SARCOPENIA IN COPD: PREVALENCE, CLINICAL CORRELATES AND RESPONSE TO PULMONARY REHABILITATION

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ONLINE SUPPLEMENT

METHODS

Sarcopenia assessment

Sarcopenia was defined according to the EWGSOP criteria, as the presence of low skeletal muscle mass, plus low handgrip strength or low physical performance.[1] Whole-body BIA was performed using a Bodystat Quadscan 4000 analyzer (Bodystat Ltd., Isle of Man, UK) applying an 800μA alternating current at 50kHz. Skeletal muscle mass (SMM, kg) was estimated using the formula developed by Janssen *et al*; ((height^2/resistance x 0.401) + (age x -0.071)] + 5.102) + 3.825 if male.[2] The skeletal muscle mass index (SMI) was also calculated as SMM/m^2. Handgrip strength was measured using the JAMAR Plus digital handheld dynamometer (Sammons Preston; Bolingbrook, IL, USA). Participants performed three maximal isometric contractions and the mean force produced was recorded. Physical performance was assessed by the 4-metre gait speed (4MGS) as previously described.[3] Participants were asked to walk at their usual pace, from a standing start, across a four-meter flat unobstructed course. The time taken to complete the course was recorded using a stopwatch, with the faster of two attempts used to calculate the 4MGS, expressed as meters per second.[3] The following cut-off values were used to identify patients with sarcopenia: SMI of ≤8.50kg/m^2 for men and ≤5.75kg/m^2 for women,[4] and either handgrip strength of <30kg for men and <20kg for women [5] or a gait speed of <0.8m/s as recommended by the EWGSOP.[1]

Additional assessments

Further measurements included the incremental shuttle walk test (ISWT),[6] five-repetition sit-to-stand test (5STS),[7] short physical performance battery (SPPB)[8]

and quadriceps maximum voluntary contraction (QMVC).[9] Predicted QMVC was calculated using a disease- and sex-specific regression equation [10] and weakness was defined as a QMVC below 1.645 standardised residuals from the healthy predicted value.[10] The St George's Respiratory Disease Questionnaire (SGRQ),[11] COPD Assessment Test (CAT),[12] Medical Research Council (MRC) dyspnoea scale [13] and spirometry were performed. Self-reported physical activity in the previous 7 days was assessed by the modified Minnesota Leisure-time Physical Activity Questionnaire and, in a sub-group, by a multisensory accelerometer (SenseWear, Bodymedia; Pittsburgh, US). Participants wore the accelerometer for 24 hours / day except when performing any tasks that might put the armband at risk of getting wet. When <22.5 hours of use were recorded during the day, data was excluded from analysis [14] Self-reported exacerbations and hospital admissions in the previous 12 months were recorded, and corroborated by primary care records. Co-morbidities were recorded using the age-adjusted Charlson Index.[15] The iBODE composite prognostic index (body mass index, airflow obstruction, dyspnea, and exercise capacity) was also calculated.[16]

Pulmonary Rehabilitation

The PR programme was an eight-week outpatient multi-disciplinary exercise and education programme comprising two supervised and at least one additional home session per week. Supervised sessions comprised of one hour exercise and one hour education. Exercise training was individualised, and in line with UK practice, primarily aerobic in nature. Initial walking speed prescription was at 80% of predicted peak oxygen consumption based on ISWT performance,[9] whilst initial endurance cycling prescription was set at a workload with the aim of patients completing ten

minutes of continuous cycling. Workloads and duration of exercise were continually reassessed and increased through the programme as tolerated. Lower limb resistance training comprised two sets of 10 leg press repetitions performed with an initial training load of 60% one-repetition maximum with one minute rest between sets, as well as sit-to-stand sets, knee lifts/extension and hip abduction with appropriate ankle weights. Upper limb resistance training comprised biceps curls, shoulder press and upright row with appropriate dumbbell weights. Workload was increased as tolerated. Education classes covered a variety of self-management topics including exercise, medication use, diet, coping strategies, increasing physical activity and recognising and managing infections.

