The German Severe Asthma Registry:
Obesity is associated with asthma parameters

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German Asthma Net e.V.

Introduction

Obesity is a risk factor for asthma severity[1]. This study aims to evaluate associations of obesity with severe asthma parameters in the German Severe Asthma Registry including 1065 patients (26% obese (BMI≥30 kg/m²)), 107 treated with anti-IgE and 237 with anti-IL5(R) antibodies, with a max. recorded therapy length of 12.5 years.

Table 1. Total patients, n=	**1065**
Mean age, years	49 ± 17
Female, %	58%
Mean BMI, kg/m² (obese, %)	27 ± 6 (26%)
Biological therapy, n=	344
FEV1, % of predicted	65 ± 21

More than 10 exacerbations/year were suffered by 11.6% of patients, whilst 16.4% had none, and 31.5% had a lifetime severe exacerbation. Furthermore, 41% were OCS-dependent.

Methods

Cross-sectional analysis of a severe asthma registry conducted at multiple tertiary referral centres in Central Europe. Patients included from Nov 2010 to Okt 2019 with evaluations including lung function scores, blood and sputum analysis, thorough patient history and medication[2], quality of life evaluations. Statistical evaluation was conducted w. SPSS, Graphpad, Excel© incl. ANOVA, ChiQ, student t-test with a cut-off level of p < 0,05.

Conclusions

In our severe asthma cohort, obesity represents a specific phenotype of severe asthma that is significantly associated with exacerbations, worse quality of life, lower blood eosinophil numbers, as well as lower FEV1, and FVC.

Bibliography

[1] Dixon et al. in Chung KF, Israel E, Gibson PG, eds. Severe Asthma (ERS Monograph). Sheffield, European Respiratory Society, 2019; pp. 93–112

[2] Holguin et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020;55(1)

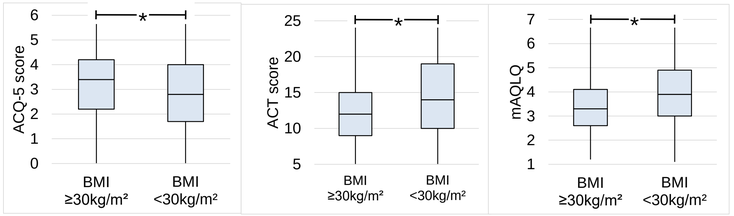
Table 2. Characteristics of obese patients

	≥30kg/m² *(n = 276)*	**<30kg/m²** *(n = 789)*
Anti-IgE therapy, n (%)	27 (10%)	80 (10%)
Anti-IL5 therapy, n (%)	53 (23%)	184 (19%)
Inhalative therapy, n (%)	196 (67%)	525 (71%)
BMI (kg/m²)	35 (5)	24 (4)
height (cm)	168 (9)	168 (12)
weight (kg)	100 (17)	69 (15)
age (years)	**53 (13)**	**48 (18)**
female, n (%)	170 (62%)	444 (57%)
onset after age of 12, n (%)	**196 (73%)**	**533 (70%)**
severe exac. (/12 mon., %)	94 (34%)	242 (31%)
OCS (mg)	7.5 (16.4)	5.8 (12.5)
OCS use, n (%)	**123 (45%)**	**308 (39%)**
IgE (U/mL)	403 (682)	412 (751)
sputum eosinophilia (%)	3.4 (6.3)	5.8 (5.2)
sputum neutrophilia (%)	60.6 (20.7)	55.0 (18.9)
pCO2 (mmHg)	36 (4)	36 (4)
pO2 (mmHg)	**71 (10)**	**75 (11)**
FEV1/FVC (%)	66 (14)	65 (15)
RV (% of norm)	175 (63)	162 (63)
TLC (% of norm)	109 (18)	108 (24)

Displayed as mean (SD). % of total are calculated from total measured. Definition of abbreviations: BMI = body mass index, OCS = oral corticosteroids, pCO2 = partial pressure of CO2 in blood, pO2 = partial pressure of oxygen in blood.

