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SPECIAL ARTICLE

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Breathlessness in older adults: What we know and what we still need to know

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Abstract

Breathlessness is common among older adults, but it is often hidden as "normal aging "or considered narrowly as a symptom of cardio-respiratory diseases. Studies on breathlessness in older adults are mostly focused on specific diseases, whereas older adults are characterized by multimorbidity and multi-system age-related impairments. This article aims to provide an overview of what is known so far on breathlessness in the general population of older adults and identify areas for further research. Research shows that breathlessness in older adults is a multifactorial geriatric condition, crossing the borders of system-based impairments and diseases, and a valuable independent prognostic indicator for adverse outcomes. Further research needs to investigate (1) the multi-factorial mechanisms of breathlessness in community-dwelling older adults including the role of respiratory sarcopenia; (2) the influence of affective and cognitive changes of older age on the perception and report of breathlessness; (3) the best way to assess and use breathlessness for risk prediction of adverse outcomes in general geriatric assessments; and (4) the most appropriate multi-modal rehabilitation interventions and their outcomes. Clinicians need to shift their approach to dyspnea from a disease symptom to a multifactorial geriatric condition that should be proactively searched for, as it identifies higher risk for adverse outcomes, and can be addressed with evidence-based interventions that can improve the quality of life and may reduce the risk of adverse outcomes in older adults.

KEYWORDS

breathlessness, dyspnea, geriatric dyspnea, geriatric syndrome, older adults

INTRODUCTION

In recent years, there has been increasing interest and calls for a systematic assessment of breathlessness in the general adult population as it is prevalent, provides valuable general prognostic information, its assessment requires minimal efforts and there are evidence-based interventions for its relief.[1–4]

Community-dwelling older adults are a special population regarding breathlessness as its prevalence increases with age, yet it is commonly hidden and attributed to "normal aging".[2,4] In addition, older adults are characterized by multimorbidity, age-related multi-system low physiological reserves, and reduced symptom perception and reporting.[2,4,5]

This article aims to provide an overview of the current research findings on breathlessness in the general population of older adults and identify potential areas for future research about its underlying causes, prognostic role, assessment, and management in general geriatric care.

The terms breathlessness and dyspnea are both used in medical literature and in this article, we use them interchangeably. Dyspnea (literal meaning 'disordered breathing') is defined as a "subjective experience of breathing discomfort",[6] but it is not a term used by patients, whereas breathlessness is more commonly used by patients and clinicians to describe breathing difficulty or discomfort.[4,7]

BREATHLESSNESS IN OLDER ADULTS: HIGH PREVALENCE

The prevalence of breathlessness in general populations of older adults ranges from 25% to 36% depending on the assessment tool and type of breathlessness (activity-related/exertional or nonexertional).[4,8,9] There is only one systematic review of studies (until 2012) on the prevalence of exertional dyspnea in older adults (≥65 years old), based on the widely used Medical Research Council breathlessness scale (MRC).[8] The MRC scale is composed of five statements describing the range of disability because of breathlessness from grade 1–5 (Table 1).[11] Out of 20 different general older adult populations (84–5119 participants) in this systematic review, the pooled prevalence for MRC grade 2–5 was 36% (95% confidence interval: 27%–47%).[8]

In a nationally representative study of 3671 adults ≥70 years old in USA, when asked "How often do you become short of breath while awake?", 25% responded "often/sometimes".[4] In a Belgian cohort of 567 adults ≥80 years old recruited in general practices, 29.9% had MRC grade 3–5.[9] In a cohort of 548 community-dwelling older adults (≥ 70 years old) in USA, more than half (56.8%) reported breathlessness severe enough to restrict their activity during their last year of life.[5]

TABLE 1 Grades and descriptions of the MRC breathlessness scale.

Grade	Description
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level ground or walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so, or after 15 min walking on the level at own pace.
4	Stops for breath after walking about 100 yds (or after a few minutes) on the level
5	Too breathless to leave the house or breathless after undressing

Note: The modified version (mMRC) or the ATS dyspnea scale uses grading from 0 to 4 and modifies Grade 3 to:" Walks slower than *people of the same age* on the level *because of breathlessness* or has to stop *for breath* when walking at own pace on the level."[10]

Key points

- Current research supports the status of breathlessness as a multifactorial geriatric condition and an independent prognostic indicator in older adults.
- Research on the contribution of multiple age-related impairments and multimorbidities to breathlessness in older adults, and the impact of cognitive and affective changes of older age on its perception and report is lacking.
- The proactive assessment for breathlessness in general geriatric health assessments and multimodal interventions that address its multifactorial and multidimensional nature may improve health outcomes and should be the focus of future research.

