Normal Weight but Low Muscle Mass and Abdominally Obese

JAMDA 18 (2017) 533–538

JAMDA

journal homepage: www.jamda.com

Original Study

Normal Weight but Low Muscle Mass and Abdominally Obese: Implications for the Cardiometabolic Risk Profile in Chronic Obstructive Pulmonary Disease

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Keywords:
COPD
exercise training
cardiovascular disease
metabolic health

A B S T R A C T

Background: It is well established that low muscle mass affects physical performance in chronic obstructive pulmonary disease (COPD). We hypothesize that combined low muscle mass and abdominal obesity may also adversely influence the cardiometabolic risk profile in COPD, even in those with normal weight. The cardiometabolic risk profile and the responsiveness to 4 months high-intensity exercise training was assessed in normal-weight patients with COPD with low muscle mass stratified by abdominal obesity.

Methods: This is a cross-sectional study including 81 clinically stable patients with COPD (age 62.5 ± 8.2 years; 50.6% males; forced expiratory volume in 1 second 55.1 ± 19.5 percentage predicted) with fat-free mass index <25th percentile eligible for outpatient pulmonary rehabilitation. Body composition, blood biomarkers, blood pressure, physical activity level, dietary intake, and physical performance were assessed at baseline and in a subgroup after 4 months of exercise training.

Results: Mean body mass index was 22.7 ± 2.7 kg/m^2, and 75% of patients had abdominal obesity. Abdominally obese patients had higher glucose, insulin, homeostatic model assessment for insulin resistance (HOMA-IR), branched chain amino acids and a higher prevalence of metabolic syndrome compared with those without abdominal obesity. Exercise training improved cycling endurance time and quadriceps strength, but did not yield a clinically meaningful improvement of the cardiometabolic risk profile. Triglycerides showed a significant decrease, while the HOMA-IR increased.

Conclusion: Abdominal obesity is highly prevalent in normal-weight patients with COPD with low muscle mass who showed an increased cardiometabolic risk compared with patients without abdominal obesity. This cardiometabolic risk profile was not altered after 4 months of exercise training.

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by persistent airflow limitation resulting from inflammation and remodeling of the airways.[1] Besides respiratory impairment, systemic disease manifestations influence disease burden and mortality risk.[1] It is well-established that both musculoskeletal impairment and elevated cardiovascular risk are common in COPD. Low muscle mass in COPD not only contributes to decreased physical performance and decreased health status,[2,3] but it is also a determinant of mortality.[4] In normal-to-overweight patients with

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This work was supported by the Lung Foundation Netherlands grant 3.4.12.023 and 3.4.09.003.

The authors declare no conflicts of interest.

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http://dx.doi.org/10.1016/j.jamda.2016.12.081
1525-8610/

COPD, low muscle mass is accompanied by a relative abundance of fat mass. There is increasing evidence that adiposity significantly contributes to the systemic inflammatory load in COPD,[5] independent of body mass index (BMI).[6] Furthermore, several studies reported an excessive abdominal visceral fat mass in COPD, independent of BMI, subcutaneous fat mass, or abdominal circumference.[7–9] Disproportionally large abdominal visceral fat mass has been associated with low-grade systemic inflammation, which in turn was strongly predictive for the risk of all-cause and cardiovascular mortality in older persons with airflow obstruction.[8]

In the current obesogenic society, low muscle mass may frequently coexist with abdominal obesity, also in normal-weight patients with COPD. In healthy persons, the "metabolically obese normal-weight" (MONW) phenotype, characterized by normal BMI but increased body fat and reduced muscle mass, was associated with metabolic abnormalities.[10,11] Furthermore, the MONW phenotype is characterized by increased amount of visceral fat, increased liver and muscle fat content, and adipose tissue inflammation.[12–14] We hypothesize that next to diet and physical activity,[15,16] (a history of) smoking[1] and specific disease induced triggers (eg, inflammation and muscle wasting) may render in particular patients with COPD susceptible to develop the MONW phenotype. Exercise training is a cornerstone of pulmonary rehabilitation (PR) to improve physical functioning in COPD. In other conditions (eg, obesity and diabetes), exercise training is also an established intervention to enhance cardiometabolic health.

