

Clinical Communications

Evaluation in a severe asthma expert center improves asthma outcomes regardless of step-up in asthma therapy

Camille Bègne, MD^a, Aurélien Justet, MD^{a,b},
Clairelyne Dupin, MD^a, and Camille Taillé, MD, PhD^{a,b}

Clinical Implications

- We report the French experience of our severe asthma expert center and confirm that a pluridisciplinary assessment at a 1-day hospital stay results in improvements in severe asthma disease management, avoiding treatment step-up in a small but clinically significant proportion of patients.

TO THE EDITOR:

The landscape of severe asthma has undergone considerable changes thanks to a clear and consensual definition of severe asthma,¹ the availability of several highly effective biologic therapies, and the regular update of practical guidelines for the global care of asthma during the past 10 years.^{1,2} All have contributed to improving the disease and reducing its burden. However, getting a severe asthma diagnosis remains a complex process, including tackling of differential diagnosis, comorbidities, and environmental triggers, evaluating adherence, and providing patient education. Severe asthma centers have been developed in several countries to provide high expertise and dedicated support. The benefits of such structures have been demonstrated to be associated with an improvement in asthma control and quality of life and a reduction in health care use, regardless of asthma phenotype.³⁻⁵ However, the improvement has been reported to therapeutic step-up, or to optimization of comorbidities.⁵ The role of overall management, including education and psychological support, has been suggested,⁵ but not investigated.

Among the 175 patients referred by pulmonologists for severe asthma in our expert center between 2014 and 2016 and attending a systematic evaluation during a 1-day visit after screening by an asthma specialist, 119 patients were retrospectively studied (see [Figure E1](#) in this article's Online Repository at www.jaci-inpractice.org). All had already received high inhaled corticosteroid doses and long-acting beta-agonist when referred to this visit. As put forward by McDonald et al,⁶ this pluridisciplinary assessment was aimed at confirming the diagnosis of asthma and severity, but also establishing asthma phenotypes, managing comorbidities, and refining the management plan. All patients underwent medical evaluation and explorations (computed tomography scan, lung function tests, blood samples),² and attended an individual interview with a nurse involved in therapeutic education to ensure a proper use of inhaler technique and to provide personalized written action plan. They were also referred to a dietitian, a psychologist, a tobaccoologist, or a social worker, when needed. All medical

reports were then discussed by the pluridisciplinary team to confirm the diagnosis of severe asthma on the basis of asthma history and symptoms, pulmonary function tests, and computed tomography scan, to list aggravating factors and to propose treatments to improve asthma control. A biologic medicine was prescribed when treatment of comorbidities was optimized and disease understanding was deemed to be suitable with appropriate self-management. We excluded 10 patients (5.7%) in whom another diagnosis than asthma was made. Patients with a 12-month follow-up were retrospectively distributed into the following 3 groups according to the medical decisions made by the pluridisciplinary team during the follow-up:

- Group 1 (N = 49) comprised patients who were prescribed a step 5 asthma therapy, such as oral corticosteroid (OCS), omalizumab, or bronchial thermoplasty or had a change in a step 5 treatment during the follow-up.
- Group 2 (N = 16) comprised patients undergoing at least 1 comorbidity intervention without any prescription of a step 5 treatment or any change in the step 5 treatment during the follow-up.
- Group 3 (N = 54) comprised patients who neither benefited from asthma treatment step-up nor from comorbidity intervention during the follow-up.

Patients in group 1 were proposed the following changes in their step 5 treatments: omalizumab (N = 25), azithromycin (N = 8), bronchial thermoplasty (N = 10), OCS (N = 4), and azathioprine (N = 2). The following scheduled medical interventions were offered in patients in group 2: pulmonary rehabilitation (N = 3), nocturnal ventilation for obstructive sleeping apnea (N = 4), smoking cessation (N = 1), psychiatric care (N = 1), nutritional follow-up by dietitian (N = 1), sleeve gastrectomy (N = 1), and hyperventilation treatment (N = 7).

