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ORIGINAL RESEARCH

Characteristics of Older Individuals with Asthma Being Treated with Biologics

Maria Aetou[1,*], Yavor Kiskinov[2,*], Sitraka Faniry Nantenaina Ratsimba[1], Maximilian Barth[1], Carmen Pizarro[2], Ingmar Bergs[1], Jens Spiesshoefer[1], Dirk Skowasch[2,*], Michael Dreher[1,*]

[1]Department of Pneumology and Intensive Care Medicine, University Hospital RWTH Aachen, Aachen, Germany; [2]Department of Internal Medicine II, Cardiology, Pneumology and Angiology, University Hospital Bonn, Bonn, Germany

*These authors contributed equally to this work

Correspondence: Maria Aetou, Department of Pneumology and Intensive Care Medicine, University Hospital RWTH Aachen, Pauwelsstrasse 30, Aachen, Germany, 52074, Tel +0049 2418088763, Email maetou@ukaachen.de

Purpose: Biologic (antibody) therapy is a safe, effective, and guideline-recommended treatment for patients with severe and otherwise uncontrolled asthma. The number of older individuals with asthma is increasing but there is a lack of data on the use of biologics in this cohort. Therefore, this study reports the characteristics of older individuals receiving biologic therapy for severe asthma.

Patients and Methods: This study was a retrospective data analysis conducted at two centers in Germany.

Results: Eighty-eight patients were included (52 aged 50–59 years and 36 aged ≥60 years). There was a high rate of comorbidities and associated pharmacological therapy use. Nearly half (49%) of participants were current or ex-smokers and 29% had chronic obstructive pulmonary disease. The older age group (≥ 60 years) had significantly more cardiovascular comorbidities, more comorbidities overall, and a worse diffusion capacity compared with the group aged 50–59 years. Baseline lung function parameters, and the change in lung function after 6 months of biologic therapy, did not differ significantly between the two age groups. Participants aged ≥60 years used self-injection less than those aged 50–59 years.

Conclusion: These data help to characterize the specific population of older people receiving biologic therapy for severe asthma, and showed a high rate of comorbidities, polypharmacy, and poor diffusion capacity in this group.

Keywords: antibodies, asthma, biologics, elderly, lung function

Introduction

The latest definition of asthma according to the 2024 Global Initiative for Asthma (GINA) Report is a heterogeneous disease, usually characterized by chronic airway inflammation and the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation.[1] Asthma is estimated to affect more than 300 million people worldwide, and its prevalence continues to increase.[2]

Asthma is often thought to be an illness primarily associated with childhood. Even when adolescents and adults describe "new" asthma symptoms, it is often excepted that there was a childhood history of asthma symptoms or an existing asthma diagnosis.[3] However, 4.5% to 12.7% of adults with asthma have a late-onset diagnosis.[4] The clinical characteristics and risk factors in these cases differ from early-onset asthma,[5,6] although there is no difference in disease severity.[7] The prevalence of asthma in individuals aged ≥65 years has been reported to have increased, and these individuals have a high mortality rate.[8] Furthermore, it has been suggested that some older individuals with asthma have recurrent symptoms and poor pulmonary function.[9] Therefore, recognition, diagnosis, and treatment of asthma in older individuals remains a clinical challenge.[10]

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There has been significant recent progress in treatments for asthma.[11] The availability of biologic therapy with monoclonal antibodies has brought significant clinical benefits to the 5–10% of the total asthmatic cohort, as this subset has persistent severe asthma despite the maximum escalation of inhaled pharmacological treatments.[12] One such biologic therapy, dupilumab, has been shown to reduce exacerbations, ameliorate respiratory symptoms, and improve lung function and quality of life, in patients with chronic obstructive pulmonary disease (COPD) and type 2 inflammation compared with placebo.[13]

The presence of non-reversible obstructive lung disease in elderly individuals can make the differential diagnosis between asthma and COPD difficult. Underlying asthma-related airway inflammation in these individuals likely differs from that in younger people and is felt to be non-type 2 mediated.[14] Other factors that need to be considered in older populations before a differential diagnosis and therapy recommendation can be made include smoking history, allergies, comorbidities, existing medication, and age-related pathophysiological changes. However, comorbidities, lung function, and polypharmacy could play an important role in older individuals with asthma who are receiving antibody treatment, and may potentially have a negative impact on the response to therapy. However, this has been rarely studied.