Why does this paper matter?

This overview of research findings highlights the need to shift the clinical and research focus of breathlessness in older adults from the disease-specific setting to the complex setting of multimorbidity and multi-system age-related impairments of this age-group and consider the use of breathlessness as a general prognostic indicator in geriatric health assessments. This has the potential to improve quality of life and reduce the risk of adverse outcomes in older adults.

Breathlessness has a high prevalence in community-dwelling older adults and it is also burdensome as it affects their functional ability, physical and mental health, and quality of life.[4,12–15] There is increasing evidence that in older adults, breathlessness is multifactorial, stretching beyond the common cardio-respiratory morbidities such as chronic obstructive pulmonary disease (COPD) and chronic heart failure that are usually attributed to it.[4,9,16,17]

BREATHLESSNESS IN OLDER ADULTS: A SYMPTOM OF AN UNDERLYING DISEASE OR A GERIATRIC SYNDROME?

The systematic review of studies published until 2012 on dyspnea in older adults identified only one study about

TABLE 2 Studies on factors associated with breathlessness in community-dwelling older adults.

Country & year of study	Participants	Prevalence of MRC ≥3	Associated factors[a]
USA 2011–2013[17]	$n = 4342$ age ≥65 years	13.2%	• Restrictive spirometric pattern 2.11 (1.61–2.76) • Obstructive spirometric pattern 1.69 (1.33–2.14) • Pulmonary hypertension 1.47 (1.08–2.00) • LV hypertrophy 1.30 (1.01–1.67) • Lower extremity weakness 2.10 (1.53–2.88) • Upper extremity weakness 1.27 (0.98–1.64) • Depression symptoms 2.41 (1.59–3.66) • Obesity 2.22 (1.75–2.81) • Renal dysfunction 1.29 (1.01–1.65) • Anemia 1.59 (1.21–2.07)
Belgium 2008–2009[9]	$n = 567$ age ≥80 years	29.9%	• Low FEV1 3.19 (1.90–5.34) • Low physical performance 2.49 (1.50–4.12) • High NTproBNP 2.36 (1.45–3.85) • Overweight/obese 2.20 (1.29–3.75) • High GDS-15 score 1.87 (1.09–4.22)
USA 1989–1990[16]	$n = 4413$ age ≥65 years	17.5%[b]	• Low FEV1 2.88 (2.37–3.49) • Respiratory muscle weakness 1.60 (1.20–2.14) • LV ejection fraction<45% 2.12 (1.43–3.16) • Diastolic dysfunction 1.32 (1.08–1.61) • Grip weakness 1.31 (1.06–1.61) • Single chair stand 2.10 (1.61–2.73) • Depressive symptoms 2.02 (1.26–3.23) • Anxiety symptoms 1.54 (1.22–1.93) • Cardiovascular medication 1.65 (1.35–2.01) • Psychoactive medication 1.71 (1.35–2.15) • Obesity 2.07 (1.67–2.55)
UK, year not reported[13]	$n = 1169$ age ≥70 years	32.3%	Prevalence in participants with versus without dyspnea: • Reversible airway disease 19.3 versus 10.3% • COPD 19.3 versus 7% • LV systolic dysfunction 17.1 versus 6.04% • Obesity 33.9 versus 23.0% • High depression & anxiety score 62.4% versus 36.4%

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; GDS-15, 15 items geriatric depression scale; LV, left ventricle; MRC, Medical Research Council breathlessness scale; n, number.

[a]The studies from USA and Belgium applied a multivariable logistic regression including all impairments. Only those with statistically significant adjusted odds ratio and their 95% confidence intervals (in brackets) are reported here. The study from UK compared population prevalence of clinically diagnosed conditions between those with and without dyspnea. Only conditions with statistically significant differences (p value >0.05) are reported here.

[b]The ATS scale grade ≥2 "Do you have to walk slower than people of your age on the level because of breathlessness?" (equivalent to MRC ≥3).

its underlying causes.[8] This study included 555 patients aged 60–79 years from four general practices in Denmark; of these, 129 who had dyspnea (MRC grade 2) went through a three-steps diagnostic protocol including electrocardiogram, spirometry, echocardiography, lung diffusion capacity, serum hemoglobin, thyroid function, cardiac MRI, bicycle exercise test, and chest radiography.[18] The identified underlying conditions were an overlap of lung conditions (53%), heart conditions (21%), obesity (16%), and general physical deconditioning (4%), whereas nearly 12% still had no identifiable cause after this step-wise diagnostic protocol.[18]

To our knowledge no other studies yet have applied a predefined diagnostic algorithm to research the underlying causes of breathlessness in community-dwelling older adults, but several cohort studies of community-dwelling older adults from different countries have reported on factors associated to breathlessness (Table 2). In these studies, the strongest independent associations with moderate–severe breathlessness (MRC grade 3–5) were for parameters of respiratory, cardiac, and muscular impairment, as well as obesity and depressive/anxiety symptoms (Table 2).[9,13,16,17] In the ARIC cohort of community-dwelling older adults in USA (5943 participants,

TABLE 3 Age -related physiological changes that might (co-) contribute to exertional dyspnea in older adults.

