found statistically significant differences between men and women in the amount of cigarettes consumption per day and in the ''cumulative consumption of tobacco'' variable. Men smoked on average 3.3 cigarettes/day more than

women (95% CI: 0.9–5.6 cigarettes/day, $p = 0.006$), and the cumulative consumption of men was higher than women by 7.8 pack-years (95% CI: 2.1–13.5 pack-years, $p = 0.007$). We did not find any significant differences between sexes in the rest of the variables analyzed,

We did not find any differences between men and women in terms of the degree of nicotine dependence or motivation to stop smoking, which has already been written about by other authors.[2] We are aware that although our sample included 314 smokers, it may not have sufficient statistical strength to identify differences between sexes, which is a possible limitation of our study. Other possible limitations would be that the findings were collected from smokers, who voluntarily attended smoking cessation clinics, and the survey was carried out in different scenarios and geographical locations which might not reflect what would happen if the tests had been administered to the general population. Another limitation could be related to the use of questionnaires in patients because results obtained are not always accurate. This variability could lead to different results.

Differences between men and women have been previously reported suggesting women are less likely to show nicotine dependence than men.[1] The behaviour of woman who smoke is influenced to a greater extent by conditioning factors related to mood and negative emotions, while for men it is more related to pharmacological signals regulated by nicotine consumption. It is worth noting that women metabolize nicotine more quickly than men and have a higher prevalence to depression, which may be related to a greater addiction. In addition, women present a more severe and different withdrawal symptoms than men[1] which makes it more difficult for them to quit smoking. Although women make the same number of attempts to quit smoking as men, they are less likely to maintain abstinence. All of the above suggests that although women's dependence on tobacco is lower, there may be other factors that make quitting more difficult.[1] Komiyama et al.[2] in a study intended to examine the interactions of factors related to tobacco consumption, found that men smoked more cigarettes per day, with a greater cumulative consumption of tobacco and had a longer time of tobacco consumption than women, but they did not find differences between men and women regarding nicotine dependence assessed by the Fagerström Nicotine Questionnaire. Women did show a higher tendency to depression and only here was a high dependency value correlated with a greater depression scale, findings that could reflect existing differences in response to psychological stress.

Gender differences have been demonstrated in terms of reinforcement and reward for nicotine, reflecting dissimilarities in dopaminergic neurotransmission regulation. It has been demonstrated that the availability as a binding potential of dopamine receptors (D2-type) is lower in the caudate nucleus and putamen of male smokers compared to non-smokers, however, this was not observed in women,[3] who responded by releasing dopamine consistently in the ventral striatum and faster than men in the dorsal putamen.[4] Okita et al.[5] found gender differences in how dopamine receptors in the midbrain influence nicotine dependence, which may explain why women would benefit less from nicotine replacement therapy, because the release of dopamine would be limited by the high density in the middle brain of D2 dopamine receptors.

Curry et al.[6] evaluated a model of both intrinsic motivation (related to health, self-control) and extrinsic motivation (immediate reinforcement and social influence) to stop smoking, and found that motivation in woman was related to immediate reinforcement which could explain their greater difficulty in quitting, because according to this model those smokers with high levels of intrinsic motivation would have better chances of stopping smoking than those with greater extrinsic motivation. The consumption of tobacco in women express higher levels of negative expectancy smoking reinforcement,[7] which indicates that reduction in negative emotions could constitute an important motivational factor that governs the consumption of tobacco in women, so treatment for women should focus more on cognitive-behavioural techniques oriented towards coping with negative emotions without smoking.[7]

Understanding individual sex differences in smoking behaviour and nicotine dependence could increase knowledge and help in the development of more effective treatment regimens.

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Conflicts of interest

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Pleural effusion negatively impacts survival of patients undergoing maintenance hemodialysis

To the Editor,

Pleural effusion (PE) is a common clinical presentation of chronic kidney disease (CKD).[1] Recently, two prospective observational studies evaluated the association of PE and mortality.[2,3] One study revealed that the presence of bilateral and transudative PE was an indicator of increased mortality.[2] The other study revealed that patients with PE caused by congestive heart failure and CKD in addition to bilateral PE had high mortality.[3] Thus, we hypothesized that PE at the time of initiating maintenance hemodialysis is closely associated with poor outcome. We examined chest X-ray (CXR) images at the time of initiating maintenance hemodialysis to evaluate the association between PE and mortality.

This was a single-center, retrospective survey study. The local ethics committee of Hikone Municipal Hospital approved this study and waived off the requirement of obtaining written informed consent for all participants.

We reviewed all medical records of the patients who were started on maintenance hemodialysis at Hikone Municipal Hospital between January 2013 and December 2017. Patients who were followed up for a minimum of 3 months post initiation of maintenance hemodialysis or until death were included. Patients who had undergone peritoneal dialysis or had values missing from their medical records were excluded. Survival data were calculated from the time of initiating maintenance hemodialysis to time of death.

PE was assessed using CXR images <1 week before the initiation of maintenance hemodialysis. PE was considered to be mild if the costophrenic angle was blunt, moderate if the effusion occupied one-third to half of the hemithorax, and severe if more than half of the hemithorax was opacified.[4]

Continuous variables were compared using Wilcoxon rank-sum test and expressed as mean ± standard deviation, whereas categorical variables were compared using chi-square test and presented as frequencies with percentage. Survival was compared using Kaplan–Meier plots and log-rank test. The multivariate Cox proportional hazards model was used for evaluating differences between survival and the following explanatory variables, age, heart disease, serum albumin level, and PE. All statistical analyses were performed using JMP® 10 statistical software package (SAS Institute; Cary, NC, USA); $p < 0.05$ was considered to be statistically significant for all analyses performed.

We screened 88 patient records, of which 6 were excluded for following reasons; 4 were followed for <3 months post initiation of maintenance hemodialysis, 1 underwent peritoneal dialysis, and another had missing CXR image before the initiation of maintenance hemodialysis. A final total of 82 patients were included in our study.

Clinical characteristics of study patients are presented in Table 1. The mean follow-up from the time of initiating maintenance hemodialysis was 765.6 ± 475.4 days. The incidence of PE at the time of initiating maintenance hemodialysis was 48.8% (40/82 patients); PE was bilateral in 21 patients (52.5%) and unilateral in 19 patients (47.5%). Patients with PE were older and had a higher frequency of heart disease than those without PE. The presence of PE, regardless of its severity, was significantly associated with lower survival probability (Fig. 1). After adjusting for age, heart disease, and serum albumin level, the presence of PE was significantly associated with lower survival probability (hazards ratio: 2.78 [95% CI, 1.047–8.23, $p = 0.040$]).

PE at the time of initiating maintenance hemodialysis was associated with poor prognosis. Studies assessing the correlation between mortality and PE caused by CKD are limited. Kwan et al. retrospectively described that PE was associated with high mortality in patients undergoing maintenance peritoneal dialysis.[5] DeBiasi et al. prospectively reported that patients with PE caused by CKD had high mortality.[3] These data are consistent with our findings. However, the underlying association between PE and mortality remains unknown. Future studies exploring the underlying association between high mortality and PE at the time initiating maintenance hemodialysis are required.

In this study, the incidence of PE at the time of initiating maintenance hemodialysis was 48.8%. Two previous studies have shown that the incidence of PE was 6.7% in patients with CKD (stage 3–5) under pre-maintenance dialysis and 20.2% in those undergoing long-term maintenance hemodialysis.[4,6] These differences could be influenced by the timing of evaluating PE.