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Original Research

Relationship between smoking and the incidence of sarcopenia: The SarcoPhAge cohort

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ABSTRACT

Introduction: The association of tobacco use and incidence of muscle impairments has not been extensively explored in research. In this study, the relationship between smoking and the incidence of sarcopenia is investigated.

Methods: The present longitudinal study used data from the Sarcopenia and Physical Impairment with advancing Age (SarcoPhAge) cohort, which includes older adults aged ≥65 years. All individuals with follow-up data on muscle health were included in this post hoc analysis. A diagnosis of sarcopenia was established, at each year of follow-up, according to the European Working Group on Sarcopenia in older People 2 (EWGSOP2) criteria. A sensitivity analysis was performed using other diagnostic criteria for sarcopenia. The smoking status and the number of cigarettes smoked per day were self-reported. The relationship between smoking status or the number of cigarettes smoked per day and the incidence of sarcopenia/severe sarcopenia throughout the 5 years of follow-up was evaluated using the Cox proportional hazards model.

Results: In total, the study population included 420 participants, with a median age of 71.7 years (P25–P75 = 67.7–76.9 years) and 59.8% were female. Over the 5 years of follow-up, 78 participants (18.6%) became sarcopenic as per the EWGSOP2 criteria and 41 individuals (9.8%) developed severe sarcopenia. There were significantly more smokers than non-smokers who developed sarcopenia (35.9% vs 16.8%, *P*-value = 0.003). A fully adjusted Cox model confirmed this observation, yielding a hazard ratio of 2.36 (95% confidence interval [CI]: 1.31–4.26), meaning that smokers have a 2.36-fold higher risk of developing sarcopenia. Furthermore, individuals who smoked had a 2.68 times increased risk of developing severe sarcopenia (95% CI: 1.21–5.93) than those who did not smoke. Sensitivity analyses globally confirmed these findings when applying other diagnostic criteria for sarcopenia.

Discussion: Smoking seems to be an important predictor for the onset of sarcopenia, highlighting, once again, that tobacco use is a major public health problem.

Introduction

Sarcopenia is currently defined by the European Working Group on Sarcopenia in older People 2 (EWGSOP2) as a loss of muscle strength coupled with a loss of muscle mass.[1] Severe forms of sarcopenia are defined when a loss of physical performance is also observed. Sarcopenia represents a major public health burden.[2] The worldwide prevalence of this disease is approximately 10%[3] in older individuals and this prevalence rate is expected to increase by 72.4% by 2045.[4] From an economic perspective, sarcopenia represents a notable cost to both the patient and society.[5] Sarcopenia has significant adverse health effects, including increased mortality,[6,7] and higher risks of falls and hospitalization.[8] Prevalence of sarcopenia in Belgium has been estimated at between 12.5%[9] and 13.7%[10] in community-dwelling older adults.

It is well known that chronic diseases developed in old age are largely influenced by lifestyle risk factors, such as smoking, alcohol consumption and physical inactivity.[11] A recent study has suggested the crucial role of a healthy diet[12,13] and physical activity[14] in sarcopenia. It is therefore probable that other lifestyle risk factors also

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influence the onset of sarcopenia. As this field of research is relatively new, the impact of unhealthy lifestyle habits needs to be further investigated. In particular, the role of tobacco use in the occurrence of sarcopenia deserves to be explored. Indeed, tobacco use is considered as one of the most important public health threats as the prevalence of smokers is considerably high and its deleterious effect on health are repeatedly proven.[15] It is therefore important to focus research on chronic diseases caused, at least in part, by tobacco,[16] because they have a high prevalence and incidence, which makes them a significant public health problem. Sarcopenia is one such chronic disease, and observational studies are useful and necessary to make advances in the understanding of these tobacco-associated diseases.

Some studies have already partially investigated the association between tobacco use and sarcopenia. Indeed, in a meta-analysis performed in 2014, Steffl et al.[17] concluded that an association between smoking and sarcopenia exists, with an overall effect size of 1.12. However, the following shortcomings of this meta-analysis must be considered: (1) all included studies presented a cross-sectional design, thus limiting the scope of the conclusions; (2) most of the included studies only focused on one component of sarcopenia (i.e. muscle mass); and (3) the dose–response relationship (i.e. the impact of the number of cigarettes consumed on the occurrence of the disease) was not studied, which is essential to determine the causality between smoking and developing sarcopenia.