This retrospective analysis of real-world data describes the characteristics of patients with severe asthma aged ≥50 years being treated with biologic therapies, including demographics and comorbidities, concomitant treatments, lung function, and the potential response to treatment.

Materials and Methods

Study Design

This retrospective study was conducted at the University Hospital Aachen and the University Hospital Bonn (both in Germany). The study protocol was reviewed by the local ethics committees (Independent Ethics Committee at the RWTH Aachen Faculty of Medicine [EK 041/21] and Faculty of Medicine in Bonn [EK 134/19]), and the requirement for informed consent to participate was waived. The study was conducted in accordance with Good Clinical Practice guidelines and Declaration of Helsinki principles.

Participants

All patients with severe asthma supervised in the pneumological outpatient-clinics of University Hospital Aachen and University Hospital Bonn between April 2014 and November 2023 who had an indication for biologic therapy were retrospectively screened for eligibility. Individuals with confirmed severe asthma based on the latest German national health care guidelines (NVL) and who were aged ≥50 years at the first administration of a biologic therapy for asthma were included.

Data Collection and Assessments

Clinical patient-related data, pulmonary and laboratory parameters were recorded anonymously in statistical spreadsheets. Patient data were retrieved from the patient data management systems (CGM MEDICO; CompuGroup Medical Clinical Europe GmbH, Koblenz, Germany and ORBIS-KAS-System). Baseline information included demographic data (age, height, weight, sex, smoking status), comorbidities, medication, biologic therapy used, whether biologic therapy was self-administered, pulmonary function test (PFT) results (obtained using full body plethysmography), and blood gas analysis (BGA) from the arterialized earlobe while breathing room air without supplemental oxygen. PFT and BGA data were also obtained after 6 months of biologic therapy. Participants were divided into two groups based on their age: 50–59 years and ≥ 60 years.

Statistical Analysis

Statistical analyses were performed using Sigma PlotTM software (Version 13.0, Systat, Erkrath, Germany). Data are expressed as mean values and standard deviation. The Shapiro–Wilk test was used to determine normality of distribution. For between-group comparisons, unpaired t-tests were used for normally distributed data and Mann–Whitney *U*-tests for non-normally distributed data. For within-group comparisons, paired t-tests were used for normally distributed data and

the Kruskal–Wallis test for non-normally distributed data, with Tukey and Bonferroni post-hoc tests, respectively, for significant differences. A p value of ≤ 0.05 was considered statistically significant.

Results

Study Population

A total of 88 individuals were included. The first biologic therapy was omalizumab in 22,7%, mepolizumab in 21,6%, benralizumab in 30,7%, dupilumab in 13,6%, and tezepelumab in 11,4%; the biologic used was changed in 40% of the total group. Nearly half of the study participants (47.7%) were current or ex-smokers, with a pack-year history of 24.7 ±17.6 years (Table 1). Nearly one-third of the total population (27%) had COPD, and cardiovascular comorbidities were common (Table 2). Multimorbidity (defined as the presence of ≥2 comorbidities) was common, and the number of non-asthma-associated comorbidities was 3.5±2.8 (Table 2). The overall number of non-asthma associated medications was 3.8±3.4 (Table 3), indicating that polypharmacy was common.