The cardiometabolic consequences of relative adiposity, however, have not been investigated in this subgroup of patients with COPD, as the focus has primarily been on adverse effects of low muscle mass on muscle function and exercise performance. Next to adiposity, loss of skeletal muscle oxidative capacity has been suggested to play a major role in "metabolic inflexibility,"[17] in which the capacity to switch from fat to carbohydrate oxidation in response to nutritional circumstances is reduced.[18] Metabolic inflexibility has been associated with insulin resistance (IR).[17] Muscle oxidative capacity is decreased in many patients with COPD because of a type I-to-II muscle fiber type shift.[19,20] In COPD patients with low appendicular muscle mass, skeletal muscle oxidative capacity is even more affected.[21] Furthermore, Maddocks et al[22] showed in normal-weight COPD patients an inverse correlation between type I muscle fibers and intramuscular fat infiltration assessed by computed tomography analysis.

The objective of the present study was to investigate the cardiometabolic risk profile of normal-weight COPD patients with low muscle mass stratified by abdominal obesity and to explore the responsiveness to 4 months of high-intensity exercise training.

Methods

A detailed methodology can be found online in the Supplementary material.

Study Design and Participants

The research question was incorporated as prescheduled analysis of the NUTRAIN-trial investigating the efficacy of targeted nutrition as adjunct to exercise training.[23] Patients were recruited from CIRO, Horn, The Netherlands, between 2011 and 2014. The study population included a total of 81 COPD patients with low muscle mass eligible for outpatient PR. Low muscle mass was defined as a fat-free mass index under the sex- and age-specific 25th percentile values,[24] assessed by DEXA (Lunar Prodigy system; GE Healthcare, Madison, WI). The study was registered at clinicaltrials.gov (NCT01344135), and ethical approval was granted by the Medical Ethics Committee from Maastricht University Medical Centre + (NL34927068.10/MEC 11-3-004). Written informed consent was obtained from all patients. Cross-sectional analysis involved the total study group, but only the placebo group of the NUTRAIN trial was included to investigate the cardiometabolic response to exercise training as the intervention group received nutritional supplementation that could have modified this response.

Measurements

Measurements were performed at CIRO during pre- and post-rehabilitation assessment. BMI was calculated and the ratio of percentage fat mass (FM) in the android to the gynoid region measured by dual energy x-ray absorptiometry (DEXA) was used as a measure for abdominal FM. Abdominal obesity was defined by android/gynoid percentage FM >1.0 for men and >0.8 for women, as previously reported.[15,25,26]

Cardiometabolic risk markers were measured including glucose, insulin, homeostatic model assessment to estimate insulin resistance (HOMA-IR), triglycerides, high and low density lipoprotein cholesterol, high-sensitive C-reactive protein, and branched chain amino acids (BCAAs). Blood pressure was measured and metabolic syndrome was defined.[27] Furthermore, medication use and comorbidities were recorded based on medical history and self-report, respectively.

Lung function was measured using forced spirometry and the diffusing capacity of the lung for carbon monoxide (DLCO) was measured using the single-breath method. Smoking status was based on self-report and was categorized as smokers, former smokers, and never smokers. Physical performance was measured by cycle endurance time (CET), isometric muscle strength, and 6-minute walk distance (6MWD). Physical activity level was measured using accelerometers. Dietary intake was assessed using a validated cross-check dietary history method.[28]

High-Intensity Exercise Training

According to the latest PR recommendations,[29] patients received 40 supervised exercise training sessions, 2 to 3 times a week, including progressive high-intensity interval and endurance exercise by cycle ergometry and treadmill walking.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS v 22 for Windows; SPSS Inc, Chicago, IL). The Shapiro-Wilk test was used to assess data for normal distribution. Parametric data were presented as mean ± standard deviation, and nonparametric data were presented as median (interquartile range). Differences between groups were compared using Student *t*-test for continuous variables, χ^2-test for categorical variables, and Kruskal-Wallis test for continuous variables with skewed distributions. Correlations were tested using Pearson's r or Spearman's ρ. The paired t-test or Wilcoxon signed-rank test was used to assess the effect of exercise training on cardiometabolic risk parameters. Differences were considered to be statistically significant at P value of $<.05$.