In view of these limitations in the research on a potential relationship between smoking and sarcopenia, the present study undertakes a post hoc analysis on data from the Sarcopenia and Physical Impairment with advancing Age (SarcoPhAge) cohort.[18] SarcoPhAge is a longitudinal study conducted over a 5-year period assessing muscle health in older individuals. The precise research question has been established as follows: Does smoking increase the risk of developing sarcopenia over 5 years of follow-up and is there a dose–response effect affecting this risk?

Methods

A post hoc analysis was performed on data from the SarcoPhAge study. The SarcoPhAge study was not specifically designed to assess the relationship between smoking and the incidence of sarcopenia, but the protocol did include an evaluation of tobacco use.

Reporting

This investigation follows the guidelines for reporting observational studies from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[19]

Population

The study population, from the SarcoPhAge cohort, has been described elsewhere.[20] Briefly, when SarcoPhAge was set up in 2013, the main objective of this prospective study was to evaluate adverse health outcomes of sarcopenia in older individuals aged ≥65 years. There were no exclusion criteria except individuals linked to the use of the dual X-ray absorptiometry (DXA) [e.g. the presence of an amputated limb or a body mass index (BMI) > 50 kg/m^2]. During the one-year recruitment period of the study (T0), 534 older adults were enrolled by means of press advertisements, and promotion in geriatric, osteoporotic, rehabilitation, and rheumatology outpatient clinics. The approval for this study (2012/277) and its subsequent amendments (2015, 2018) were obtained from the Ethics Committee at the University of Liège, Belgium. All older individuals included in the study were informed of the study objectives and signed the informed consent form. Participants were interviewed annually during the 5 years of follow-up (T1, T2, T3, T4, T5). The final follow-up assessment occurred in 2019 (T5).

Exposure assessment

Smoking status (yes/no) was recorded at the initial assessment (T0) of participants in the SarcoPhAge study. A current smoker was defined as a person who has smoked more than 100 cigarettes (or other tobacco products) in his/her whole lifetime and has smoked in the last 28 days.[21] The data were self-reported by the participant. The number of cigarettes consumed per day was also self-reported at this initial consultation.

Outcomes assessment

Sarcopenia is defined as an alteration in two muscle components:

1. Muscle strength, which was evaluated by a hand-held dynamometer (Saehan Corporation, MSD Europe Bvba, Brussels, Belgium) calibrated, each year, for 10, 40, and 90 kg. The Southampton protocol was applied for this test: participants were asked to squeeze the dynamometer, as hard as possible, three times with each hand. The highest value of the six measurements was recorded.[22]
2. Muscle mass, which was evaluated by DXA (Hologic Discovery A, USA), calibrated daily. The appendicular lean mass was obtained and adjusted for height squared to obtain the appendicular lean mass index in kg/m^2 (ALMI).

In the present analysis, a diagnosis of sarcopenia was established as per the EWSOP2 operational definition.[1] Being sarcopenic implies an impairment of muscle strength plus an impairment of muscle mass. Low muscle strength was defined as <27 kg in men and <16 kg in women, and low muscle mass was defined as an ALMI <7.0 kg/m^2 in men and <5.5 kg/m^2 in women.

As a severity index of sarcopenia, physical performance was evaluated by the Short Physical Performance Battery (SPPB) test,[23] which includes an assessment of balance (/4 points), gait speed (/4 points), and chair stand (/4 points), scored on a maximum of 12 points. Severe sarcopenia is determined as an impairment of physical performance of ≤8 points/12, in addition to the diagnosis of low muscle strength and low muscle mass.