Table 1 Participant Demographic and Clinical Characteristics, Overall and by Age Group

Variable	Total (n = 88)	Age Group		
		50–59 Years (n = 52)	≥60 Years (n = 36)	*p* value
Age, years	59.1±6.5	54.9±2.7	65.1±5.5	0.00
Male sex, n (%)	44 (50.0)	28 (53.9)	16 (44.4)	0.39
Height, m	1.7±0.1	1.7±0.1	1.7±0.1	0.71
Body weight, kg	84.0±17.2	84.6±18.1	83.1±16.1	0.68
Body mass index, kg/m²	28.6±5.9	28.8±6.4	28.5±5.3	0.81
Duration of biologic treatment, years	4.2±2.2	4.1±2.3	4.3±2.1	0.73
Exacerbation in the year before initiation of biologic treatment, n (%)	75 (85.2)	45 (90.0)	30 (93.8)	0.56
Self-injection, n (%)	68 (77.3)	45 (86.5)	23 (63.6)	**0.01**
Smoker or ex-smoker, n (%)	42 (47.7)	24 (47.1)	18 (51.4)	0.69
Smoking pack-years, n	24.7±17.6	22.8±16.2	27.2±19.7	0.46
First treatment, n (%)				
Omalizumab	20 (22.7)	10 (19.2)	10 (27.8)	0.35
Mepolizumab	19 (21.6)	13 (25.0)	6 (16.7)	0.36
Dupilumab	12 (13.6)	10 (19.2)	2 (5.6)	0.07
Tezepelumab	10 (11.4)	7 (13.5)	3 (8.3)	0.46
Benralizumab	27 (30.7)	11 (21.2)	16 (44.4)	0.02

Notes: Values are mean ± standard deviation or number of patients (%). P values ≤0.05 are highlighted bold to indicate statistical significance.

Table 2 Details of Comorbidities, Overall and by Age Group

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
COPD, n (%)	24 (27.3)	13 (25)	11 (30.6)	0.63
OSAS, n (%)	11 (12.5)	6 (11.5)	5 (13.9)	0.75
EGPA, n (%)	8 (9.1)	3 (5.8)	5 (13.9)	0.20
ABPA, n (%)	6 (6.8)	3 (5.8)	3 (8.3)	0.64
HES, n (%)	3 (3.4)	2 (3.9)	1 (2.8)	0.79
Chronic rhinosinusitis, n (%)				
Without polyps	19 (21.6)	13 (25.0)	6 (16.7)	0.36
With polyps	13 (14.8)	7 (13.5)	6 (16.7)	0.68

(*Continued*)

Table 2 (Continued).

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
GERD, n (%)	9 (10.2)	6 (11.5)	3 (8.3)	0.63
Atopic neurodermatitis, n (%)	6 (6.8)	6 (11.5)	0 (0.0)	**0.04**
Allergic rhinitis, n (%)	6 (6.8)	3 (5.8)	3 (8.3)	0.64
AERD, n (%)	4 (4.6)	2 (3.9)	2 (5.6)	0.71
Allergic to inhaled allergens, n (%)	59 (67.1)	39 (75.0)	20 (55.6)	0.06
Food allergies, n (%)	10 (11.4)	5 (9.6)	5 (13.9)	0.54
Cardiovascular disease, n (%)	40 (45.5)	19 (36.5)	21 (58.3)	**0.04**
Arterial hypertension, n (%)	45 (51.1)	23 (44.2)	22 (61.1)	0.12
Hyperlipidemia, n (%)	15 (28.4)	12 (23.1)	13 (36.1)	0.19
Type II diabetes, n (%)	13 (14.8)	7 (13.5)	6 (16.7)	0.68
Chronic kidney disease, n (%)	1 (1.1)	1 (1.9)	0 (0.0)	0.41
History of malignancy, n (%)	7 (8.0)	2 (3.9)	5 (13.9)	0.09
Connective tissue disease, n (%)	2 (2.3)	1 (1.9)	1 (2.8)	0.79
Steroid-associated side effects, n (%)	19 (21.6)	13 (25.0)	6 (16.7)	0.49
Number of comorbidities	2.1 ± 2.1	2.1 ± 1.9	2.1 ± 2.4	0.96
Number of non-asthma-associated comorbidities	3.5 ± 2.8	3.1 ± 2.5	3.9 ± 3.1	0.18
Patients without non-asthma-associated comorbidities, n (%)	6 (6.8)	5 (9.6)	1 (2.8)	0.22
Number of non-asthma-associated comorbidities, n (%)				
1	20 (22.7)	12 (23.1)	8 (22.2)	0.93
2	13 (14.8)	9 (17.3)	4 (11.1)	0.43
3	10 (11.4)	6 (11.5)	4 (11.1)	0.95
>3	33 (37.5)	15 (28.9)	18 (50.0)	**0.04**

Notes: Values are mean ± standard deviation or number of patients (%). P values ≤0.05 are highlighted bold to indicate statistical significance.