All baseline characteristics, including asthma control and annual rate of exacerbations, were not significantly different among the groups ([Tables I and II](#)). From the first evaluation at 6 months, the proportion of patients achieving an Asthma Control Test score of 20 or more increased in the 3 groups, then continued to progress at 12 months, with group 3 demonstrating the largest proportion (increased from 11% to 20% at 6 months and 29.5% at 12 months) of controlled patients. This was associated with a decrease in daily dose of OCS and hospitalizations rate ([Table II](#)). No significant changes on FEV₁ were observed ([Table II](#)).

These results on a team-based care approach are close to those previously observed in other health care systems,³⁻⁵ showing similar extend in Asthma Control Test changes⁵ and reduction in asthma exacerbation.³⁻⁵ We also confirm that severe asthma diagnosis was reviewed in a sizable part of the cohort,⁴ although most patients were referred by lung specialists.

Many challenges remain in the management of severe asthma before prescribing biological therapies. In this context, it is relevant to point out that a small but clinically significant proportion of patients in group 3 improved without any add-on therapies (step-up treatment and medical interventions) after a 12-month period. This effect "patient care" may explain a part of

TABLE 1. Demographic and clinical baseline characteristics of the population (N = 119) according to the medical decision making by a pluridisciplinary team at the end of a 1-d visit

Characteristic	All (N = 119)	Group 1 (N = 49)	Group 2 (N = 16)	Group 3 (N = 54)	P value
Demographic					
Age (y)*	50.8 ± 1.3	49.2 ± 2.0	47.4 ± 2.8	53.0 ± 2.0	NS
Sex: female	80 (67.2)	31 (63.3)	13 (81.3)	36 (66.7)	NS
BMI (kg/m ²)*	26.9 ± 0.6	27.2 ± 0.8	27.7 ± 2.0	26.3 ± 0.7	NS
Current smokers	13 (11)	5 (10.2)	3 (18.75)	5 (9.2)	NS
Former smokers	34 (28.5)	17 (34.6)	3 (18.75)	14 (26)	NS
Asthma history					
Age of asthma onset (y)*	26.5 ± 1.8	20.5 ± 2.6	25.8 ± 5.4	32.0 ± 2.7	.013
Asthma treatment					
LAMA	37 (31.1)	15 (30.5)	5 (31.0)	17 (31.5)	NS
Omalizumab	12 (10.1)	6 (12.2)	1 (6.2)	5 (9.2)	NS
Montelukast	60 (50.4)	32 (65.3)	7 (43.8)	21 (38.9)	.023
Azithromycin	15 (12.6)	5 (10.2)	1 (6.2)	9 (16.5)	NS
Daily oral corticoids	31 (26.1)	14 (28.6)	2 (12.5)	15 (27.8)	NS
Dose of prednisone (mg/d)	18.0 ± 2.0	20.4 ± 2.0	45.0 ± 15.0	13.0 ± 1.3	NS
Comorbidities					
Atopy	64 (53.8)	36 (73.5)	9 (56.3)	19 (35.1)	.0005
GERD	60 (50.4)	27 (55.1)	9 (56.3)	24 (44.4)	NS
Chronic rhinosinusitis	58 (48.7)	26 (53.1)	10 (62.5)	22 (40.7)	NS
Nasal polyps	39 (32.7)	15 (30.6)	3 (18.8)	21 (38.9)	NS
OSA	13 (10.9)	6 (12.2)	3 (18.8)	4 (7.4)	NS
Anxiety	29 (24.4)	14 (28.6)	3 (18.8)	12 (22.2)	NS
Depression	16 (13.4)	7 (14.3)	1 (6.2)	8 (14.8)	NS
HVS	40 (33.6)	15 (30.6)	10 (62.5)	15 (27.8)	NS
Cardiovascular disease	28 (23.5)	11 (22.4)	3 (18.8)	14 (25.9)	NS
Diabetes and/or dyslipidemia	23 (19.3)	7 (14.3)	1 (6.3)	15 (27.8)	NS
Lung function testing					
FEV ₁ (% pred)	71.0 ± 2.2	66.6 ± 3.0	82.0 ± 6.5	72.0 ± 3.0	NS
FEV ₁ post-BD (% pred)	78%	73%	90%	78%	NS
FEV ₁ /FVC (%)*	62.0 ± 1.4	59.0 ± 2.3	71.5 ± 1.5	63.3 ± 2.0	NS
RV (% pred)*	148 ± 4.2	147 ± 7.0	144 ± 6.0	149 ± 6.0	NS
RV/TLC*	53.0 ± 3.1	47.0 ± 3.6	60.0 ± 9.0	53.0 ± 5.0	NS
Maximum blood eosinophil count (/mm ³)*,†	532 ± 101	613 ± 160	597 ± 207	596 ± 160	NS