Sensitivity analyses were performed as per four other definitions of sarcopenia (see Table 1), which included the European Working Group on Sarcopenia in Older People 1 (EWGSOP1),[24] the International Working Group on Sarcopenia (IWGS),[25] the Society on Sarcopenia, Cachexia and Wasting Disorder (SSCWD),[26] and the Foundation for the National Institutes of Health (FNIH).[27]

Covariates

Each year, the SarcoPhAge study also gathered a large number of sociodemographic, clinical, and physical data. Some of these covariates have been studied in the present analysis because they may potentially have an impact on sarcopenia status, including age, from medical record; gender, from medical record; number of concomitant medications per individual, self-reported; number of comorbidities per individual, self-reported; alcohol consumption (yes or no), self-reported; cognitive status using the Mini Mental State Examination (MMSE),[28] scored on 30-points scale (higher score suggesting better cognitive status); level of physical activity using the Minnesota instrument,[29] reported in kcal/day; and

Table 1
Four other operational definitions of sarcopenia and their cutoff limits.

Organization, year	Muscle mass		Muscle strength		Physical performance
EWGSOP, 2010	Women: SMI ≤5.50 kg/m^2 Men: SMI ≤7.26 kg/m^2	AND	Women: grip strength <20 kg Men: grip strength <30 kg	AND/OR	SPPB ≤8 points OR gait speed ≤0.8 m/s
IWGS, 2011	Women: SMI ≤5.67 kg/m^2 Men: SMI ≤7.23 kg/m^2			AND	Gait speed <1.0 m/s
SSCWD, 2011	Women: SMI ≤5.18 kg/m^2 Men: SMI ≤6.81 kg/m^2			AND	Gait speed <1.0 m/s
FNIH, 2014	Women: ALM_{BMI} <0.512 Men: ALM_{BMI} <0.789	AND	Women: grip strength <16 kg Men: grip strength <26 kg	AND	Gait speed <0.8 m/s

ALM_{BMI}, appendicular lean mass body mass index; EWGSOP1, European Working Group on Sarcopenia in Older People 1; FNIH, Foundation for the National Institutes of Health; IWGS, International Working Group on Sarcopenia; SPPB, Short Physical Performance Battery test; SSCWD, Society on Sarcopenia, Cachexia and Wasting Disorder; SMI, skeletal muscle mass index.

nutritional status via the Mini Nutritional Assessment,[30] scored on 30-points scale (higher score suggesting better nutritional status).

Statistical analyses

All data were processed using R version 3.6.2 and SPSS 24 (IBM Corporation, Armonk, NY) software packages. To verify the distribution of the continuous variables, four different methods were used: Shapiro–Wilk test, quantile–quantile plot, histogram and mean ≈ median. For all variables following a skewed distribution, quantitative observations have been expressed as median and quartiles (P25–P75). Group comparison between smokers and non-smokers has been undertaken by the U Mann–Whitney test (non-parametric test). Qualitative variables have been reported in absolute (n) and relative (%) frequencies, and were compared using the Chi-squared test.

Regarding the incidence of sarcopenia, individuals presenting the disease at baseline (T0) were excluded from the data set, so at T0 all study participants were free from sarcopenia. New cases of sarcopenia at each year of follow-up (i.e. any new cases during, at least, one of the years of follow-up [T1, T2, T3, T4, T5]) were recorded. Individuals with a missing diagnosis of sarcopenia at T1, T2, T3, T4, and T5 were excluded from the analysis. The same process was undertaken for the incidence of severe sarcopenia. To reduce the risk of selection bias due to differences in lost-to-follow-up rate at different follow-up times, a sensitivity analysis was performed only in older adults still present in the cohort at the 5-year follow-up, allowing conclusions about the association between smoking and the 5-year incidence of sarcopenia. Therefore, only older adults who have undergone evaluations for sarcopenia at the end of the study (T5) were retained in this analysis.