Location	Changes and the mechanisms leading to exertional dyspnea (→)
LUNGS	Reduced lung compliance (due to reduced elastic recoil) ➢ Reduced forced expiratory volume in 1 s ➢ Reduced vital capacity ➢ Increased functional residual capacity Increased airway resistance ➢ Increased functional residual capacity ➢ Increased residual volume ➢ Lung hyperinflation → *Increased mechanical loading of respiratory muscles* Reduced gas exchange efficiency due to: – Increased dead space & ventilation/perfusion mismatch – Reduced DLCO (diffusion capacity for carbon monoxide) → *Increased ventilatory demand during exercise*
CHEST WALL	Reduced chest wall compliance (stiffening of the chest wall) Changes in the shape of thorax (dorsal kyphosis) → *Increased mechanical loading of respiratory muscles*
RESPIRATORY MUSCLES	Reduced inspiratory and expiratory muscles' strength due to: – Increased mechanical loading from changes in lung & chest wall – Age-related sarcopenia → *Decreased ventilatory capacity*
LOCOMOTOR MUSCLES	Reduced mass and strength (age-related sarcopenia, deconditioning) ➢ Reduced anaerobic threshold and mechanical efficiency → *Increased ventilatory demand during exertion*
CARDIO-VASCULAR	Reduced compliance of myocardium, arteries, and veins (stiffening) Calcification of valves; Atherosclerosis. ➢ Hypertension ➢ Reduced end-diastolic and stroke volume ➢ Reduced cardiac output Reduced response of beta receptor stimulation and reduced function of atrial pacemakers' cell ➢ Reduced heart rate and contractile response to exertion → *Increased ventilatory demand during exertion &* *decreased ventilatory capacity (through restrictive lung changes)*

mean age 76 years), after the exclusion of participants with dyspnea-associated conditions (heart failure, COPD, obesity, and severe kidney dysfunction), 27% still had undifferentiated dyspnea that in 13.2% was moderate-to-severe (MRC grade 3–5).[17] After adjusting for several noncardiovascular impairments (restrictive and obstructive spirometry patterns, obesity, depression, upper and lower extremity weakness, anemia, and renal dysfunction), left ventricular systolic and diastolic dysfunctions were poor discriminators of moderate–severe dyspnea.[17] These findings caution that undifferentiated dyspnea in older adults "should not be assumed to be caused by occult heart failure" and support the "multifactorial nature of dyspnea in older adults".[17]

Older adults are characterized by multimorbidity especially co-occurrence of cardio-respiratory diseases, but they also have multi-system age-related impairments that may contribute to exertional dyspnea (Table 3, Supplementary Material S1). Respiratory, cardiovascular, musculoskeletal, and neuropsychological impairments have been consistently shown to be associated with exertional dyspnea in older adults even after adjustment for potential confounders, and from a physiological point of view these age-related impairments, especially when accumulative, could have a primary contribution in the different levels of the development of the experience of dyspnea (Figure 1).[9,16,17,19] Obesity has also been consistently reported as associated with exertional dyspnea in older adults possibly as a result of its effect on respiratory function and exercise capacity, but its primary contribution in the mechanisms of dyspnea is not clear yet.[18,20]

Breathlessness and sarcopenia

Several studies in community-dwelling older adults have reported an independent association between moderate–

