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The absence of dyspnoea, cough and wheezing: a reason for undiagnosed airflow obstruction?

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Summary

Objectives: The diagnosis of obstructive lung disease (OLD) may be overlooked because of the poor correlation between the intensity of symptoms and the severity of airway obstruction (AO). Undiagnosed airflow obstruction (UDAO) is associated with health impairment and mortality. Questions remain such as the reasons for its occurrence and the underlying diseases. In a pulmonologist's private practice, the objectives were to detect UDAO in the absence of dyspnoea, cough and wheezing, to improve its screening following other anamnestic data, and to separate UDAO patients into "silent asthma" (SA) or "persistent obstruction".

Methods: Patients were subjected to a verbal questionnaire for the detection of alternative indication for pulmonary function tests (PFTs), to a physical examination and, in the case of a severe smoking habit, to a chest X-ray. PFTs were performed whenever an OLD history or another lung disease was present and, in the absence of any dyspnoea, cough and wheezing, when other symptoms and conditions occurred (sputum, chest tightness, fatigue, rhinitis, snoring; active/passive smoking, recurrent lower respiratory tract infections, asthma in childhood or in family, atopy).

Results: Of 3762 consecutive patients, 1389 patients with AO were identified. Among them, 147 UDAO patients were detected with no history of dyspnoea, cough and wheezing (3.9% and 10.6%, respectively). All these patients had other suggestive symptoms and AO risk factors which justified PFTs. They presented with mild (65%), moderate (21%) or even severe (16%) AO. SA patients normalized their spirometric values under treatment.

Conclusion: The absence of dyspnoea, cough and wheezing is a fairly frequent finding and a reason for UDAO. PFTs are warranted with any suggestive symptoms and AO risk factors. The favourable follow-up underlines the importance of screening for UDAO.

Key words: asthma; pulmonary disease; chronic obstruction; spirometry; respiratory system abnormalities; airflow obstruction, undiagnosed airflow obstruction; asymptomatic; screening; symptoms; perception

Introduction

Obstructive lung disease (OLD) is a health problem worldwide with a major impact on health and economics [1]. Studies carried out since the 1990s highlight a prevalence range of undiagnosed airflow obstruction (UDAO) of 3 to 12% [2–4]. It may be a manifestation of asthma and chronic ob-

Abbreviations/definitions

AO	airway obstruction
BX	bronchodilator
COPD	chronic obstructive pulmonary disease
DLCO	diffusion capacity of the lung for carbon monoxide
FEF 25–75	forced expiratory flow between 25 and 75% of forced vital capacity
FEV_1	forced expiratory volume in 1 second
ΔFEV_1 % pred.	variation of the FEV_1 expressed in percentage of the predicted value (20)
FVC	forced expiratory vital capacity
LRTIs	lower respiratory tract infections
PFT(s)	pulmonary function test(s)
PO	"persistent obstruction"
SA	"silent asthma"
SA-PO	"silent asthma" and "persistent obstruction"
SES	socioeconomic status (level 1, 2, or 3)
UDAO	undiagnosed airflow obstruction

Competing interests: none declared.

structive pulmonary disease (COPD), or of a less frequent disorder [3]. Its screening is biased by the fact that several patients have never smoked and/or are asymptomatic [2–4]. Questions remain as to its frequency, the reasons for its occurrence, the underlying diseases, the type of intervention needed, and the role of screening [3].

Dyspnoea, cough and wheezes are commonly associated with airway obstruction (AO) in asthma and in COPD [1, 5, 6]. However, the diagnosis can be overlooked if assessed only on clinical grounds. The lack of correlation between the intensity of symptoms and the severity of obstruction has been documented [5–8]. Moreover, both diseases are poorly perceived by patients and by doctors [2, 3, 5, 9–11]. The need to measure AO for their management has been mentioned [1–9, 12]. Further inflammation and remodelling can induce partly reversible AO at the time the health impairment is present [1, 12, 13].

AO in the absence of wheezes or/and dyspnoea has been observed in asthma [5, 7, 12, 14]. In children, AO occurring without dyspnoea, cough and wheezing has been described by Wolf as "silent asthma" [15]. In adults, the term "silent obstruction" was introduced for clinical warning purposes, and also because of the possible absence of these symptoms in COPD [16–18]. However, patients referred to, or consulting a pulmonologist, frequently present a respiratory background, such as smoking and sputum production, which is not "silent".

This prospective study was performed on consecutive patients attending for a private pulmonological consultation in Geneva (Switzerland). The objectives were to detect UDAO in the absence of three typical AO symptoms, namely, dyspnoea, cough and wheezing, to improve UDAO screening following other anamnestic data, to separate UDAO patients into underlying diseases, mainly, into "silent asthma" (SA) and "persistent obstruction" (PO) patients, and to monitor follow-up under treatment [1, 5–9, 12, 19]. We also queried whether these atypical patients would become aware of a functional improvement when treated, and feature differences in AO reversibility over time.