To determine the relationship between smoker status and incidence of sarcopenia, a univariate analyses was initially performed. A contingency table was produced and the Chi-squared test applied. A Cox proportional hazards model was then performed with the incidence of sarcopenia as a dependent variable and smoking status as an explanatory variable. A second Cox model, adjusted on the covariates identified above and potentially being explanatory, was then launched. The hypothesis of proportional hazards was verified for all covariates. The covariates included in the model (i.e. age, gender, number of concomitant medications per individual, number of comorbidities per individual, cognitive status, level of physical activity and nutritional status) were chosen because they are known to potentially affect muscle status.[12,20] The model did not include BMI and ALMI to avoid over adjustment. The same statistical principles were performed in the investigations related to severe sarcopenia. To determine the incidence of (severe) sarcopenia or not over time, Kaplan–Meier curves and log rank tests were used. To elucidate the relationship between the number of cigarettes consumed per day and incidence of (severe) sarcopenia, a test of comparison between groups was performed (i.e. U Mann–Whitney test). A Cox proportional hazards model was undertaken to explore univariate and multivariate relationships. The 5% critical level was set to interpret statistically significant results.

Results

Characterization of the studied population

Of the initial 534 enrolled participants in the SarcoPhAge study, 420 were included in the present analysis, after the exclusion of those with baseline sarcopenia (n = 24) and those who were never assessed during the 5 years of follow-up (n = 90) [Fig. 1]. Various reasons have been identified for this lack of follow-up, including death, refusal to participate and not being able to contact the individuals. Therefore, all older individuals for whom evaluations for sarcopenia had been performed during at least one of the follow-up times (T1, T2, T3, T4, and/or T5) were retained in this analysis.

The baseline characteristics of the 420 included individuals are presented in Table 2. The study population had a median age of 71.7 years (P25–P75 = 67.7–76.9 years) and 59.8% were female. In total, 39 individuals (9.3%) were smokers and 381 were non-smokers (90.7%). When looking at the baseline characteristics as per smoking status, a significantly lower BMI was seen in smokers than in non-smokers (*P*-value <0.001). ALMI was also observed to be significantly lower in men and women who smoked (respectively, *P*-values = 0.02 and 0.01).

When considering clinical differences between individuals lost to follow-up and individuals remaining in the study, it was observed that individuals who were not interviewed at follow-up were significantly older than interviewed individuals (respectively, 75.3 years [P25–P75 = 71.2–78.6] vs 71.6 years [P25–P75, 67.7–76.8], *P*-value <0.001). Furthermore, the physical performance of those not interviewed at follow-up was significantly lower than in interviewed individuals (respectively, 9 points [P25–P75 = 7–10.75] in the SPPB test vs 10 points [P25–P75 = 9–11], *P*-value <0.001). No significant difference between the groups was seen regarding smoking status (*P*-value = 0.44) or the number of cigarettes smoked per day (*P*-value = 0.60).

Relationship between smoking status and incidence of sarcopenia

Over the 5 years of follow-up of the SarcoPhAge study, 78 participants (18.6%) became sarcopenic as per the EWGSOP2 criteria. These criteria were also used to highlight the severity gradient of the disease and, in this sample, 41 individuals (9.8%) developed severe sarcopenia at one follow-up point over the 5 years.