The same proportion of obese patients received biologics as non-obese patients, but obese patients were more frequently on **LAMA therapy** (60% vs. 51% **p=0.01**).
OCS-dependent patients were more obese than patients without OCS (27.7 ± 5.9kg/m² vs. 26.5 ± 6.3kg/m², **p=0.001**). In regression analysis, OCS-dependency was predicted in severe asthmatics with a BMI cut-off above 39 kg/m². An increase in BMI conferred an OR of 1.034 per kg/m² for OCS-dependency (**p=0.001**).
Patients with later **asthma onset** had higher BMI (27.4 ± 5.7 vs. 26.0 ± 7.1, **p=0.004**). Obese patients were **older** (**p<0,001**).
Obesity was associated with worse partial pressure of oxygen in blood (**pO2**, **p=0.001**).

Obesity leads to worse **quality of life** and asthma control

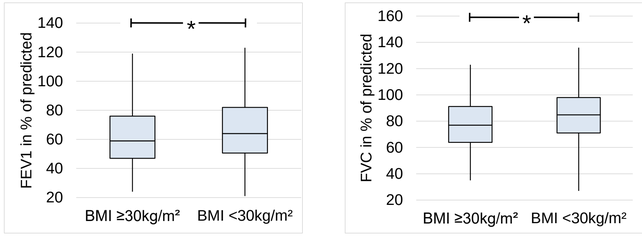


Obese patients had worse quality of life, as reflected by worse ACQ (3.2±1.4 vs. 2.8±1.5), ACT (12±5 vs. 15±5) and mAQLQ scores (3.5±1.2 vs. 4.0±1.3; all **p<0.001**). Patients reaching asthma control (defined as ACQ score ≤ 1,5 ACT score ≥ 20, mAQLQ ≥ 5.4) were significantly less often obese than uncontrolled patients (ACQ 88% vs. 78%, **p=0.002**; ACT 89% vs. 78% and mAQLQ 93% vs. 83%, both **p<0.001**; also see table 3.b).
Obesity was also associated with worse quality of life under anti-IgE or anti-IL5 therapy (table 3.a). No post-hoc difference could directly be detected between therapies.

Table 3.a, quality of life:	**anti-IgE ≥30kg/m²**	**anti-IgE <30kg/m²**	**anti-IL5 ≥30kg/m²**	**anti-IL5 <30kg/m²**	*p-value*
ACQ-5 score	3.6 (1.3)	3.3 (1.3)	3.3 (1.3)	3.0 (1.4)	*<0.0001*
ACT score	11 (5)	13 (5)	13 (5)	15 (5)	*<0.0001*
mAQLQ score	2.9 (0.8)	3.7 (1.3)	3.5 (1.2)	3.9 (1.2)	*<0.0001*

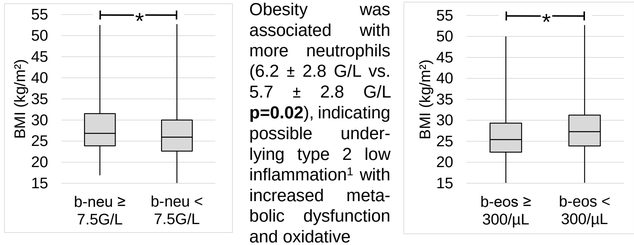
Table 3.b BMI:	**Un-controlled**	**Controlled**	*p-value*
ACQ	27.4 (6.3)	25.1 (5.9)	*<0.0001*
ACT	27.4 (6.0)	25.4 (5.9)	*<0.0001*
mAQLQ	27.4 (6.2)	24.3 (6.2)	*<0.0001*

Obesity is associated to worse **lung function values**



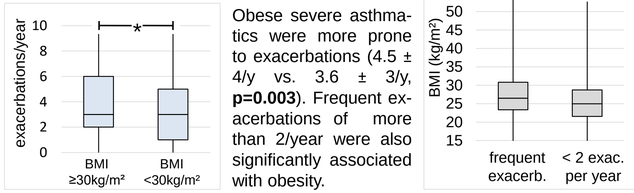
Obesity was associated with lower lung function parameters: FEV1 (1.8±0.7L vs. 2±0.8L, or in % of predicted: 62±21% vs. 66±21%, **p=0.01**) and FVC (2.8±1L vs. 3.1±1L , or: 77±19% vs. 84±19%, **p<0.001**).