Material and methods

Study design: From 1984 to 1997, we examined adults and elderly patients (≥65 years of age) referred to, or freely attending the pulmonology practice. In order to detect an alternative indication for PFTs, patients were subjected to a verbal questionnaire concerning the purpose of the consultation, current symptoms, the presence or absence of respiratory symptoms, exercise tolerance, active/passive smoking, current medical diagnoses and treatment, medical and family history, and socioeconomic status. It was elaborated by an experienced pulmonologist, but was not validated in a population-based study. Patients underwent a physical examination and, in the case of severe smoking habit, a chest X-ray.

PFTs were performed whenever an OLD history or another lung disease was present, and when other suggestive symptoms and clinical conditions, such as AO risk factors, isolated or in combination were present. Thus, in patients not presenting the three usual AO symptoms, i.e. dyspnoea, cough and wheezing, PFTs were also performed for other indication(s), such as: sputum, inability to bring out sputum, chest tightness, fatigue, rhinitis, snoring, fainting, tachycardia, active smoking, passive exposure in childhood, recurrent lower respiratory tract infections (LRTIs), LRTIs in childhood, asthma in childhood and/or in family, atopy, hyperinflation on chest X-ray, and pre/post-operative evaluation [1–7, 9–13, 15–19].

We identified patients with AO as a consequence of pulmonary function tests (PFTs) [1–19]. Obstruction was defined as FEV_1/FVC ratio below 88% predicted in men and 89% in women [17]. The level of separation between asthma and COPD may be difficult to assess [1, 13, 19–22]. We applied the criterion of the variation of the FEV_1 expressed as a percentage of the predicted (% pred.) value, more than 15% in asthma, and less than 15% in COPD [20]. ΔFEV_1 % pred. allows estimation of the response to treatment independent of age, height and sex. Its value is expected to be low in severe, but also in slight degree obstruction. In chronic bronchitis, an asthma-like response may be featured although less pronounced. Thus, we also considered a history of smoking, the number of pack-years, persistent functional anomalies (severe hyperinflation, FEF 25–75 lower than 20% of predicted, reduced DLCO), as well as suggestive chest X-ray (hyperinflation, zones of hyperlucency).

Patients presenting with both an alternative indication for a PFT and an UDAO demonstration were included and defined the study group. Those presenting an OLD disease diagnosed in adult life and/or having recourse to an inhaled therapy were excluded. Approval for the study was given by the ethics committee of the Association des Médecins du Canton de Genève. See Appendix for abbreviations/definitions.

Definitions of "silent asthma", "persistent obstruction", and socioeconomic status

As three usual symptoms of AO were absent, we adopted a working definition of "silent asthma" (SA) (ΔFEV_1 % pred. >15%) versus "persistent obstruction" (PO) (ΔFEV_1 % pred. <15%) on the basis of the ΔFEV_1 % pred. between baseline value at first visit and at 1 to 3 months under treatment [15, 20, 21]. SA and PO patients composed the SA-PO study group. Definition of socioeconomic status (SES): A Educational levels 1) elementary level, 2) baccalauréat level and equivalent, 3) university level; B Professional levels 1) low-level employee, 2) intermediate level, 3) executive level. The categorization of SES was based on the patient's educational and professional level, and was defined as the higher of the two levels if these were different.

Lung function testing

Spirometry was performed by the principal investigator in an identical manner, according to ATS recommendations. It was made at the first assessment visit, 1 to 3 months after initiation of treatment, and after 2 years under therapy. Reversibility at first assessment visit was tested by repeating spirometry after administration of a bronchodilator (2 × 200 µg inhaled salbutamol). Func-

tional improvement under treatment was assessed at baseline post bronchodilator. Predicted values: European Coalworkers [19]. Equipment: Gould Godart Pulmonet III with DLCO (Bilthoven, Netherlands, EU) and SensorMedics Vmax 229 V6200 Autobox bodyplethysmograph with DLCO (Yorbalinda, California, USA).

Follow-up

For the first follow-up, SA-PO patients were examined from one to three months after introduction of the treatment. In case of FEV_1 normalization after one month, the value measured at that time was taken into consideration. Otherwise, the best value of FEV_1 obtained one or two months later was considered. For the second follow-up, the FEV_1 value was considered two years after introduction of the treatment. In the meantime, renewal of prescriptions and usual follow-up were provided by the pulmonologist. Several patients also attended the consultation of their general practitioner for other reasons.

Treatment

Treatment consisted of inhaled beta-agonists (daily dose 800 mcg salbutamol, or 1000 mcg terbutaline, or 100 mcg salmeterol) and corticosteroids (daily dose 1000 mcg beclomethasone, or 800 mcg budesonide, or 1000 mcg fluticasone), on a twice-daily schedule [1, 12, 13]. The therapy was not modified during the 2-year follow-up. UDAO patients were informed of the characteristics of their disease, the need for better understanding of less symptomatic AO, the purpose of the treatment, the side effects and the necessity for close observance. Oral consent was obtained for inclusion. Treatment compliance was assessed anamnestically.