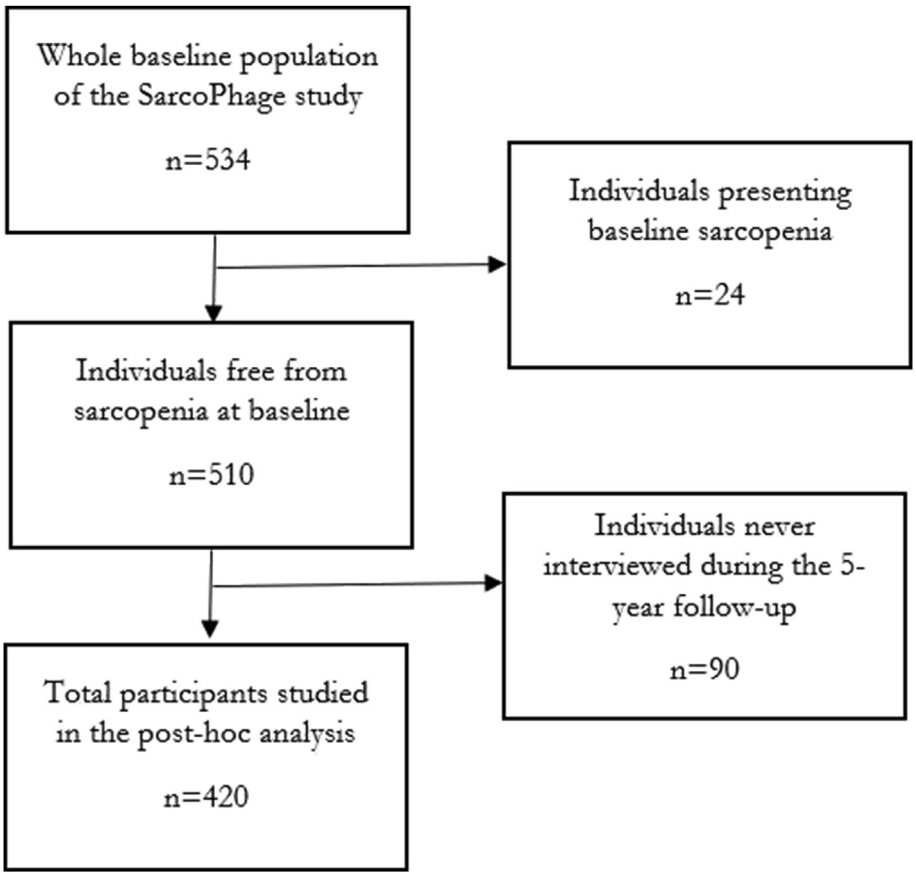

Fig. 1. Flowchart for inclusion of participants in the present analysis.

In Table 3, it can be seen that there were significantly more smokers than non-smokers who developed sarcopenia (incidence of sarcopenia of 35.9% in smokers vs 16.8% in non-smokers, *P*-value = 0.003). Crude and adjusted Cox proportional hazards models produced hazard ratios (HRs) of 2.29 and 2.37, respectively, revealing a higher risk of developing sarcopenia for individuals who were smokers. A significant Kaplan–Meier curve (log rank *P*-value <0.001) graphically represents this relationship between smoking status and incidence of sarcopenia (Fig. 2A).

A relationship between smoking status and incidence of severe sarcopenia was also observed: there were significantly more smokers than non-smokers who developed severe sarcopenia

Table 2
Baseline characteristics of the participants of the SarcoPhAge study.

Characteristics	All (n = 420)	Smoking status		*P*-value
		Yes (n = 39)	No (n = 381)	
Age in years [median (P25–P75)]	71.7 (67.7–76.9)	69.0 (67.0–74.6)	72.1 (67.8–77.4)	0.05
Gender [n (%)]				
Men	169 (40.2)	16 (41.0)	153 (40.2)	0.91
Women	251 (59.8)	23 (59.0)	228 (59.8)	
No. of concomitant medications per individual [median (P25–P75)]	5 (3–8)	6 (3–8)	5 (3–8)	0.34
No. of concomitant conditions per individual [median (P25–P75)]	4 (2–5)	4 (3–5)	4 (2–5)	0.68
Alcohol consumption [n (%)]				
Yes	215 (51.2)	22 (56.4)	193 (50.7)	0.49
No	205 (48.8)	17 (43.6)	188 (49.3)	
Cognitive status (/30 points) [median (P25–P75)]	29 (28–29)	28 (28–29)	28 (28–29)	0.17
Level of physical activity (kcal/day) [median (P25–P75)]	779.75 (280–1526)	773 (288.5–1554)	960 (105–1529)	0.65
Body mass index (kg/m^2) [median (P25–P75)]	26.3 (23.8–29.8)	23.2 (20.1–26.9)	26.7 (24.0–29.9)	<0.001
ALMI (kg/m^2) [median (P25–P75)]				
Men	7.98 (7.28–8.79)	7.49 (6.83–8.45)	8.05 (7.30–8.84)	0.02
Women	5.98 (5.50–6.54)	5.47 (5.21–6.35)	6.01 (5.54–6.58)	0.01
Muscle strength (kg) [median (P25–P75)]				
Men	40 (36–45)	40.1 (32–42)	40 (36–45)	0.55
Women	23 (18–27)	22.7 (18–26)	24 (20–28)	0.24
SPPB test (/12 points) [median (P25–P75)]	10 (9–11)	10 (9–11)	10 (9–11)	0.86
Nutritional status (/30 points) [median (P25–P75)]	29 (22–30)	28 (22–29)	28 (22.25–30)	0.17

ALM_{BMI}, appendicular lean mass index; SPPB, Short Physical Performance Battery test.