Results

Mean ± standard deviation age of the patients was 63 ± 8 years, and 50.6% were male patients. The proportion of smokers, former smokers, and never smokers was 25.0%, 73.8%, and 1.3%, respectively. The majority of the patients had moderate-to-severe COPD (Global Initiative for Chronic Obstructive Lung Disease I/II/III/IV: 11.1%/49.4%/30.9%/8.6%). The average DLCO was 49.4 ± 14.6 %predicted, indicative of emphysema.[30,31]

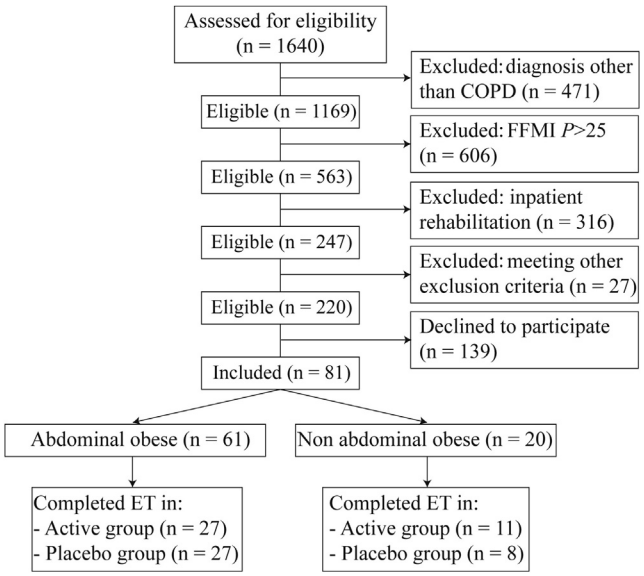

Fig. 1. Participant flowchart. ET, exercise training; FFMI, fat free mass index.

Abdominal vs Non-abdominal Obesity

Abdominal obesity was present in 61 of the 81 patients (75%) (Figure 1). Forced expiratory volume in 1 second and DLCO were comparable between groups, but patients with abdominal obesity had lower residual volume, total lung capacity, and intra-thoracic gas volume (Table 1). Although patients with abdominal obesity had a higher BMI, their fat-free mass index was not significantly different from those without abdominal obesity. Furthermore, the groups were not significantly different in bone mineral density.

Table 1
Characteristics of COPD Patients With Low Muscle Mass Stratified by Abdominal Obesity

	Abdominal Obesity (n = 61)	Nonabdominal Obesity (n = 20)	*P* Value
General Characteristics			
Age, years	63.3 ± 8.1	60.0 ± 8.2	.111
Males, n (%)	33 (54.1)	8 (40.0)	.274
Smoking status*			
Current smoker, n (%)	14 (23.0)	6 (31.6)	.574
Former smoker, n (%)	46 (75.4)	13 (68.4)	
Never smoker, n (%)	1 (1.6)	0 (0.0)	
Lung function			
FEV_1, %pred	54.1 ± 17.9	58.1 ± 24.0	.432
FVC, %pred	97.8 ± 16.3	98.2 ± 16.9	.924
FEV_1/FVC, %	39.3 ± 11.0	43.9 ± 12.8	.215
DLCO, %pred	49.0 ± 15.1	50.7 ± 13.0	.680
RV,% pred	141.8 ± 42.7	166.8 ± 50.4	**.037**
TLC, %pred	112.1 ± 16.2	122.7 ± 16.6	**.021**
ITGV, %pred	136.6 ± 28.9	161.2 ± 32.5	**.002**
Body composition			
BMI, kg/m^2	23.6 ± 2.4	20.0 ± 0.8	**<.001**
FFMI, kg/m^2	15.9 ± 1.6	15.6 ± 1.6	.424
SMI, kg/m^2	6.3 ± 0.9	6.1 ± 0.8	.332
Fat percentage, %	32.4 ± 8.0	22.0 ± 9.0	**<.001**
BMD, g/cm^2	1.1 ± 0.1	1.0 ± 0.1	.154