Perception of a functional improvement under treatment

Because of a reduced perception of AO in the absence of three main symptoms, SA-PO patients were evaluated on their faculty to perceive functional improvement under treatment. Perception was considered to be present if a subjective improvement was noticed. It was confirmed by an affirmative answer to both questions: "Do you feel better?", and "Do you feel that your respiration has improved?" A free report of a better well-being and an affirmative answer to additional specific questions were also considered, such as: "Do you have less sputum?", "Are you less tired?", "Do you have fewer respiratory infections?"; "Do you have any other observation?"

Statistical methods

For the 147 patients included and for the subsample of 76 patients with complete 2-year follow-up data, a comparison of the SA and PO patients with respect to their FEV_1 baseline was first done using the Mann-Whitney-U-test. Temporal changes in ΔFEV_1 % pred. within groups were assessed using the sign test and compared between groups using the Mann-Whitney-U-test. Differences in variability of change between groups were assessed using the Siegel-Tukey-test. Both distributions of FEV_1 % pred. at given time points, and of temporal changes in ΔFEV_1 % pred. were represented by box plots referring to the mentioned subsample (n = 76). The Mann-Whitney-U-test and the Wilcoxon signed rank test were used to assess the perception of a functional improvement under treatment (n = 76). Since our study is descriptive, no level of significance has been specified. Each p-value should therefore only be interpreted as the probability that the observed difference, or an even larger one, would have arisen by chance alone.

Results

In a cohort of 3762 consecutive patients, 1389 AO patients were identified (figure 1). Among them, 147 UDAO patients were detected with no history of dyspnoea, cough and wheezing: 3.9% of consecutive patients and 10.6% of patients with AO (103 adults and 44 elderly patients, age range 18 to 85 years, median 57 years). Median age is slightly higher in AO and SA-PO patients (table 1). In PO patients, the amount of pack-years is nearly twice as high as in SA patients (table 2). In SA-PO male and female patients, SES level 3 is associated with a higher mean of pack-years than in levels 1 and 2.

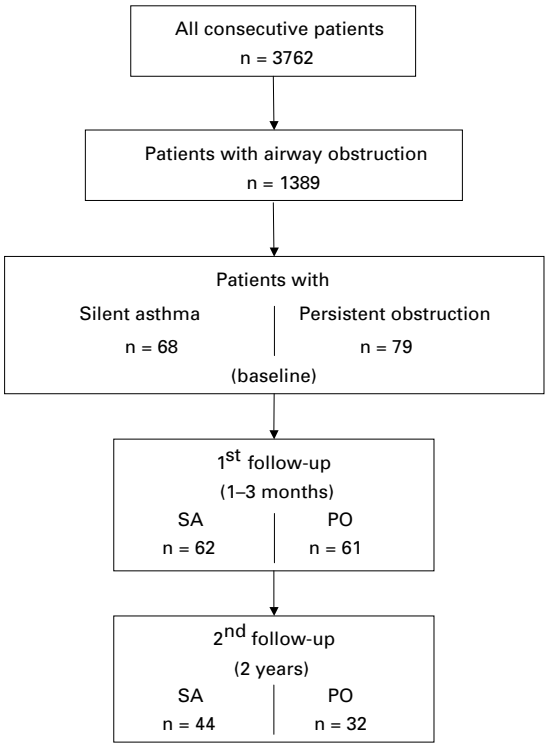

Figure 1

Flow chart describing selection of study sample and follow-up. The flow chart describes the selection process having led to the study sample of UDAO patients with silent asthma (SA) or persistent obstruction (PO). Moreover, it shows the number of patients in each of the two study subgroups having participated in a given follow-up assessment. Among the 76 patients assessed after 2 years (52%), none had skipped the first follow-up assessment.

All SA-PO patients had suggestive symptoms and clinical conditions, such as AO risk factors, isolated or in combination, which justified PFTs (table 3). Table 4 shows the distribution of the SA-PO patients according to the severity of AO. Finally, 23 cases (15.6% of SA-PO patients) were associated with a severe degree of AO. There was no apparent difference between adults and elderly patients, or between men and women.