BD, Bronchodilator; BMI, body mass index; FVC, forced expiratory capacity; GERD, gastroesophageal reflux disease; HVS, hyperventilation syndrome; LAMA, long-acting muscarinic antagonist; OSA, obstructive sleeping apnea; NS, not significant; RV, residual volume; TLC, total lung capacity.

Allergy was defined by an allergen-driven asthma confirmed by a skin prick test and/or a specific IgE level of >0.35 ku/L, and/or food allergy and/or atopic dermatitis. HVS was diagnosed in our center by a hyperventilation test.

Data are expressed as n (%).

*Mean ± SD.

†Higher blood eosinophil count in the previous 12 mo.

the dramatic effect observed in the placebo arm in some randomized studies.⁷ More importantly, this emphasizes the role of information and patient education to improve inhalation technique and adherence and increase confidence in treatments and action plan use, and highlights the importance of a pluridisciplinary and expert evaluation, which may give benefits before considering a biologic. Indeed, because patients were mainly referred for treatment step-up, we can consider that a biologic prescription may have been avoided in about 10 patients in group 3 and 2 in group 2 (13.4% of the study population).

Our findings also highlight the importance of asthma training courses for all health care professionals, in order to provide a pluridisciplinary management of severe asthma patients. It is noteworthy to mention that there are no asthma nurses in

France, contrarily in the United Kingdom, for example. Such an approach meets patient expectations because they often ask for some explanation on disease and treatment,⁸ express concern about potential side effect of medications,¹ and claim to access consistent quality care by a specialized severe asthma team.⁹ All this highlights the need for building up health care networks to shorten times for care management, optimize prescribing of costly biotherapies, and facilitate a pluridisciplinary collaborative setting in asthma management.

Of course, this study has a monocentric retrospective design, which may seem like a drawback but is a strength actually, because this study reflects the routine clinical practices in an expert asthma center. Although already well described,⁶ organization of specialized centers depends on local health care systems

TABLE II. Comparison of asthma control, frequency of exacerbations and asthma-related hospital admissions, the use of OCSs, and lung function over the 12-mo follow-up in the analysis population according to the medical decision making by a pluridisciplinary team