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; AERD, aspirin-exacerbated respiratory disease; COPD, chronic obstructive pulmonary disease; EGPA, eosinophilic granulomatosis with polyangiitis; GERD, gastroesophageal reflux disease; HES, hypereosinophilic syndrome; OSAS, obstructive sleep apnea syndrome.

Table 3 Medication Details, in the Overall Population and by Age Group

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
SABA, n (%)	61 (70.1)	41 (80.4)	20 (54.6)	**0.01**
ICS, n (%)	4 (4.6)	4 (7.8)	0 (0.0)	0.09
LAMA, n (%)	53 (60.9)	35 (68.6)	18 (51.5)	0.08
LABA, n (%)	3 (3.5)	3 (5.9)	0 (0.0)	0.14
ICS/LABA, n (%)	62 (71.3)	36 (70.6)	26 (75.8)	0.87
LAMA/LABA, n (%)	2 (2.3)	2 (3.9)	0 (0.0)	0.23
ICS/LAMA/LABA, n (%)	20 (23.0)	11 (21.6)	9 (24.2)	0.44
OCS, n (%)	29 (33.3)	17 (33.3)	12 (33.3)	1.00
Montelukast, n (%)	32 (36.8)	19 (37.3)	13 (36.4)	0.91
Azithromycin, n (%)	1 (1.2)	1 (2.0)	0 (0.0)	0.40
Antihistamine, n (%)	19 (21.8)	13 (25.5)	6 (18.2)	0.33
Antiplatelet, n (%)	17 (19.8)	10 (19.6)	7 (21.9)	0.96
β-blocker, n (%)	6 (7.1)	3 (6.0)	3 (9.4)	0.65
Other antiarrhythmics, n (%)	5 (5.9)	4 (8.0)	1 (3.1)	0.33
Statin, n (%)	24 (28.2)	12 (24.0)	12 (37.5)	0.31

(*Continued*)

Table 3 (Continued).

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
ACEi/ARB, n (%)	28 (33.0)	14 (28.0)	14 (37.5)	0.25
CCB, n (%)	13 (15.3)	6 (12.0)	7 (18.8)	0.32
NOAK, n (%)	6 (7.1)	2 (4.0)	4 (12.5)	0.19
Diuretics, n (%)	17 (20.0)	9 (18.0)	8 (18.8)	0.59
Number of concomitant medications	2.5±2.4	2.3±2.3	2.8±2.4	0.50
Number of non-asthma associated medications	3.8±3.4	3.5±3.6	4.2±3.1	0.33

Notes: Values are mean ± standard deviation or number of patients (%). P values ≤0.05 are highlighted bold to indicate statistical significance.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; ICS, inhaled corticosteroids; LABA, long-acting β2-agonist; LAMA, long-acting muscarinic receptor antagonist; NOAK, novel oral anticoagulants; OCS, oral corticosteroids; SABA, short-acting β2-agonist.

There were no significant difference between the groups aged 50–59 years and ≥60 years with respect to demographic and clinical characteristics (Table 1), most comorbidities (Table 2), and medication usage (Table 3). However, self-injection of biologic therapy was significantly more common in those aged 50–59 versus ≥60 years (Table 1), a significantly higher proportion of the ≥60 versus 50–59 years group had cardiovascular comorbidities and a significantly lower proportion had atopic neurodermatitis (Table 2).