We could define 68 cases of SA (age range 16 to 85 years, median age 56) and 79 cases of PO (age range 33 to 78 years, median age 58). Not all PO patients with severe obstruction were smokers [1–4]. In addition, some PO smokers showed a good response to treatment (ΔFEV_1 % pred. close

Table 1
Demographic data.

	all patients (n = 3762) median[1] (quartiles)	AO patients (n = 1389) median[1] (quartiles)	SA-PO patients (n = 147) median[1] (quartiles)
all	50	54	57
(n = 3762, 1389, 147)	(34, 63)	(38, 65)	(45, 64)
men	51	56	55
(n = 1792, 766, 79)	(36, 64)	(41, 66)	(43, 62)
women	49	52	58
(n = 1970, 623, 68)	(33, 63)	(35, 65)	(48, 65)
all smokers	55	59	56
(n = 1387, 718, 95)	(40, 66)	(48, 68)	(46, 64)
male smokers	57	59	55
(n = 818, 460, 60)	(43, 68)	(48, 68)	(45, 62)
female smokers	52	58	58
(n = 569, 258, 35)	(35, 65)	(43, 67)	(48, 65)

[1] medians and quartiles of age
Patients attending a pulmonology practice from 1984 to 1997. 1) Collective: all consecutive patients, 2) AO patients: patients with airway obstruction (as a part of the collective), mainly asthma and chronic obstructive pulmonary disease patients, 3) SA-PO patients: "Silent asthma" and "Persistent obstruction" patients (as a part of the AO patients).

Table 2
Smoking history (pack-years), gender and socioeconomic status.

Smokers	SA-PO patients (n = 95) median[1] (quartiles)	SA patients (n = 39) median[1] (quartiles)	PO patients (n = 56) median[1] (quartiles)
all	40	25	47.5
(n = 95, 39, 56)	(25, 50)	(10, 40)	(36.5, 60)
men	40	30	45
(n = 60, 23, 37)	(25, 52.5)	(10, 40)	(40, 60)
women	35	22.5	50
(n = 35, 16, 19)	(25, 50)	(10, 35)	(35, 55)
SES 1	40	25	45
(n = 54, 16, 38)	(25, 50)	(12.5, 35)	(35, 55)
SES 2	35	20	57.5
(n = 25, 13, 12)	(20, 60)	(10, 35)	(41, 60)
SES 3	52	58	58
(n = 16, 10, 6)	(25, 50)	(15, 50)	(40, 55)

[1] medians and quartiles of pack-years smoked
SA–PO patients: "Silent asthma" (SA) and "Persistent obstruction" (PO) patients.
Number of smokers n = 95, representing 65% of the SA–PO patients (first assessment visit: n = 147).
SES: socioeconomic status categorized based on educational level (1) elementary level, 2) baccalauréat level and equivalent, 3) university level) and professional level (1) low-level employee, 2) intermediate level, 3) executive level). SES was defined as the higher of the two levels if those were different.

to 15%, or above) as observed in chronic bronchitis [1]. Even though 55 PO patients presented COPD features, we refrained from defining an additional category, as overlap between asthma and COPD needs accurate investigation [22]. We maintained the more general expression "persistent obstruction" for the whole of the less responsive group.

At 1 to 3 months after initiation of treatment, the SA group emerged as evidenced by the normalisation of the mean value of FEV_1 and by a mean ΔFEV_1 % pred. of 25%. After 2 years' follow-up, the ΔFEV_1 % pred. remained higher for the SA than for the PO patients. Median values of FEV_1 % pred. were higher among SA than among PO within the subsample of 76 patients with complete follow-up data (SA n = 44, PO n = 32) (figure 2). The values increased until the first follow-up assessment, and tended to drop slightly in both groups between the first and the second follow-up assessment. This decrease in FEV_1 % pred. mean values was not associated with a recurrence of initial symptoms or with clinical worsening. No apparent difference between adults and elderly patients could be discerned.

The median increase in ΔFEV_1 % pred. post bronchodilator assessment was higher in the SA than in the PO group (figure 3). In SA, it continued to be slightly steeper in the second time interval. The decrease in ΔFEV_1 % pred. between the

two follow-ups was the same in both groups. The variability of change between post bronchodilator assessment and the first follow-up was higher among SA than among PO patients. Thus, SA emerges as a clinical entity featuring specific characteristics, namely: 1) a different follow-up under treatment in regards to FEV_1 and ΔFEV_1 % pred. mean values, 2) a lower incidence of smoking, and 3) far less sputum production (tables 2 and 4, figures 1 to 4).

At 1 to 3 month follow-up, a lack of compliance due to side effects was observed in 23 cases. We included these in our subdivision: 5 non-smoking SA patients featured a ΔFEV_1 % pred. value

Table 3

Alternative indication for performing PFTs in UDAO screening.