Asthma control	All	Group 1	Group 2	Group 3
ACT score				
ACT score				
Baseline	13.4 ± 0.6	12.5 ± 1.0	12.0 ± 1.0	15.0 ± 0.8
At 6 mo	16.3 ± 0.7	15.07 ± 1.1	14.6 ± 1.6	17.2 ± 1.2
At 12 mo	15.7 ± 0.6	14.3 ± 1.0	15.4 ± 1.7	17.3 ± 0.9
<i>P</i> value	<.05	<.05	NS	<.05
Distribution of ACT scores at baseline	(N = 119)	(N = 49)	(N = 16)	(N = 54)
ACT score ≥ 20	10 (8.4)	4 (8.1)	0	6 (11.1)
16 ≤ ACT score ≤ 19	14 (11.7)	5 (10.2)	2 (12.5)	7 (13)
15 ≤ ACT score	95 (79.8)	40 (81.6)	14 (87.5)	41 (76)
Distribution of ACT score at 6 mo	(N = 112)	(N = 47)	(N = 15)	(N = 50)
ACT score ≥ 20	20 (17.8)	9 (19)	1 (6.2)	10 (20)
16 ≤ ACT score ≤ 19	34 (30)	11 (22.4)	7 (43.7)	16 (32)
15 ≤ ACT score	58 (51.7)	27 (57.4)	7 (43.7)	24 (48)
<i>P</i> value	<.05	<.05	<.05	<.05
Distribution of ACT score at 12 mo	(N = 119)	(N = 49)	(N = 16)	(N = 54)
ACT score ≥ 20	29 (24.3)	11 (22.4)	2 (12.5)	16 (29.6)
16 ≤ ACT score ≤ 19	50 (42)	15 (30)	10 (62.5)	25 (46.3)
15 ≤ ACT score	40 (33.6)	23 (47)	4 (25)	13 (24)
<i>P</i> value	<.05	<.05	<.05	<.0001
ACT score increased by ≥3 points				
At 6 mo (N = 112)	37 (33)	15 (32)	4 (26.6)	18 (36)
At 12 mo (N = 119)	51 (42.8)	23 (47)	5 (31.2)	23 (42.6)
Annual exacerbations rate	(N = 119)	(N = 49)	(N = 16)	(N = 54)
Baseline	7.2 ± 0.7	7.3 ± 1.0	8.2 ± 2.0	6.9 ± 1.2
At 12 mo	1.5 ± 0.2	1.8 ± 0.4	1.3 ± 0.4	1.3 ± 2.2
<i>P</i> value	<.001	<.001	<.05	<.001
Annual hospitalizations rate	(N = 119)	(N = 49)	(N = 16)	(N = 54)
Baseline	0.40 ± 0.07	0.40 ± 0.12	0.30 ± 0.15	0.30 ± 0.11
At 12 mo	0.10 ± 0.03	0.10 ± 0.06	0.06 ± 0.06	0.10 ± 0.06
<i>P</i> value	<.001	<.05	NS	<.05
Patients with hospitalizations for asthma	(N = 119)	(N = 49)	(N = 16)	(N = 54)
Baseline	30 (25.2)	11 (22.4)	5 (31.2)	14 (26)
At 12 mo	10 (8.4)	5 (10.2)	1 (6.2)	4 (7.4)
<i>P</i> value	<.001	<.05	NS	<.05
Use of OCSs				
Daily dose of OCS (mg)				
Baseline	16.4 ± 7.3	19 ± 2.0	22.5 ± 3.5	15 ± 5.6
At 12 mo	12.6 ± 5.5	11.2 ± 4.5	5 ± 0	12 ± 5.4
<i>P</i> value	<.05	<.05	NS	NS
Proportion of patients treated with daily OCS	(N = 119)	(N = 49)	(N = 16)	(N = 54)
Baseline	27 (22.6)	15 (30.6)	2 (12.5)	10 (27.7)
At 12 mo	27 (22.6)	16 (32.5)	2 (12.5)	9 (26)
<i>P</i> value	NS	NS	NS	NS
FEV ₁ (%)				
Baseline	71.0 ± 2	66.5 ± 3	82.0 ± 6	72.0 ± 3
At 12 mo	73.0 ± 2	69.0 ± 4	88.0 ± 5	74.0 ± 4
<i>P</i> value	NS	NS	NS	NS

ACT, Asthma Control Test.