BMD, bone mineral density; BMI, body mass index; DLCO, diffusing capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FFMI, fat free mass index; FVC, forced vital capacity; ITGV, intra-thoracic gas volume; %pred, percentage of predicted; RV, residual volume; SD, standard deviation; SMI, skeletal muscle mass index; TLC, total lung capacity.
Data are presented as mean ± SD unless indicated otherwise. Boldface indicates statistical significance ($P < 0.05$).
*Only available for 80 patients.

Table 2
Cardiometabolic Risk Profile in COPD Patients With Low Muscle Mass Stratified by Abdominal Obesity

	Abdominal Obesity (n = 61)	Nonabdominal Obesity (n = 20)	*P* Value
Glucose, mmol/L*	5.2 (4.9–5.7)	4.9 (4.4–5.3)	**.003**
Insulin, mIU/L*	8.0 (5.6–12.0)	4.9 (3.3–8.1)	**.007**
HOMA-IR*	1.9 (1.3–2.8)	1.1 (0.7–1.8)	**.005**
Triglycerides, mmol/L*	1.3 (1.0–1.7)	1.1 (0.9–1.3)	.065
HDL cholesterol, mmol/L*	1.5 (1.2–1.9)	1.8 (1.3–2.2)	.181
LDL cholesterol, mmol/L	3.2 ± 1.1	3.1 ± 1.1	.793
Systolic blood pressure, mm Hg†	124.7 ± 18.4	122.5 ± 13.7	.638
Diastolic blood pressure, mm Hg†	73.4 ± 11.2	70.3 ± 9.0	.277
Metabolic syndrome, n (%)‡	26 (44.1)	1 (5.0)	**.001**
Hs-CRP, mg/L*	2.5 (1.0–6.1)	2.0 (0.2–5.6)	.273
BCAAs, μm/L*	469 (421–507)	415 (377–468)	**.013**

BCAAs, branched chain amino acids; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment to estimate insulin resistance; Hs-CRP, high-sensitive C-reactive protein; IQR, interquartile range; LDL, low density lipoprotein; SD, standard deviation.
Data are presented as mean ± SD unless indicated otherwise. Boldface indicates statistical significance ($P < 0.05$).
*Median (IQR).
†Only measured in 53 abdominally obese patients.
‡Only measured in 59 abdominally obese patients.

Abdominally obese COPD patients had higher glucose and insulin levels and higher HOMA-IR than those without abdominal obesity (Table 2), resulting in a higher prevalence of IR (32% vs 7%, $P = .055$). Furthermore, almost one-half of the abdominally obese patients had metabolic syndrome vs 1 patient in the non-abdominally obese group ($P = .001$). Plasma concentration of BCAAs was significantly higher in abdominally obese patients compared with those without abdominal obesity and significantly correlated with HOMA-IR in the group as a whole ($\rho = 0.49$; $P < .001$, Figure 2). The prevalence of cardiovascular disease (27.9% vs 40.0%) and diabetes (6.6% vs 0%) as well as cardiometabolic medication use was not significantly different between patients with and without abdominal obesity (Supplementary Table 1).

Peak work rate, CET, maximal isometric strength, and 6MWD were comparable between patients with and without abdominal obesity (Table 3). Total physical activity level was significantly lower in abdominally obese patients. Furthermore, abdominally obese patients tended to spend more time sedentary and less time in moderate to