Suggestive symptoms[1]	"Silent asthma" n = 68	"Persistent obstruction" n = 79	Clinical conditions[1]	"Silent asthma" n = 68	"Persistent obstruction" n = 79
Fatigue	13	17	Recurrent LRTIs	19	15
Chest tightness	19	15	LRTIs in childhood	18	15
Burning sensation	3	5	Active smoking	47	71
Tachycardia	3	3	Passive smoking exposure in childhood	7	28
Rhinitis	15	5	Asthma in childhood	6	1
Sputum production	19	46	Asthma in family	16	14
Inability to bring out sputum		9	Pre/post-operative evaluation	12	8
Fainting		3 *	Hyperinflation on chest X-ray		61
Snoring	1	8 **	Known atopy	6	1

[1] expressed in percentage of "silent asthma" patients (SA) and of "persistent obstruction" patients (PO).
* was associated with severe air trapping and hyperinflation.
** was associated with sleep apnea obstructive syndrome.
LRTIs: lower respiratory tract infections. PFTs: pulmonary function tests.

Table 4

Severity of airway obstruction seen at first assessment visit.

Severity of obstruction	Slight n = 93	Moderate n = 31	Severe n = 23
FEV_1 at first visit	>69% pred.	50–69% pred.	<50% pred.
"Silent asthma", n = 68	78%	16%	6%
"Persistent obstruction", n = 79	51%	25%	24%
SA-PO patients, n = 147	63%	21%	16%

Percentage of patients across different severity levels of airway obstruction [19].
SA-PO patients: patients with airway obstruction, presenting without any dyspnoea, cough, and wheezing, and subdivided in "silent asthma" and "persistent obstruction" patients.
FEV_1 = forced expiratory volume in 1 second. % pred. = percentage of predicted value.

Figure 2

Variability of FEV_1 % pred. at four assessment times.
"Silent asthma" (SA) and "Persistent obstruction" (PO) patients with complete follow-up data, n = 76. FEV_1 % pred.: forced expiratory volume in 1 second expressed as percentage of predicted value. For each group, the distribution of the variable FEV_1 % pred. at different times is represented by four box plots, indicating the minimum and the maximum values (end points of the two whiskers), the lower quartile (lower end of the box), the median (horizontal line within the box) and the upper quartile (upper end of the box). Observed medians: a) initial assessment: SA 80.0, PO 66.0, p = 0.002; b) post bronchodilator assessment: SA 93.5, PO 75.5, p = 0.0004; c) 1–3 months' follow-up: SA 102.0, PO 79.5, p <0.0001; d) 2 years' follow-up: SA 99.0, PO 75.0, p <0.0001. P-values obtained from Mann-Whitney-U-test.

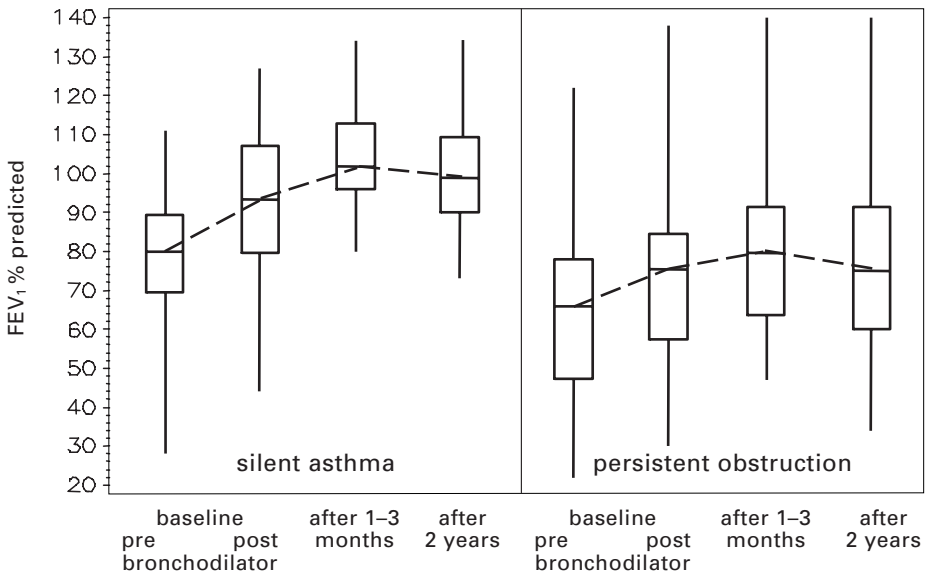

Figure 3

Variability of change in ΔFEV_1 % pred. between different assessment times.
"Silent asthma" (SA) and "Persistent obstruction" (PO) patients with complete follow-up data, n = 76. ΔFEV_1 % pred.: variation of forced expiratory volume in 1 second expressed as percentage of the predicted value (ref. [20]). For each group, the distribution of the change in ΔFEV_1 % pred. between different assessment times is represented by three box plots (see figure 2). Observed median changes in ΔFEV_1 % predicted: a) between initial and post bronchodilator assessment: SA 13.5, p <0.0001, PO 9.0, p <0.0001, with p = 0.004 for difference between groups; b) between post bronchodilator assessment and 1–3 months' follow-up: SA 9.0, p <0.0001, PO 4.5, p = 0.0002, with p = 0.13 for difference between groups; c) between 1–3 months' and 2 years' follow-up: SA - 4.0, p <0.0001, PO - 4.0, p = 0.0005, with p = 0.60 for difference between groups. P-values obtained using the sign test and the Mann-Whitney-U-test, respectively. Variability of change in ΔFEV_1 % pred. between post bronchodilator and first follow-up assessment differed between the two groups (p = 0.02, Siegel-Tukey-test).