Pulmonary Function Data

PFT data at baseline are shown in Table 4, and the percentage change in PFT parameters from baseline to 6 months after initiation of biologic therapy are shown in Table 5. Apart from a significantly more impaired diffusion capacity in

Table 4 Pulmonary Function Test Data at Baseline, Overall and by Age Group

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
TLC, L	6.53 ± 1.54	6.55 ± 1.65	6.51 ± 1.40	0.92
TLC, % predicted	107.19 ± 16.44	106.70 ± 18.13	107.89 ± 13.93	0.74
VC, L	2.91 ± 0.86	3.00 ± 0.85	2.78 ± 0.86	0.24
VC, % predicted	78.85 ± 18.36	76.84 ± 17.85	81.69 ± 18.94	0.23
IC, L	2.50 ± 0.88	2.47 ± 0.80	2.56 ± 1.00	0.65
RV, L	3.56 ± 1.31	3.51 ± 1.45	3.63 ± 1.12	0.69
RV, % predicted	166.26 ± 51.20	170.39 ± 56.73	160.40 ± 42.23	0.37
RV/TLC, % predicted	143.41 ± 33.49	146.67 ± 37.40	138.89 ± 27.00	0.29
FRC, L	4.11 ± 1.33	4.15 ± 1.46	4.05 ± 1.15	0.74
FEV_1, L	14.20 ± 114.73	1.94 ± 0.73	31.57 ± 178.36	0.24
FEV_1, % predicted	62.41 ± 22.53	60.83 ± 21.80	64.69 ± 23.68	0.43
FEV_1/FVC, % predicted	67.69 ± 15.35	68.68 ± 15.55	66.28 ± 15.16	0.48
PEF, L/sec	5.02 ± 1.97	5.04 ± 2.01	4.99 ± 1.96	0.92
MEF 75, L/sec	3.40 ± 2.11	3.50 ± 2.17	3.27 ± 2.03	0.61
MEF 50, L/sec	1.87 ± 1.31	1.97 ± 1.46	1.74 ± 1.08	0.42
MEF 25, L/sec	0.70 ± 0.50	0.73 ± 0.53	0.65 ± 0.46	0.44
Reff, kPa/(L/sec)	0.42 ± 0.20	0.43 ± 0.20	0.40 ± 0.21	0.72
sReff, kPa*sec	2.03 ± 1.23	2.12 ± 1.36	1.91 ± 1.01	0.46

(*Continued*)

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Table 4 (Continued).

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
Rtot, kPa/(L/sec)	0.50 ± 0.25	0.49 ± 0.24	0.51 ± 0.26	0.79
sRtot, kPa*sec	2.38 ± 1.62	2.42 ± 1.65	2.33 ± 1.59	0.81
DLCO SB, % predicted	66.28 ± 20.08	67.26 ± 15.45	64.85 ± 25.69	0.65
RV SB, % predicted	108.38 ± 51.40	100.61 ± 27.51	119.72 ± 72.92	0.16
DLCO/VA, % predicted	80.89 ± 21.12	85.43 ± 19.79	74.27 ± 21.65	**0.05**
PaO_2, mmHg (MV, STD)	70.85 ± 9.87	71.60 ± 10.25	69.80 ± 9.35	0.44
$PaCO_2$, mmHg (MV, STD)	35.17 ± 4.28	34.96 ± 4.32	35.47 ± 4.27	0.61
pH	7.44 ± 0.03	7.44 ± 0.03	7.44 ± 0.03	0.98
Base excess, mmol/L	0.31 ± 1.98	0.12 ± 2.13	0.58 ± 1.75	0.33
Carboxyhemoglobin, Vol%	1.26 ± 1.04	1.43 ± 1.25	1.00 ± 0.57	0.13

Notes: Values are mean ± standard deviation. P values ≤0.05 are highlighted bold to indicate statistical significance.