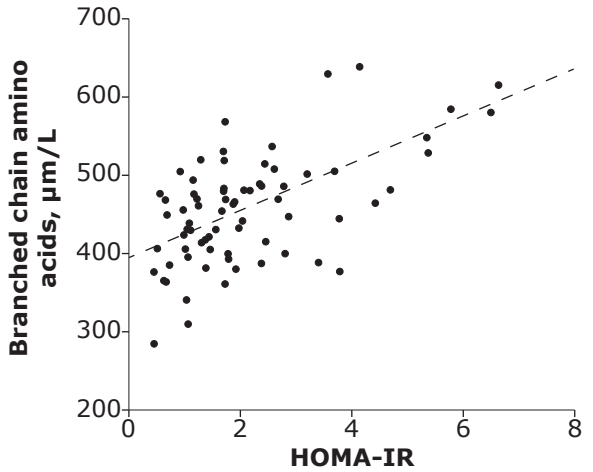

Fig. 2. Correlation between HOMA-IR and branched chain amino acids in patients with COPD ($\rho = 0.492$; $P < .001$).

Table 3
Physical Performance, Physical Activity, and Dietary Intake of COPD Patients With Low Muscle Mass Stratified by Abdominal Obesity

	Abdominal Obesity (n = 61)	Nonabdominal Obesity (n = 20)	*P* Value
Physical Performance			
Peak work rate, Watt	78 ± 28	81 ± 34	.754
CET, seconds	277 ± 178	279 ± 172	.969
Maximal isometric strength, Nm	123 ± 39	108 ± 41	.166
6MWD, m	487 ± 79	512 ± 93	.254
Physical activity level			
Total activity, counts/min	172.95 ± 77.49	217.13 ± 88.19	**.042**
Time spent in sedentary PA, % of wear time	71.67 ± 7.77	67.62 ± 10.34	.077
Time spent in lifestyle PA, % of wear time	21.91 ± 5.10	23.74 ± 6.41	.213
Time spent in MVPA, % of wear time	6.42 ± 3.97	8.64 ± 4.91	.051
Dietary intake			
Total energy, kcal*	2050 (1779–2487)	2378 (1681–3499)	.121
Protein, E%	15.9 ± 3.5	14.6 ± 2.0	.056
Carbohydrates, E%	44.3 ± 9.8	44.5 ± 10.1	.937
Fat total, E%	36.3 ± 7.5	39.3 ± 9.0	.154

6MWD, six minute walking distance; CET, cycling endurance time; E%, energy percentage; IQR, interquartile range; MVPA, moderate to vigorous physical activity; PA, physical activity; SD, standard deviation.
PA level was measured in 55 abdominally obese patients and 19 nonabdominally obese patients. Data are presented as mean ± SD unless indicated otherwise. Boldface indicates statistical significance ($P < .05$).
*Median (IQR).

vigorous physical activity (MVPA) compared with the patients without abdominal obesity. No significant differences were seen in dietary intake or dietary quality.

Responsiveness to High-Intensity Exercise Training

Of the placebo group in the NUTRAIN-trial 35 patients (90%) completed the exercise training program, of which 27 had abdominal obesity whereas 8 had no abdominal obesity. Quadriceps strength ($P < .001$) and CET ($P < .001$) significantly increased, whereas 6MWD did not change after completion of the exercise training (Table 4). However, no changes were found in glucose, high and low density lipoprotein cholesterol, systolic and diastolic blood pressure, high-sensitive C-reactive protein, and BCAAs. Triglycerides showed a significant decrease ($P = .011$), while the HOMA-IR increased ($P = .042$) because of an increase in insulin.

Discussion

To our knowledge, this is the first study investigating the cardiometabolic risk profile in normal-weight COPD patients with low muscle mass stratified by abdominal obesity. The main finding is that abdominal obesity frequently concurs with low muscle mass in patients with COPD eligible for outpatient PR and that these patients are characterized by higher glucose, insulin, HOMA-IR, and BCAAs levels, and lower total physical activity level compared to those without abdominal obesity. No differences were seen in other lifestyle factors including smoking behavior and dietary quality. The prevalence of metabolic syndrome was high in patients with abdominal obesity. This metabolic profile resembles the recently highlighted MONW phenotype. The cardiometabolic risk profile of the abdominally obese patients, however, was not altered immediately after 4 months of high-intensity exercise training and HOMA-IR, but not BCAAs, actually increased because of an increase in insulin.