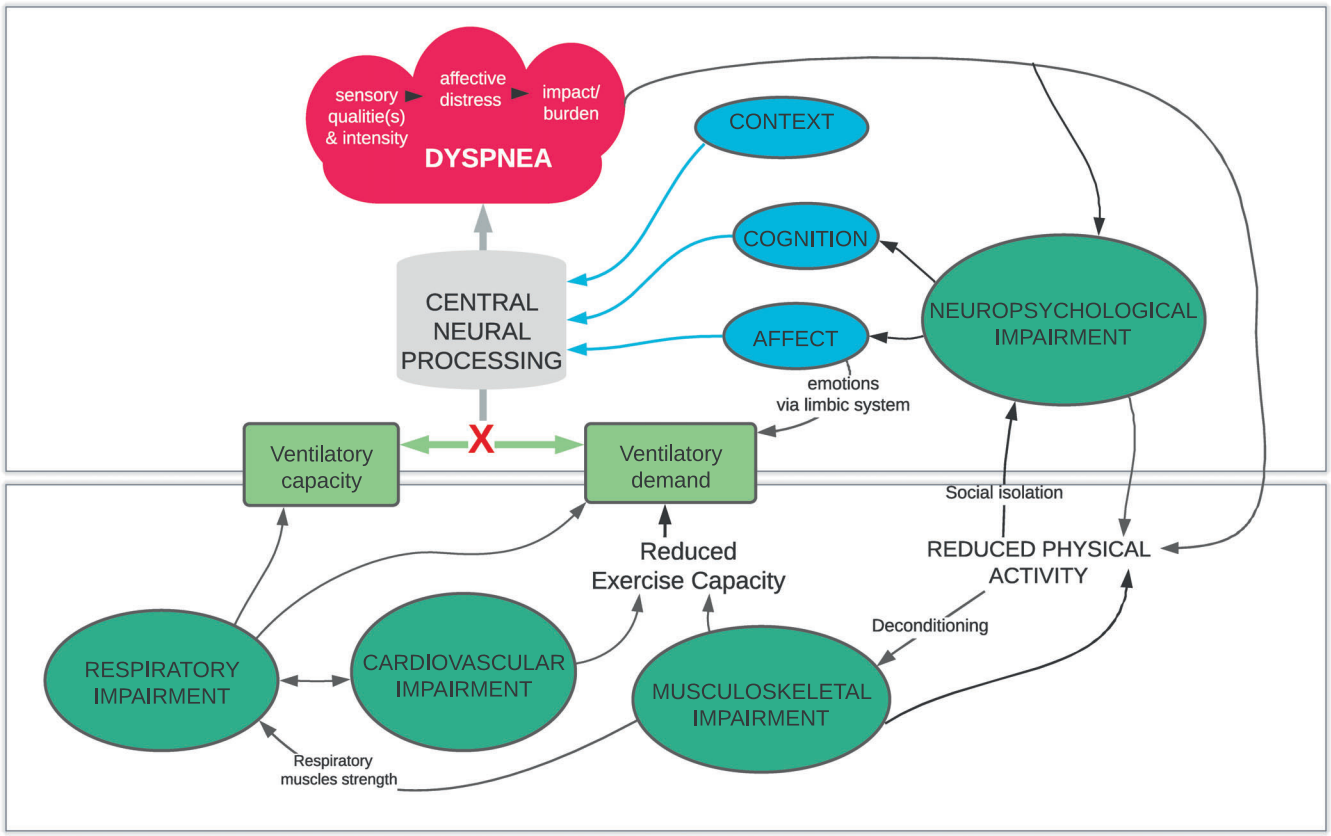

FIGURE 1 Schematic presentation of the key contributing factors and processes/pathways that may be involved in the perception of exertional dyspnea in older adults. The green oval shapes represent the four key impairments that may contribute to dyspnea in older adults in peripheral (lower part of the schema) and central (upper part of the schema) levels of the processing of the experience of dyspnea. These impairments may be due to age-related changes and/or chronic (co)morbidity in these systems. They may (co)-contribute through different pathways (black arrows) to the imbalance between ventilatory capacity and ventilatory demand that leads to the generation of the sensation(s) of dyspnea in the brain (awareness of the neuromechanical dissociation). A complex central neural processing in a cortico-limbic network (the neuromatrix of dyspnea) integrates the sensory input with the brain's expectations based on previous experiences of dyspnea (cognition), context and affect/mood leading to the multidimensional experience of dyspnea that consists of the intensity and quality of sensation(s), the related affective distress, and the impact/burden on activities of daily living. Through its impact, breathlessness may contribute back to the contributing impairments leading to potential vicious cycles.

severe exertional dyspnea and sarcopenia.[9,17,21–23] In the Cardiovascular Health Study in USA (4413 participants, mean age 72.6 years), low grip strength, respiratory muscle weakness, and poor performance in a single chair stand test were independent correlates of moderate–severe exertional dyspnea.[16] In addition, frailty (Fried phenotype) and poor performance in a single chair stand test were competing variability factors of moderate–severe exertional dyspnea.[21] In the Belgian cohort of adults ≥80 years old, low grip strength or low scores of a battery of physical performance tests were independently associated to exertional dyspnea.[9] Among 411 community-dwelling adults aged ≥60 years old in Brazil, higher MRC grades were associated with poorer scores of the short physical performance battery of tests independently of age, sex, smoking status, number of morbidities, and frailty status.[22]