Abbreviations: DLCO, diffusing capacity of the lungs for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FRC, functional residual capacity; FVC, forced vital capacity; IC, inspiratory capacity; MEF 75, mean expiratory flow at 75% of vital capacity; MEF 50, mean expiratory flow at 50% of vital capacity; MEF 25, mean expiratory flow at 25% of vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; PEF, peak expiratory flow; pH, potential of hydrogen; Reff, effective airway resistance; Rtot, total resistance; RV, residual volume; SB, spontaneous breathing; sReff, effective specific airway resistance; sRtot, total specific resistance; TLC, total lung capacity; VC, vital capacity.

Table 5 Percent Change From Baseline in Pulmonary Function Test Data After 6 Months' Treatment with a Biologic, Overall and by Age Group

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
TLC, L	–2.5 (–5.9, 0.8)	–2.6 (–7.7, 2.6)	–2.5 (–6.3, 1.3)	0.99
TLC, % predicted	–2.4 (–5.8, 1.1)	–2.6 (–7.7, 2.6)	–2.1 (–6.3, 2.1)	0.91
VC, L	9.8 (–0.7, 20.4)	4.0 (–1.2, 9.15)	18.12 (–6.4, 42.7)	0.2
VC, % predicted	3.8 (–0.9, 8.5)	1.4 (–5.2, 8.0)	7.3 (1.0, 13.6)	0.23
IC, L	–1.3 (–6.6, 4.0)	–0.7 (–7.9, 6.41)	–2.2 (–10.2, 5.8)	0.80
RV, L	–3.3 (–13.8, 7.2)	2.7 (–14.4, 19.8)	–11.6 (–18.7, –4.4)	0.2
RV/TLC, % predicted	–4.3 (–10.8, 2.2)	–0.3 (–10.4, 9.8)	–9.6 (–16.1, –3.2)	0.18
FRC, L	–3.0 (–8.9,3.0)	–1.2 (–10.7, 8.3)	–5.2 (–10.9, 0.5)	0.17
FEV_1, L	27.1 (–11.3, 65.6)	9.2 (–0.1, 18.5)	52.8 (–40.0, 145.6)	0.28
FEV_1, % predicted	10.7 (4.5, 16.8)	9.0 (–0.18, 18.2)	13.1 (6.1, 20.1)	0.53
FEV_1/FVC, % predicted	4.4 (0.7, 8.1)	1.9 (–3.3, 7.2)	7.9 (3.2, 12.6)	0.13
PEF, L/sec	6.2 (0.1, 12.2)	6.7 (–2.2, 15.6)	5.6 (–2.3, 13.2)	0.85
MEF 75, L/sec	19.0 (8.6, 29.5)	19.5 (3.4, 35.6)	18.4 (7.2, 29.6)	0.92
MEF 50, L/sec	15.0 (3.0, 26.9)	15.6 (–3.0, 34.3)	14.1 (1.5, 26.6)	0.90
MEF 25, L/sec	16.6 (2.8, 30.4)	9.7 (–7.37, 26.8)	25.7 (2.8, 48.5)	0.28
Reff, kPa/(L/sec)	10.0 (–0.3, 20.4)	13.0 (–2.1, 28.1)	5.1 (–8.2, 18.5)	0.72
sReff, kPa*sec	–6.1 (–12.8, 0.6)	–5.8 (–15.5, 3.9)	–6.5 (–15.1, 2.2)	0.93
Rtot, kPa/(L/sec)	8.0 (–6.1, 22.0)	14.9 (–7.3, 37.0)	–1.8 (14.2, 10.8)	0.27
sRtot, kPa*sec	–4.1 (–12.3, 4.1)	–2.9 (–15.4, 9.5)	–5.6 (–15.3, 4.1)	0.76
DLCO SB, % predicted	3.9 (–1.4, 9.2)	1.1 (–3.7, 5.8)	7.5 (–3.5, 18.4)	0.53
RV SB, % predicted	10.9 (4.3, 17.5)	5.5 (–2.6, 13.7)	17.6 (6.5, 28.6)	0.34
DLCO/VA, % predicted	–1.3 (–4.2, 1.7)	1.4 (–1.3, 4.1)	–4.6 (–10.5, 1.4)	0.29
PaO_2, mmHg	2.0 (–1.8, 5.7)	0.0 (–5.4, 5.5)	4.4 (–0.5, 9.3)	0.40

(*Continued*)

Table 5 (Continued).