Obesity is associated with **neutrophilia**, less eosinophils



Obesity was associated with more neutrophils (6.2 ± 2.8 G/L vs. 5.7 ± 2.8 G/L **p=0.02**), indicating possible underlying type 2 low inflammation[1] with increased metabolic dysfunction and oxidative stress (see comorbidities). Obesity was also associated with reduced blood eosinophils with a threshold of 300 cells/µL (37% vs. 53%, **p<0.001**). Patients with blood eosinophilia had a mean BMI of 26.2±5.6, with less than 300 eos/µL 28.1±6.2 kg/m². Total IgE or sputum data did not yield significant results.

Obesity and **exacerbation** frequency



Obese severe asthmatics were more prone to exacerbations (4.5 ± 4/y vs. 3.6 ± 3/y, **p=0.003**). Frequent exacerbations of more than 2/year were also significantly associated with obesity.

Obesity is associated with **comorbidities**

Table 4. Comorbidities

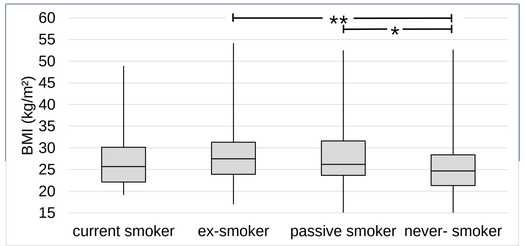
% comorbidity	*in obese:*	*in non-obese:*	*sign.*
GORD	124 (45%)	255 (34%)	*p=0.001*
depression	49 (18%)	87 (11%)	*p=0.009*
art. hypertonia	159 (58%)	199 (26%)	*p<0.001*

mean BMI	*with comorb.:*	*without c.m.:*	*sign.*
GORD	28.1 (6)	26.4 (6)	*p<0.001*
depression	28.6 (7)	26.8 (6)	*p=0.004*
art. hypertonia	30.0 (6)	25.5 (6)	*p<0.001*
CSwNP	27.3 (6)	26.6 (6)	*p=0.067*
bronchiectasis	25.3 (6)	27.1 (6)	*p=0.075*
COPD	28.4 (7)	27.0 (6)	*p=0.082*

Displayed as mean (SD) or n (%). Definition of abbreviations: GORD: Gastro-esophageal reflux disease, CSwNP: chronic sinusitis with nasal polyps, COPD: chronic obstructive pulmonary disease

Obese severe asthmatics had a higher burden of comorbidities than non-obese patients, including GORD, depression and hypertonia. GORD had a prevalence of 45% in obese patients, vs. a third of non-obese (**p=0.001**). More than half of obese patients had arterial hypertonia, double as much as non-obese asthmatic patients (**p<0.001**). Patients with arterial hypertonia had a mean BMI of 30 kg/m², compared to 25.5 kg/m² in patients without. Likewise, depression had a significantly increased prevalence in obese patients (**p=0.009**). Pathophysiologically disconnected comorbidities such as COPD, bronchiectasis and CSwNP were not associated with obesity in severe asthmatic patients.

Any smoking is associated with obesity



Non-obese patients were significantly more often non-smokers (**p<0.001**). Obese patients however were significantly more ex-smokers, and more passive smokers (ANOVA: **p<0.001**).

Table 5. Smoking behavior	**obese (≥30kg/m²)**	**non-obese (<30kg/m²)**	*p-value*
	(n = 276)	*(n = 789)*	
current smoker, n (%)	6 (2%)	20 (3%)	*ns*
ex-smoker, n (%)	**132 (48%)**	**296 (38%)**	***p=0.003***
passive smoker, n (%)	64 (23%)	139 (18%)	*p=0.050*
never-smoker, n (%)	**74 (27%)**	**334 (42%)**	***p<0.001***