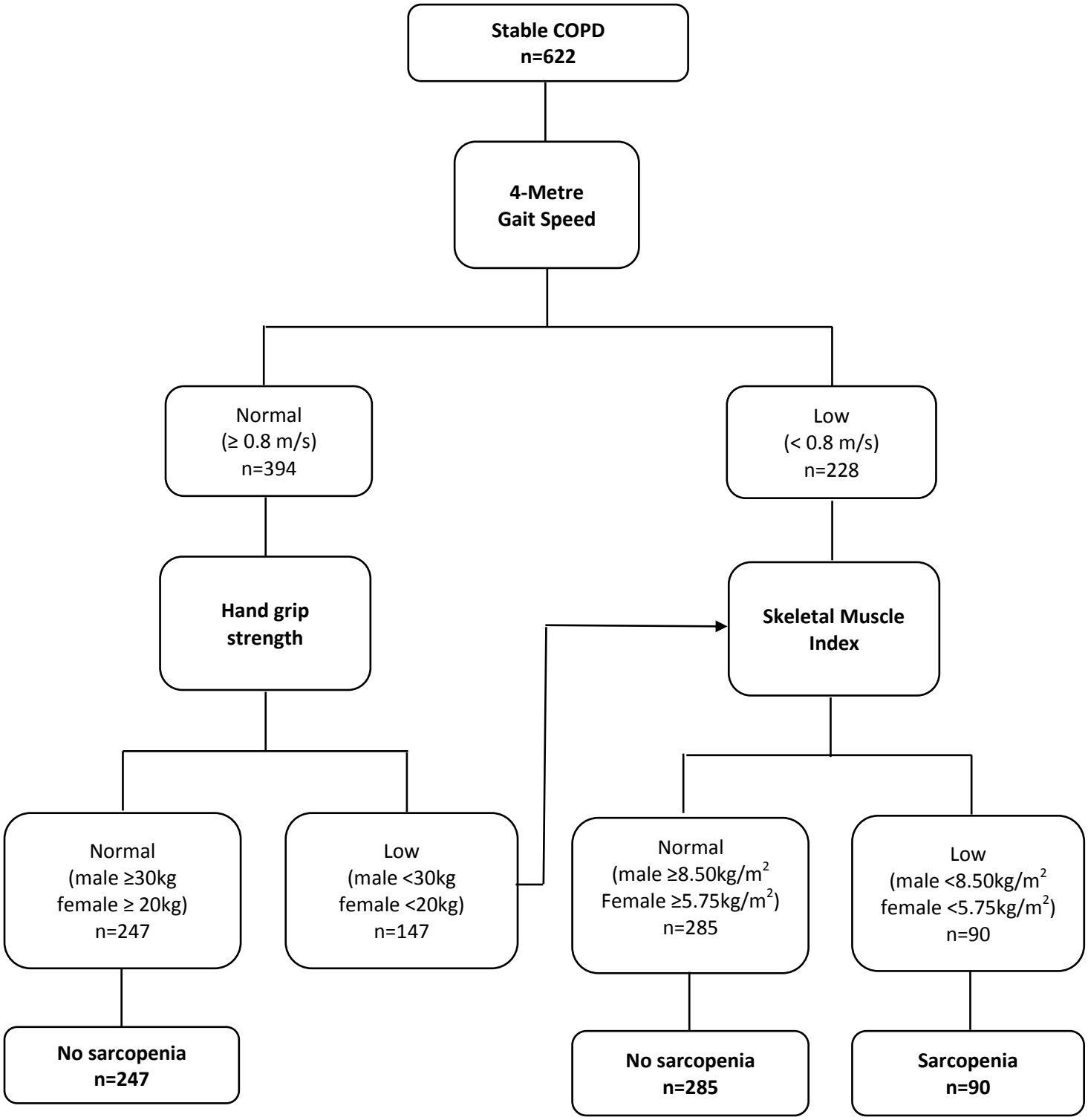
TABLE S1: Baseline clinical characteristics expressed as mean (SD) and median (25^{th}, 75^{th} centiles) based presence of quadriceps weakness, sarcopenia or both.