Variable	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
$PaCO_2$, mmHg	1.4 (–1.1, 4.0)	–0.1 (–3.7, 3.5)	3.4 (–0.2, 6.9)	0.33
pH	–0.1 (–0.2, –0.03)	–0.1 (–0.3, –0.0)	–0.1 (–0.3, 0.0)	0.86
Base excess, mmol/L	96.3 (–99.1, 291.7)	62.6 (–243.7, 368.9)	139.7 (–67.3, 346.6)	0.78
Carboxyhemoglobin, Vol%	24.8 (13.4, 36.2)	24.2 (10.7, 37.7)	25.8 (5.3, 46.3)	0.93

Notes: Values are mean change from baseline (95% confidence interval).
Abbreviations: DLCO, diffusing capacity of the lungs for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FRC, functional residual capacity; FVC, forced vital capacity; IC, inspiratory capacity; MEF 75, mean expiratory flow at 75% of vital capacity; MEF 50, mean expiratory flow at 50% of vital capacity; MEF 25, mean expiratory flow at 25% of vital capacity; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; PEF, peak expiratory flow; pH, potential of hydrogen; Reff, effective airway resistance; Rtot, total resistance; RV, residual volume; SB, spontaneous breathing; sReff, effective specific airway resistance; sRtot, total specific resistance; TLC, total lung capacity; VC, vital capacity.

Table 6 Biomarker Details, in the Overall Population and by Age Group

Variable at Baseline	Total	Age Group		
		50–59 Years	≥ 60 Years	*p* value
Eosinophilic blood count (MV, STV); /nl	422.21±448.37	423.92±471.50	419.71±419.09	0.97
IgE level (MV, STD); kU/l	542.12±840.16	560.95±837.30	513.57±857.55	0.81

Notes: Values are mean ± standard deviation.
Abbreviation: IgE, Immunglobuline E.

participants aged ≥60 versus 50–59 years, there were no significant differences in baseline or follow-up PFT data between the two age groups.

Biomarker

Asthma associated biomarker data at baseline are shown in Table 6. There was no statistical significance whether related to the eosinophilic blood count nor the total IgE level in serum between the two age groups.

Discussion

This retrospective study describes the clinical characteristics of an older population of individuals with asthma who were being treated with biologic therapy. Overall, these people had a significant smoking history, and therefore comorbid COPD was quite common; in particular, the older age group (≥60 years) had impaired diffusion capacity. In addition, more than two-thirds of participants had comorbidities, polypharmacy was common, and self-injection of biologics was less common in the older age group. Although it has been shown that biologics are effective in patients with asthma who have a smoking history,[15] and in patients with COPD and those with impaired diffusion capacity,[13] it is still not clear how smoking overall impacts on antibody selection and the long-term effects of biologic therapy.

Our findings are clinically relevant due to the growing proportion of patients with asthma who are diagnosed at an older age. In addition, the first positive results for biologics in patients with COPD[13] mean that it is likely that more older individuals will be treated with these agents. In that context, the factors identified in this study will be important to take into account, including comorbidities, polypharmacy, ability to self-inject biologics, smoking history, and impaired diffusion capacity.

Although biologics have played a crucial role in the treatment of severe asthma since 2009,[16] all landmark trials for biologic therapy used to support regulatory approvals primarily included patients aged <75 years and had exclusion criteria relating to comorbidities that are common in the elderly; the average age of the patients included in these studies was around 50 years.[17–21] This limits the applicability of clinical trial data to older adults.[22] There is therefore a need to address the knowledge gap regarding use of biologic therapy for respiratory disease in adults aged ≥50 years. The

coexisting conditions in this population make the diagnosis and therapy challenging.[23] As highlighted by our data, two of these challenges are multimorbidity and polypharmacy. However, most clinical practice guidelines focus on single diseases, leading to care that is sometimes inadequate and potentially harmful.[24]