Results are expressed as mean ± SD or as n (%). Exacerbation was self-reported by the patient and defined as OCS treatment for more than 3 d, or a 50% increase in daily OCS for more than 3 d, or an emergency department visit, or a hospital admission.

and human and material resources. We also acknowledge that group 1 and group 2 were heterogeneous and somewhat artificial: group 1 gathered patients receiving various drug types and those undergoing bronchial thermoplasty, and group 2 gathered patients undergoing various interventions. As a result, the benefit seems to be low in group 1 and group 2. However, the aim of the study was not to assess the effect of step 5 treatments. The reduction in OCS consumption in some patients may have been masked by the introduction of OCSs in 4 patients in group 1. Finally, the data on asthma exacerbations and hospitalizations were based on self-report, as in the Dutch study,⁴ and may suffer a recall bias. Similarly, during patient education sessions, self-management skills of the disease are taught to avoid hospitalizations. This means a better knowledge of the disease for the patient, but not necessarily better asthma control.

In conclusion, a systematic assessment of severe asthma by a pluridisciplinary team in an expert center improves severe asthma control in a small but clinically significant part of the patients, sometimes without any step up in asthma treatments. This study highlights the importance of setting up specialized asthma centers to provide an appropriate environment for optimizing overall patient care before considering biologic prescription.

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^aService de Pneumologie et Centre de Référence Constitutif des Maladies Pulmonaires Rares, Hôpital Bichat, Groupe Hospitalier Universitaire AP-HP Nord-Université de Paris, Paris, France

^bINSERM UMR 1152, LabEx Inflamex, Paris, France

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Corresponding author: Camille Taillé, MD, PhD, Service de pneumologie, Hôpital Bichat, 46 rue Henri Huchard, 75018 Paris, France. E-mail: camille.taille@aphp.fr. 2213-2198

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METHODS

Study population

Patients were all adult patients who were referred to the asthma expert center at Bichat University Hospital for difficult-to-severe asthma and were eligible for a systematic asthma assessment at a 1-day visit between January 2014 and January 2016. They were identified in the National Hospital Discharge database, and all files were reviewed by 2 pulmonologists (C.B. and C.T.). All patients who refused the use of data from their medical reports in a research setting were excluded from the study.

In our center, patients referred for difficult-to-severe asthma are first assessed over a 45-minute outpatient visit with an asthma specialist. All patients are systematically assessed for asthma-associated comorbidities (dysfunctional breathing, anxiety or depression, obesity, obstructive sleeping apnea, chronic rhinosinusitis and/or nasal polyps, atopy, and gastroesophageal reflux disease). Medication use (adherence and inhaler technique) is evaluated. The level of asthma control is reported using Asthma Control Test, frequency of exacerbations, and number of asthma-related visits/admissions in an emergency department in past 12 months. Lung computed tomography scan and pulmonary function tests, when available, are examined.

At the end of this visit, all patients with an obvious diagnosis, other than severe asthma, and/or failing to take their treatment and/or receiving step 2-3 treatments (Global Initiative for Asthma) are proposed an appropriate treatment and an inclusion in an educational program. They are reassessed, and if they are still uncontrolled, a second outpatient visit can be scheduled. Such patients were excluded from the present study.

Other patients are proposed a second visit (baseline), which takes place a few weeks after first evaluation and is a 1-day stay at hospital for a multidisciplinary assessment, confirming (or not)

the diagnosis of asthma, of severe asthma, establishing severe asthma phenotypes, managing comorbidities and confounding diseases, and refining the management plan. Patients attend an individual interview with a nurse involved in therapeutic education, during which they are asked about medication use issues, including treatment adherence and those related to OCSs, such as phobia, beliefs, and disease understanding, using an interview guide. All patients undergo a nurse-led therapeutic education to ensure a proper use of inhaler technique and to reinforce medication adherence. Personalized written action plan and prescription are provided. In addition, inhaler technique can be changed and/or a spacer prescribed to make adherence easier. Incentives to promote smoking cessation and physical activity are given. If necessary, patients can be referred to a dietitian, a psychologist, a tobaccologist, a physiotherapist, an ENT specialist, a social worker, or any other professional if a visit has been scheduled.