Table 3
Relationship between smoking status and incidence of sarcopenia (n = 420).

Smoking status	Incident sarcopenia		*P*-value	Crude HR (95%CI)	Adjusted[a] HR (95%CI)
	Yes (n = 78)	No (n = 342)			
Yes (n = 39)	14 (35.9)	25 (64.1)	0.003	2.29 (1.28–4.09)	2.36 (1.31–4.26)
No (n = 381)	64 (16.8)	317 (83.2)			
	Incident severe sarcopenia				
Yes (n = 41)	No (n = 379)				
Yes (n = 39)	8 (20.5)	31 (79.5)	0.02	2.42 (1.12–5.23)	2.68 (1.21–5.93)
No (n = 381)	33 (8.6)	348 (91.4)			

CI, confidence interval; HR, hazard ratio.
[a] Adjusted for age, gender, number of concomitant medications per individual, number of comorbidities per individual, alcohol consumption, cognitive status, level of physical activity, nutritional status.

(20.5% vs 8.6%, *P*-value = 0.02). The risk of developing severe sarcopenia was increased by 2.42 times for individuals who smoked. In a fully adjusted model, this risk was increased to 2.69 times. Fig. 2B shows the incidence of severe sarcopenia between smokers and non-smokers (log rank *P*-value <0.001).

Sensitivity analyses, performed only on individuals assessed at the 5-year follow-up (n = 268), have confirmed these findings, and even suggest an increased magnitude of risk. In the fully adjusted analysis, smokers had a 4.90-fold increased risk of developing sarcopenia after 5 years of follow-up compared with non-smokers. Smokers also had a 20.47-fold increased risk of developing severe sarcopenia after 5 years of follow-up. Detailed analyses are available in the online Supplementary Materials.

When applying sensitivity analyses using other sarcopenia criteria, we observed the following adjusted HRs (95% CI): 2.42 (1.45–4.07) for the EWGSOP1; 2.52 (1.44–4.44) for IWGS; and 4.19 (1.99–8.82) for SSCWD. For the three criteria, there was significantly higher risks for developing sarcopenia when being a smoker. The calculation of an HR for the FNIH definition was impossible as there were no smokers in the group of individuals identified with sarcopenia by the FNIH criteria.

Relationship between the number of cigarettes smoked per day and incidence of sarcopenia

This study also investigated the relationship between the number of cigarettes consumed per day and the incidence of sarcopenia over the 5 years of follow-up (Table 4). In the sarcopenia and severe sarcopenia groups, the number of cigarettes consumed per day was significantly higher than in the non-sarcopenia and non-severe sarcopenia groups (respectively, *P*-values = 0.002 and 0.011). Through fully adjusted Cox models, it was observed that an increase in the consumption of one cigarette per day resulted in a 5% higher risk of developing sarcopenia over 5 years. The risk rose to 6% for developing severe sarcopenia.

A sensitivity analysis was performed on the sample of 268 individuals who remained in the cohort at the 5-year follow-up. In this sample, the risk of developing sarcopenia or severe sarcopenia caused by each additional cigarette was even greater: it was increased by 10% and 19%, respectively. Detailed data are available in the Supplementary Materials.

When considering other criteria for defining sarcopenia, three definitions also showed an impact of the number of cigarettes consumed per day on the risk of developing sarcopenia, which was significantly increased for each additional cigarette consumed per day (adjusted HRs: 1.05 [95% CI 1.03–1.08] for EWGSOP1; 1.04 [95% CI 1.01–1.07] for IWGS; and 1.06 [95% CI 1.03–1.10] for FNIH). Again, the calculation of an HR for the FNIH definition was impossible as there were no smokers in the group of individuals identified with sarcopenia by the FNIH criteria.