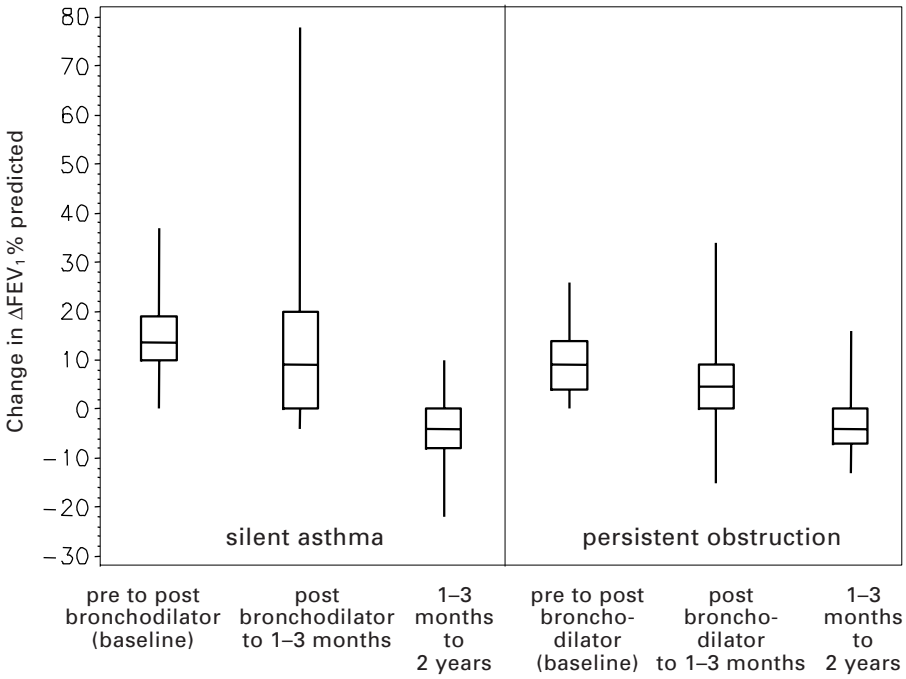

Figure 4

Perception of a functional improvement under treatment.
"Silent asthma" (SA, *white*) and "Persistent obstruction" (PO, *black*) patients with complete follow-up data, n = 76. ΔFEV_1 % pred.: variation of forced expiratory volume in 1 second expressed as percentage of the predicted value (ref. [20]). For perception definition, see Material and Methods. For the two groups, mean values of ΔFEV_1 % pred. are given for different assessment times. **I)** A Patients with perceived clinical improvement: a) at 1–3 months' follow-up: SA 30, PO 19, p = 0.003; b) at 2 years' follow-up: SA 26, PO 14, p = 0.002. B Patients without perceived clinical improvement: a) at 1–3 months' follow-up: SA 20, PO 9 , p = 0.008; b) at 2 years' follow-up SA 15, PO 4, p = 0.01 (p-values obtained from Mann-Whitney-U-test). **II)** Changes in ΔFEV_1 % pred. between the two follow-up assessments reached the following p-values (Wilcoxon signed rank test): a) SA patients in group A: p <0.0001; b) PO patients in group A: p <0.0001; c) SA patients in group B: p = 0.02; d) PO patients in group B: p = 0.02. **III)** Differences in ΔFEV_1 % pred. after 2 years of follow-up between groups A and B reached the following p-values (Mann-Whitney-U-test): p = 0.02 in SA patients and p = 0.001 in PO patients. The corresponding p-values for the comparison after 1–3 months of follow-up were 0.05 and 0.0007, respectively.

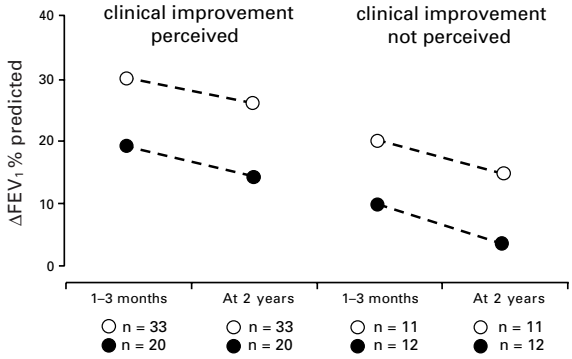

Table 5

Comparison of FEV_1 % predicted between subjects with and without complete follow-up.