Then, patients undergo functional and laboratory assessments including lung function tests, lung and sinus computed tomography scan, bronchial fibroscopy or induced sputum, skin prick tests, blood tests, and screening for steroids side effects. All medical reports, including the final diagnosis, are then discussed by the multidisciplinary team to decide treatments to improve asthma control. A biologic drug is prescribed when treatment of comorbidities has been optimized and disease understanding is deemed to be suitable with appropriate self-management.

Severe asthma diagnosis is considered on the basis of uncontrolled asthma despite regular high-dose inhaled corticosteroid/long-acting beta-agonist treatment, daily OCS, and after optimal treatment of comorbidities and aggravating factors.

Finally, patients are assessed and managed over a 12-month period. Two outpatient visits are scheduled at 6 months and 12 months, at which treatment can be modified. After 12 months, controlled patients are generally proposed to be referred back to their own pulmonologist.

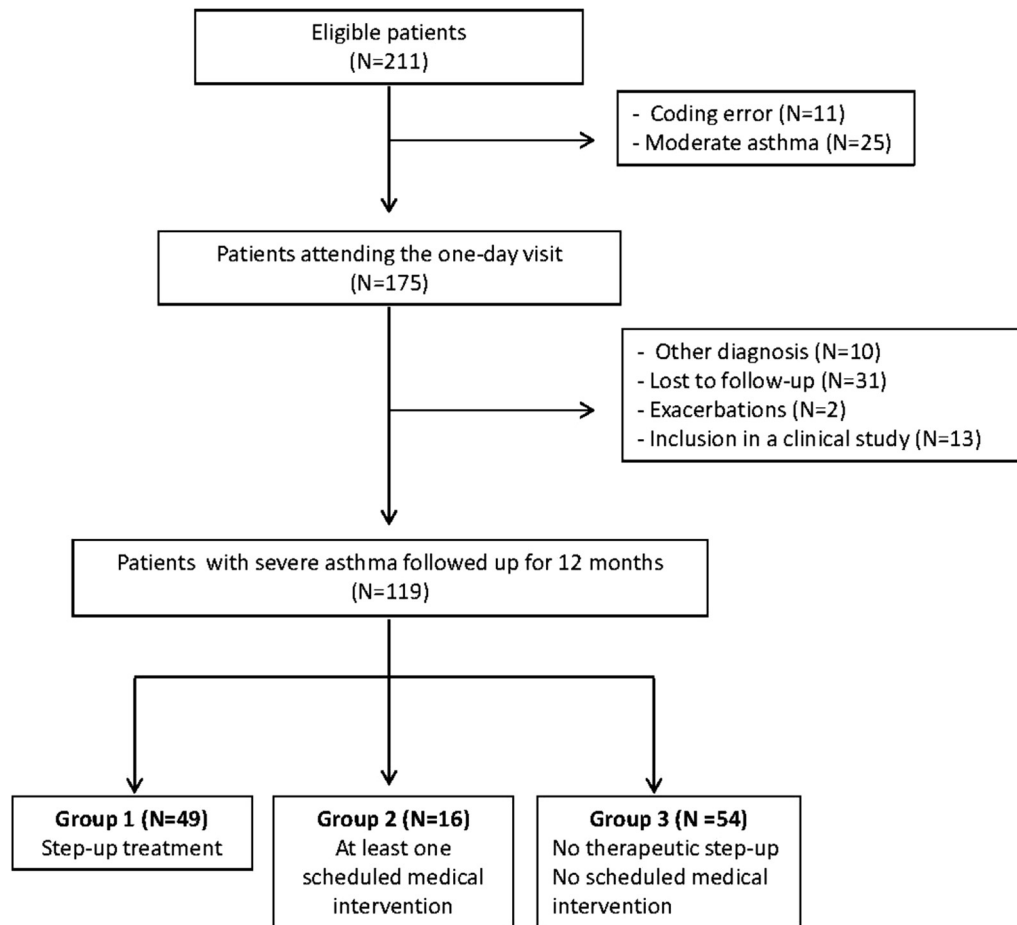


FIGURE E1. Flowchart of patients included in the study analysis.