Discussion

Based on data from the SarcoPhAge cohort, this study aimed to explore, through a post hoc analysis, the longitudinal relationship between smoking status and incidence of (severe) sarcopenia. The results show a significantly higher risk of developing sarcopenia when being a smoker. The importance of this association was shown by the adjusted HR observed in the study sample of 2.37 (95% CI 1.32–4.27) for sarcopenia and of 2.69 (95% CI 1.22–5.95) for severe sarcopenia. This study also demonstrated a biological gradient: for each additional cigarette consumed per day, the risk of sarcopenia or severe sarcopenia increased by 5% or 6%, respectively. Sensitivity analyses performed only on the sample of individuals who remained at the 5-year follow-up confirmed these findings, and revealed an even more pronounced association between smoking and the onset of (severe) sarcopenia. This high magnitude

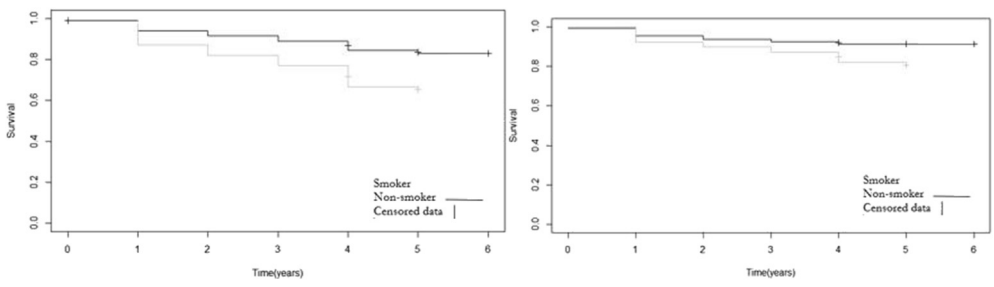

Fig. 2. Incidence of (a) sarcopenia and (b) severe sarcopenia in relation to smoking status, log-rank p < 0.001.

Table 4
Relationship between number of cigarettes per day and incidence of sarcopenia (n = 420).

Variable of interest	Incident sarcopenia		*P*-value	Crude HR (95% CI)	Adjusted[c] HR (95% CI)
	Yes (n = 78)	No (n = 342)			
Number of cigarettes per day	3.0 ± 8.0[a]	0.9 ± 4.2[a]	0.002[b]	1.05 (1.0[b]-1.08)	1.04 (1.02–1.07)
	Incident severe sarcopenia				
	Yes (n = 41)	No (n = 379)			
Number of cigarettes per day	3.8 ± 9.4[a]	1.0 ± 4.2[a]	0.011[b]	1.05 (1.02–1.09)	1.0[b] (1.02–1.09)

CI, confidence interval; HR, hazard ratio.
[a] For a better visualization of data, expressed in mean ± SD; however, non-parametric test was applied.
[b] Because of skewed variable.
[c] Adjusted for age, gender, number of concomitant medications per individual, number of comorbidities per individual, alcohol consumption, cognitive status, level of physical activity, nutritional status.

of association was, however, very imprecise given the very wide 95% CIs (see Supplementary Materials), probably related to the low number of cases of (severe) sarcopenia.

Based on this study and other previous studies, some specific points can suggest a causal relationship, as per Hill criteria,[31] between exposure to tobacco and the occurrence of sarcopenia. First, there was quite a strong association between tobacco and the occurrence of sarcopenia in this and previous studies (all HRs were >2 and may even be > 10 in sensitivity analyses). Second, in this analysis, a temporal sequence was observed (i.e. the smoking habit precedes the onset of sarcopenia). Third, the results show a biological gradient (i.e. smoking more cigarettes leads to an increased risk of sarcopenia). Fourth, a biological plausibility has been proposed in several studies. Rom et al.[32] suggested that smoking could promote the deterioration of muscle proteins due to the oxidative stress generated. Nogueira et al.,[33] in a study conducted in mice, suggested a role for capillary regression induced by tobacco consumption, resulting in an impairment of skeletal muscle function. Fifth, the results of the present study are in accordance with previous findings, such as the meta-analysis by Steffl et al.,[17] which, although carried out on cross-sectional studies and thus having limitations, demonstrated that being a current smoker is associated with sarcopenia (overall effect size = 1.12). More specifically, the cross-sectional studies included in the meta-analysis by Steffl et al. focussed on sarcopenia defined as an impairment of three components (i.e. muscle mass, muscle strength, and physical performance) and showed higher magnitudes of association. Similar to the current findings, the study of Jo et al.[34] yielded an odds ratio (OR) of 3.34 and the study of Akune et al.[35] yielded an OR of 2.82 in females. Other studies included in the meta-analysis provided conflicting results, yet, most finding support a causal relationship between smoking status and sarcopenia. However, it is probably premature to definitively conclude that a real cause and effect relationship exists between smoking and the onset of sarcopenia. Indeed, other Hill criteria[31] for imputing causality are not met at this time, such as experimental evidence, reversibility of association, specificity, and analogy.