Table 4
Effect of 4 Months High-Intensity Exercise Training on Physical Performance, PA, Dietary Intake, and the Cardiometabolic Risk Profile in Low Muscle Mass patients With COPD With Abdominal Obesity

	Baseline (n = 27)	After 4 Months (n = 27)	*P* Value
Physical Performance			
CET, seconds	237 ± 77	533 ± 388	**<.001**
Maximal isometric strength, Nm	126 ± 40	139 ± 41	**<.001**
6MWD, m	487 ± 72	490 ± 96	.781
PA*			
Total activity, counts/min	165.94 ± 73.21	165.20 ± 93.90	.949
Time spent in sedentary PA, % of wear time	74.04 ± 5.58	73.79 ± 8.28	.845
Time spent in lifestyle PA, % of wear time	19.79 ± 3.35	19.87 ± 5.00	.949
Time spent in MVPA, % of wear time	6.17 ± 3.60	6.33 ± 4.27	.773
Dietary intake			
Total energy, kcal*	2176 (1930–2590)	2155 (1656–2773)	.532
Protein, E%	15.7 ± 3.7	15.6 ± 3.5	.886
Carbohydrates, E%	45.4 ± 11.4	43.4 ± 8.4	.273
Fat total, E%	35.1 ± 8.0	36.8 ± 7.4	.262
Cardiometabolic risk parameters			
Glucose, mmol/L	5.2 (5.0–5.8)	5.5 (4.9–6.0)	.515
Insulin, mIU/L	7.7 (6.3–11.2)	9.1 (7.0–11.9)	.074
HOMA-IR	1.9 (1.4–2.7)	2.4 (1.8–3.0)	**.042**
Triglycerides, mmol/L	1.4 (1.0–1.8)	1.0 (0.9–1.4)	**.011**
HDL cholesterol, mmol/L	1.6 (1.1–1.9)	1.5 (1.2–1.8)	.572
LDL cholesterol, mmol/L	3.2 (2.4–4.0)	3.0 (2.24.0)	.149
Systolic blood pressure, mmHg*	130 ± 20	128 ± 22	.761
Diastolic blood pressure, mmHg*	77 ± 13	76 ± 15	.853
Hs-CRP, mg/L†	2.8 (1.3–3.7)	1.9 (0.5–8.4)	.895
BCAAs, μm/L†	470 (449–508)	461 (443–519)	.428

6MWD, six minute walking distance; BCAAs, branched chain amino acids; CET, cycling endurance time; E%, energy percentage; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment to estimate insulin resistance; Hs-CRP, high-sensitive C-reactive protein; IQR, interquartile range; LDL, low density lipoprotein; MVPA, moderate to vigorous physical activity; PA, physical activity; SD, standard deviation.
Data are presented as mean ± SD unless indicated otherwise. Boldface indicates statistical significance ($P < .05$).
*Only measured in 22 patients after 4 months of training.
†Median (IQR).

Within this selected population of COPD patients with low muscle mass, the proportion of those with abdominal obesity was high (75%). This seems to be more related to lifestyle factors, in particular low physical activity level, than to specific disease characteristics. Although we did not characterize emphysema by high-resolution computed tomography, patients with and without abdominal obesity were comparable in terms of airflow limitation and diffusion capacity as proxy for emphysema. The slightly lower static hyperinflation in the abdominally obese patients might be related to effects of adiposity on functional residual capacity as shown in studies by O'Donnell et al.[32–34]

Differences in physical activity level were characterized by a 20% lower total physical activity level. Furthermore, the time spent sedentary and in MVPA seems to be higher and lower, respectively, in the abdominally obese patients. It would be worthwhile to explore how the amount of sedentary time in COPD can be decreased. In diabetes-oriented research, a shift has occurred in physical activity targets from more time in MVPA toward sitting less and increasing standing and stepping as means to improve cardiometabolic health.[35] However, efficacy and feasibility of such interventions and eventual added value in other chronic diseases such as COPD needs to be established.