	Neither quads weakness or sarcopenia (n=206)	**Quads weakness (n=268)**	**Sarcopenia (n=33)**	**Both (n=47)**	**p-value**
Age (years)	68 (11)	70 (9)	73 (7)	72 (9)	0.012
Sex (M:F)	126:80	148:120	23:10	30:17	0.262
MRC	3 (1)	3 (1)*	3 (1)	4 (1)*	0.001
FEV1 (% predicted)	46.3 (18.3)	44.8 (18.1)	39.4 (20.5)	40.1 (18.3)	0.067
BMI (kg/m)	27.9 (5.0)	28.2 (5.9)	20.6 (3.1)*	21.6 (4.3)*	<0.001
SMM (kg)	24.5 (6.8)	24.2 (6.9)	19.8 (4.8)*	18.9 (5.3)*	<0.001
SMI (kg/m^2)	8.69 (1.71)	8.72 (1.85)	7.09 (1.18)*	6.84 (1.37)*	<0.001
Handgrip (kg)	31.2 (10.2)	26.0 (9.3)*	23.6 (8.8)*	20.3 (5.6)*	<0.001
Peak QMVC (kg)	33.7 (9.8)	22.1 (7.3)*	25.0 (7.8)*	16.1 (4.8)*	<0.001
QMVC % predicted	77.3 (11.2)	51.5 (11.0)*	68.7 (13.0)*	45.1 (10.1)*	<0.001
4MGS (m/s)	0.98 (0.22)	0.87 (0.22)*	0.82 (0.19)*	0.77 (0.24)*	<0.001
5STS (secs)	12.3 (10.1, 14.9)	15.0 (12.2, 22.7)*	15.9 (11.8, 21.4)*	24.7 (13.2, 60.0)*	<0.001
SPPB	11 (10, 12)	9 (7, 11)*	9 (8, 11)*	7 (6, 10)*	<0.001
ISWT (m)	278 (162)	195 (128)*	181 (115)*	149 (112)*	<0.001
CAT	21 (8)	21 (8)	23 (9)	25 (9)*	0.008
SGRQ Total	50.2 (17.7)	52.7 (16.4)	52.4 (17.2)	60.6 (17.1)*	0.003
Smoking status (current:former:never)	42:155:9	40:212:16	6:24:3	9:35:3	0.700
Charlson Index	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 3)	0.018
Hospital inpatient days previous 12 months	0 (0, 2)	0 (0, 4)	0 (0, 1)	0 (0, 5)	0.363
Number of exacerbations previous 12 months	2 (1, 4)	2 (1, 3)	2 (1, 4)	2 (1, 4)	0.991
Self-report physical activity					
Energy expenditure (kcal / week)	645 (293, 1428)	525 (156, 1251)	452 (284, 779)	210 (8, 656)*	<0.001
Time in moderate activity (mins / week)	185 (80, 406)	150 (45, 318)	130 (81, 221)	60 (4, 183)*	<0.001

Legend: 4MGS = 4-metre gait speed, 5STS = five-repetition sit-to-stand test, BMI = body mass index, CAT = COPD Assessment Test, FEV^1 – Forced expiratory volume in one second, iBODE = body mass index, obstruction, dyspnoea, exercise capacity index, ISWT = incremental shuttle walk test, kcal = kilocalorie, MRC = Medical Research Council, SGRQ = St George's Respiratory Disease Questionnaire, SMI = skeletal muscle mass index, SMM = skeletal muscle mass, SPPB = short physical performance battery, QMVC = quadriceps maximum voluntary contraction.

*indicates a statistical significant difference compared to neither quadriceps weakness or sarcopenia.

FIGURE S1: Study cohort using the European Working Group on Sarcopenia in Older People (EWGSOP) algorithm for diagnosing sarcopenia.



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