Our study did not find any significant difference between patients aged 50–59 years versus ≥60 years in the rate of COPD as comorbidity, smoking pack-years, lung function (other than diffusion capacity), and the lung function response to 6 months of biologic therapy and the biomarkers at baseline. These data suggest that, among older individuals with asthma, age does not appear to have a strong influence on the choice of and response to biologic therapy. These results are in line with data from the few other available observational studies that have shown similar benefits of antibody therapies in elderly individuals as seen in non-elderly adults.[22] To the best of our knowledge, data for this comparison are only available for benralizumab,[25] whereas participants in our study were being treated with a variety of different biologic agents.

Our finding that individuals with severe asthma being treated with biologics who were aged ≥ 60 years had more cardiovascular comorbidities than those aged 50–59 years could be clinically relevant because underlying cardiovascular comorbidities could have an impact on the effectiveness and tolerability of biologic therapy. However, our analysis did not show any difference in lung function parameters after 6 months of biologic therapy in the group aged ≥60 versus 50–59 years. The high rate of cardiovascular comorbidity in the group aged ≥ 60 years suggests that screening for these conditions should be performed routinely.

Another interesting finding of our study was that the group aged 50–59 years were significantly more likely to self-inject biologic therapy than those aged ≥ 60 years. This is another thing that needs to be taken into account when prescribing biologics to older individuals. Self-administration of biologics has always been a possibility but the home administration of biologics became more frequent during the COVID-19 pandemic. The transition from hospital to home administration is an important innovation because it could help relieve the burden on stressed health system components such as medical centers and practices. However, set-up of home administration of biologics needs to be performed clinicians with adequate expertise in the field of severe asthma and biologic therapies, in cooperation with other health professionals, pharmacists, and general practitioners.[26]

Despite the considerable size of the elderly asthma population and the economic societal burden imposed by this specific demographic, there is currently limited research focusing on this group.[16] As the options for pharmacologic therapy of asthma expand, it will be crucial to include older participants in large clinical trials so that the effects of therapy in this at-risk and growing population are better understood.[14] Topics that need to be addressed and evaluated in detail include possible differences in biologic responses based on age-related physiologic and immunologic changes in combination with comorbidities and concomitant medication, along with the potential use of new biomarkers to predict treatment response (in addition to those that have already been established (such as immunoglobulin E and eosinophil levels).

Although addressing an important knowledge gap regarding the real-world characteristics of older individuals with severe asthma being treated with biologics, our study does have important limitations that needs to be taken into account when interpreting the findings. This is its retrospective design, which means that we do not have data on important parameters such as blood inflammatory and cellular biomarkers of asthma disease severity, long-term observational follow-up, and a comprehensive assessment of patient symptoms. These data should be addressed by future studies, aiming to a better understanding and subsequently targeted therapy of this subset of asthmatic patients.

Conclusion

In conclusion, the present real world clinical study shows that older patients with asthma are facing a significant number of comorbidities, with more cardiovascular comorbidities and more impaired diffusion capacity with increasing age. Yet, older age does not seem to alter lung function response and general tolerability of antibody treatment in the present study. In addition, our study highlights that polypharmacy is present in this patient population and while no specific systematic difference in the particular type of antibody chosen was found in the present trial very old patients were less able to self-inject the antibody.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement of Ethics

Study approval statement: The study protocol was approved by the Institutional Review Boards for Human Studies at RWTH University, Aachen, Germany and University of Bonn, Germany. All study procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki and its latest revision.

Consent to participate statement: Due to the retrospective study design, the requirement for informed consent to participate was waived by the local ethics committees (Independent Ethics Committee at the RWTH Aachen Faculty of Medicine [EK 24-130] and Faculty of Medicine in Bonn [EK 134/19]). All patient related data was pseudonymised and saved on password protected computer in our university hospitals. Hence patient related data confidentiality was ascertained.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors have no conflicts of interest in the context of the present manuscript to declare. This study was not supported by any sponsor or funder.

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