Although further investigations in this area are required, the present study brings original new findings, having a two-fold advantage: (1) it is the first study to be interested in the prospective relationship between smoking and the onset of sarcopenia over time, while using the latest updated relevant algorithm for operationally defining sarcopenia (i.e. EWGSOP2 criteria[1]); and (2) the present study demonstrates that, regardless of the diagnostic definition applied to define sarcopenia, the link between smoking and sarcopenia seems to be established, which reinforces the robustness of the current findings. Only the FNIH definition of sarcopenia was an exception because none of the sarcopenic individuals identified were smokers, probably because the definition identifies as sarcopenic, individuals with another phenotype. Indeed, the BMI in the sarcopenic group was significantly higher than in the non-sarcopenic group when using FNIH criteria (30.13 ± 5.41 kg/m^2 vs 25.67 ± 4.68 kg/m^2, *P*-value <0.001). It should also be noted that the FNIH diagnostic definition of sarcopenia identified fewer cases of sarcopenia (5.7%) than the other definitions (around 25% depending on the criteria).

Some limitations of the present study should be considered and a critical appraisal of the scientific process is important. Indeed, this study is probably exposed to a selection bias: individuals from the SarcoPhAge study with poor physical performance are more reluctant to attend their annual interviews and either refuse to come or cannot be contacted anymore, as mentioned in the Results section. However, this does not seem to influence the analyses on the relationship between tobacco and incidence of sarcopenia because there were not more smokers among those who were lost to follow-up. Sensitivity analyses also reduced the likelihood of selection bias because by being more rigorous in the selection criteria of the population (i.e. only older individuals reviewed after 5 years), the relationships were still observed, and even to a greater extent. However, regarding the data on tobacco use, there could be a social desirability bias: being a smoker was likely perceived as a negative behavior and could thus be under-reported. Recall bias could also be present when recording the number of cigarettes smoked per day. It would have been interesting to carry out a sensitivity analysis with the 'former smoker' status (data not available in the current study) and in a younger population (<65 years old). A distinction between age-related and non–age-related sarcopenia could not be made within the SarcoPhAge cohort. Although the current results are adjusted for comorbidities per individual, this does not clearly distinguish between individuals experiencing age-related or condition-related sarcopenia. Finally, it cannot be ruled out that certain potentially confounding factors were not taken into account (e.g. stress, sleep, change of smoking status during the 5-year follow-up).

In conclusion, this study shows, once again, the significant damage of cigarettes on health; namely, here, on the muscle health of older individuals. Therefore, even if an older person's muscle condition may seem satisfactory, the clinician should conduct a history to obtain the individual's tobacco consumption, to anticipate the effects that this unhealthy lifestyle behavior could have on the patient's muscle health. Smoking remains a lifestyle habit that can be changed to reduce a large number of health risks, including, it seems, sarcopenia. Reducing the prevalence of smokers, and consequently, the incidence of sarcopenia, would therefore reduce a huge public health burden. Given the suggested link between smoking status and the incidence of sarcopenia, and the resulting biological gradient, clinicians have one more reason to promote better lifestyle habits by stopping smoking.

Author statements

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Ethical approval

The agreement for this study (2012/277) and its subsequent amendments (2015, 2018) were obtained from the Ethics Committee at the University of Liège, Belgium.

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Competing interests

All authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2021.01.017.

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