	patients with 2 years follow-up mean[1] (n)	patients with incomplete follow-up mean[1,2] (n)		patients with 1 to 3 months follow-up mean[1,2] (n)	
PO patients					
baseline pre bronchodilator	64 (32)	73 (47)	(p = 0.05)	68 (29)	(p = 0.41)
baseline post bronchodilator	74 (32)	82 (47)	(p = 0.04)	77 (29)	(p = 0.29)
after 1 to 3 months	80 (32)	80 (29)	(p = 0.67)	80 (29)	(p = 0.67)
SA patients					
baseline pre bronchodilator	78 (44)	83 (24)	(p = 0.40)	83 (18)	(p = 0.43)
baseline post bronchodilator	92 (44)	96 (24)	(p = 0.51)	95 (18)	(p = 0.71)
after 1 to 3 months	105 (44)	102 (18)	(p = 0.41)	102 (18)	(p = 0.41)

[1] mean of FEV_1 in percent of predicted
[2] p-values from Mann-Whitney-U-test, reference group = patients with complete follow-up (2 years)
Patients with incomplete follow-up tended to start from higher FEV_1 values than patients with a 2-year follow-up (n = 76).
PO patients: "persistent obstruction" patients
SA patients: "silent asthma" patients

higher than 15%, and 18 heavy smoking PO patients low to very low FEV_1 and ΔFEV_1 % pred. values, as well as hyperinflation (PFTs, chest X-ray). Before the end of 2 year follow-up, we failed to keep track of 48 patients for similar reasons, or because they felt well enough to deny the disease, or because some physicians stopped the treatment in the absence of symptoms. Also, patients with incomplete follow-up tended to start from higher FEV_1 values than patients with a 2-year follow-up (table 5).

In SA patients with perception of functional improvement, ΔFEV_1 % pred. was high at first follow-up assessment and remained high later (figure 4). We made the same observation for PO patients, although with lower ΔFEV_1 % pred. In this group, some patients responded to therapy as seen in chronic bronchitis but could not be classified as SA. This was characterized by a mean ΔFEV_1 % pred. of 19%, lower than the mean value of 30% seen in SA, featuring some overlap between SA and PO patients (figures 2 and 3). ΔFEV_1 % pred. of patients with no perception of improvement was lower for both groups at 1 to 3 month follow-up and even worse after two years.

Discussion

This study illustrates the outcome of UDAO occurring without dyspnoea, cough and wheezing. To our knowledge, it is the first attempt to describe this situation in a private pulmonology practice. The condition was identified in 10.6% of the patients with AO and in 3.9% of the collective. The prevalence may be higher in an unbiased setting as seen in the cohort SAPALDIA: 5.4% [18]. Although our data should not be compared to a population-based study, both results highlight that the lack of these symptoms is not rare. It is a reason for UDAO, mainly in SA. AO seen in PO patients, associated with smoking and sputum, might have been previously diagnosed [1, 6]. The absence of treatment before inclusion induced discomfort, fatigue, recurrent infections and limitation in the quality of life [1, 12, 15, 16, 19, 23, 24].

A poor correlation between the intensity of usual symptoms and the OLD severity has been mentioned [1, 5–9, 11, 12, 16, 18, 25–30]. Teeter et al. extended this discordan**ce** to nocturnal awakening, chest tightness and sputum production, describing "underestimator patients" [7]. However, there are reasons for performing PFTs in the absence of usual AO symptoms (table 3) [1–7, 9, 11–13, 15–19, 28–31]. Sputum for instance, largely present in PO, highlights its belonging to COPD main symptoms [1, 5–7, 13, 14, 19]. Concerning fatigue, a relationship has been shown between its intensity and pulmonary function, exercise tolerance, or quality of life [15, 32]. As even a mild disease may compromise the quality of life, other anamnestic data have to be considered for improving UDAO screening [33].

A less symptomatic AO is not necessarily associated with a slight degree of AO. SA-PO patients presented with moderate or even severe AO (table 4). This observation was seen in adults and elderly patients. Thus, UDAO is related to a higher-than-expected AO degree [2–4, 16, 26, 29]**.** The clinical implications are high. For instance, the risks for surgery performed under general anaesthesia are underestimated if an underlying obstructive disease is not diagnosed [1, 16]. Other risks, such as increased morbidity and mortality, have also been mentioned [2–4]. Finally, misdiagnosed lung volume anomalies might serve as a base for further respiratory impairment, infections and failure [1, 3, 12, 19, 34]. It is of primordial interest that the new COPD classification mentions that some patients do not experience AO symptoms [1].

The treatment could not be standardized because of the subsequent introduction of budesonide, salmeterol and fluticasone. Also, there was a fairly high drop-out rate over time (48%). These facts may limit our ability to draw conclusions from the response seen in each group. However, a separation into SA and PO patients could be made, featuring specific characteristics for the underlying diseases which is an objective of UDAO screening [2–4, 20–22]. SA emerged as a clinical entity with relevance in adults also (tables 2 and 4, figures 1 to 4). SA patients normalized their spirometric values, whereas PO patients did not [1, 12, 13, 19]. On average, both groups showed a decrease in FEV_1 % pred. suggestive of altered AO reversibility and potential ongoing remodelling [1, 12, 13] (figures 2 and 3).