Metabolic syndrome is a constellation of risk factors that has been shown to increase the risk of developing type II diabetes mellitus and cardiovascular disease in the general population. The prevalence of metabolic syndrome in this group of patients with low muscle mass was 34.2%, which corresponds to the recently reported prevalence (34%) in normal-to-overweight patients with COPD in a systematic review.[36] Although metabolic syndrome was determined based on the National Cholesterol Education Program's Adult Treatment Panel III definition with no obligatory component for abdominal obesity, the high proportion of abdominal obesity appears to be the main driver because only 1 patient in the group without abdominal obesity had metabolic syndrome.

In line with the low prevalence of metabolic syndrome in COPD patients without abdominal obesity, the prevalence of IR, based on the HOMA-IR, was also low in this group (7%). Compared to the patients without abdominal obesity, the abdominally obese group had a significantly higher prevalence of IR. Although we are aware HOMA-IR is not a definitive tool to assess IR, we also found higher levels of BCAAs in patients with abdominal obesity, which was significantly correlated with HOMA-IR. The causality of BCAAs and IR is still unclear but BCAAs have recently been positioned as biomarker of IR.[37,38] Several potential mechanisms have been proposed to explain the contribution of BCAAs to IR.[37,39] BCAAs are proposed to activate the mammalian target of rapamycin complex 1 signaling pathway, which could lead to an impaired insulin action. Furthermore, increased BCAAs are proposed to be a biomarker of impaired BCAA metabolism causing β-cell dysfunction and IR. In addition, increased BCAAs can cause secretion of the 3-hydroxyisobutyrate from muscle, which activates endothelial fatty acid transport and uptake, resulting in lipid accumulation in muscle and IR.[39] These are interesting observations, which seem clinically relevant, but because the biological and clinical relevance of the HOMA-IR has been questioned, euglycemic clamp studies are needed to gain more insight into the pathophysiology of IR and increased BCAA levels in this phenotype.

Despite that exercise training has been shown to improve the cardiometabolic risk profile in overweight and obese persons without COPD,[40–42] less is known about its effects in the MONW phenotype. We, therefore, investigated as proof-of-concept the effects of high-intensity exercise training on the cardiometabolic risk profile of the abdominally obese COPD patients. A remarkable finding was the raised HOMA-IR after this high-intensity exercise training. This is in line with a recent study by Cebron et al[43] showing significant improvements in HOMA-IR after short-term (4 weeks) high-intensity exercise training only in COPD patients with normal muscle mass, whereas COPD patients with low muscle mass did not improve. Furthermore, in line with the current study the non-IR COPD patients with low muscle mass even increased in HOMA-IR, because of an increase in insulin (personal communication). It could be speculated that the increase in HOMA-IR, primarily because of increased insulin levels, reflects an adaptive anabolic response to the exercise training, as increased insulin signaling stimulates muscle anabolism. No studies are available in literature that have related changes in plasma insulin and HOMA-IR to muscle insulin/insulin-like growth factor 1 signaling after exercise training in patients with COPD. This could be further investigated in future research.

Some limitations of the current study deserve discussion. First, the cardiometabolic profile was assessed in cross-sectional design. This was suitable to answer our research question but not to unravel the cause of the elevated cardiometabolic risk and the development of cardiometabolic diseases over time. Another limitation is that the proof-of-concept exercise intervention was studied in a subset of patients that nevertheless showed a consistent response.

In conclusion, this study showed that abdominal obesity is highly prevalent in COPD patients with low muscle mass who showed an increased cardiometabolic risk in comparison to COPD patients without abdominal obesity. The effectiveness of the current exercise program in terms of maximizing exercise performance was confirmed as shown by significant improvements in CET and quadriceps strength. However, no clinically meaningful alterations in cardiometabolic risk parameters were observed. Future studies should give more insight into the underlying pathophysiology of the elevated cardiometabolic profile in COPD. Subsequently the modulating potential of different exercise training types and intensities and nutritional or pharmacologic interventions on the cardiometabolic profile could be opportunistic to investigate.

Supplementary Data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.jamda.2016.12.081.

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