For most SA-PO patients, the evolution was clinically good. This study also highlights the necessity of a treatment as a decisive intervention [1, 12, 13, 21, 22, 29]. As for asthma, SA patients have to be evaluated following remission versus relapse [12]. About 20% could interrupt medication after two years' follow-up. However, 80% had to maintain it due to a relapse, preceded by an asymptomatic decrease in FEV_1 and ΔFEV_1 % pred. mean values (figures 2 to 4) corresponding to persistent asthma [12]. As for COPD, PO patients have to be assessed following the response. Bronchodilators should not be discontinued [1]. Further studies will better define indication to inhaled corticosteroids [1, 13]. The favourable follow-up underlines the importance of UDAO screening but points to its financial impact [2–4].

Less symptomatic AO raises the issue of non-perceiving variations in AO. Reduced perception of dyspnoea was described in asthma and in COPD

[1–11, 30]. A slow increment in bronchoconstriction could induce subjective adaptation to AO [27]. Habituation to symptoms might account for blunted perception of progressive AO [25]. Reduced afferent information, impaired perception of airway tone, and brain centre defect could be involved in a decreased cough reflex [9, 11, 26]. Airflow limitation may precede the onset of wheezing, and some explanations have been proposed for its absence [5, 14, 15, 35]. Research on less symptomatic AO also focuses on the psychological mechanisms by which symptoms are perceived [9, 28, 36, 37].

In this study, differences in AO perception levels have been found under treatment. Although the evaluation could be carried out in only 76 SA-PO patients (52%), it suggests a correlation with the response expressed by the ΔFEV_1 % pred. (figure 4). Patients showing no perception of improvement belong to the group with the lowest increase of ΔFEV_1 % pred., in comparison with patients showing a perception. The absence of perception of improvement is associated with lesser increases of FEV_1. This fact also suggests that a small variation in AO is related to a lesser perception [9, 10, 27].

Reduced perception of AO, even by the physician, is a striking predicament. It appears to be one reason for the drop-out seen in our study, and another one for UDAO [2–3, 5, 7–12, 15, 16, 25–28]. For instance, AO has been described as common but unsuspected by physicians working in a general medical service [38]. Moreover, many UDAO patients had reported AO symptoms without any subsequent diagnosis [2–4]. Therefore, UDAO screening should be improved, especially among non-smokers, by systematic PFTs in the presence of any suggestive symptoms and of AO risk factors, mainly: passive smoking in childhood or adult life, recurrent LRTIs, asthma in childhood and/or in family, rhinitis, and atopy [1–4, 9, 12, 13, 18–19, 31, 39–41].

We conclude that the occurrence of AO in the absence of three main symptoms, i.e. dyspnoea, cough and wheezing, is a fairly frequent finding and a reason for UDAO. It is associated with slight, moderate or even severe AO. The value of ΔFEV_1 % pred. is of clinical interest in identifying UDAO patients, particularly those with SA. This paediatric entity has thus also developed a clinical relevance in adults. Risk factors for UDAO include smoking and other causes, such as reduced AO perception by patients and even by physicians. Therefore, UDAO screening should be improved, especially among non-smokers. The decision regarding long-term treatment must be defined on the basis of response, follow-up and clinical experience.

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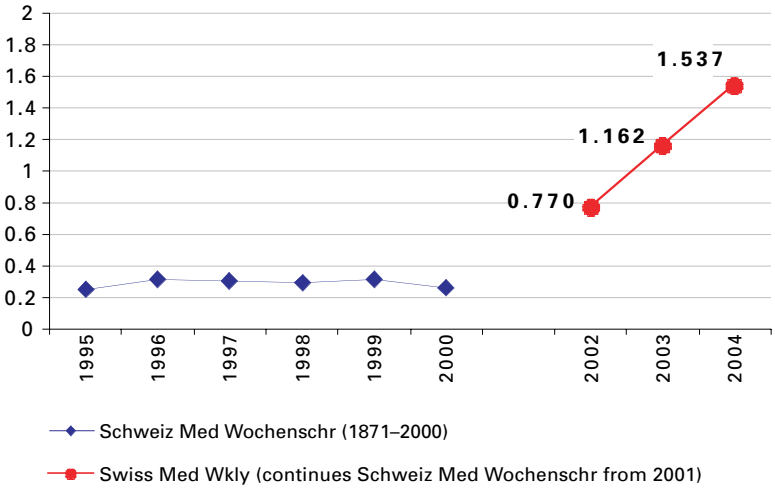

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