There is a possible bidirectional association between dyspnea and sarcopenia.[2,21] Dyspnea limits physical activity that causes disuse atrophy and weakness of skeletal muscles in particular the leg muscles, followed by muscle deconditioning with increased ventilation demand for same level of activity, leading to further increase of breathlessness and development of a vicious cycle (Figure 1).[2,6,21]

In older adults, the age-related sarcopenia and muscle deconditioning due to chronic morbidities and a sedentary lifestyle could be primary causes of breathlessness or associate causes together with the age-related reduced ventilation capacity due to respiratory impairment (Figure 1).[2,7,19,21] The age-related sarcopenia may cause or exacerbate dyspnea by increasing ventilatory demand through the weakness of ambulatory/locomotor muscles, as well as by reducing ventilatory capacity through the

weakness of inspiratory and expiratory muscles that are crucial in the development of dyspnea (Figure 1).[2,21,23,24] The weakness of respiratory muscles, recently termed respiratory sarcopenia and defined as low maximal inspiratory pressure, may even be an indicator of systemic sarcopenia and frailty in older adults.[23–25] Both age-related and disease-related respiratory sarcopenia may cause sarcopenic respiratory disability (recently defined as MRC grade 3–5 and corresponding to moderate–severe exertional dyspnea).[24]

Recently a large longitudinal study of community-dwelling older adults in Italy (2322 participants ≥65 years old) has reported a bidirectional relationship between dyspnea and depression.[26] In 4.4 years follow-up, study participants with persistent, incident or worsening dyspnea in daily activities (MRC grade ≥2) had a 2–3 times higher risk for incident or worsening depressive symptoms, and those with persistent or incident depression had a 2 times higher risk for developing dyspnea in daily activities, compared with study participants without baseline dyspnea or depressive symptoms, respectively.[26] Similar longitudinal studies are needed to investigate the interaction of the multi-system factors that contribute to breathlessness in community-dwelling older adults.

The findings from cross-sectional studies on factors contributing to breathlessness in older adults do not allow inference of causality, although the identified contributing factors and their mechanisms have a robust clinical and physiological basis.[16,17] They are also secondary data analyses from cohort studies that were not originally designed to answer questions about the underlying causes of dyspnea in older adults, so there is variety in measurements of different impairments/dysfunction, and the diagnoses of chronic diseases such as COPD or heart failure are often based on self-reports or derived from secondary sources or evaluations.

Despite the need for further robust research in this area, the current findings from different cohorts of community-dwelling older adults consistently support the consideration of breathlessness in older adults as a multifactorial geriatric health condition similar to falls, dizziness, and delirium, having multiple contributing factors in multiple domains.[7,9,16,17] Breathlessness has the features that characterize a geriatric syndrome: a high prevalence in older adults; a substantial impact on their disability and quality of life; and multifactorial etiology across multiple organ systems.[9,16,27,28]

The complex interactions and contributions of the multiple factors associated to breathlessness in community-dwelling older adults, especially the role of respiratory and ambulatory sarcopenia, need further research. This could lead to interventions that address several contributing conditions, for example, exercise rehabilitation, with the potential of reducing the considerable burden of dyspnea and the general independent risk for adverse outcomes that is associated with it.[6,24,29,30]

BREATHLESSNESS IN OLDER ADULTS: AN INDEPENDENT RISK MARKER FOR ADVERSE OUTCOMES

In the general adult population, breathlessness has been shown to be associated with mortality independent from cardio-respiratory impairments and their risk factors.[31,32] Recently, in a large study of hospitalized patients in USA (median age 60 years), dyspnea on admission (assessed with a simple numerical rating scale) was strongly associated with mortality (in-hospital and after 2 years) and use of hospital resources, independent of demographics, comorbidity, and illness severity, especially in patients *without* a primary cardio-respiratory discharge diagnosis.[33] This study highlights the powerful general prognostic value of breathlessness beyond primary cardio-respiratory morbidities and supports the call for assessing it systematically like vital signs or pain.[3,33]

To our knowledge, no study, so far, has tested the proactive search for breathlessness in real-life geriatric assessments of community-dwelling older adults and followed up its impact on adverse outcomes, but several prospective cohort studies from different countries have reported associations of moderate–severe exertional dyspnea with all-cause mortality, unplanned hospitalizations and disability in activities of daily living, independent of age, sex, smoking status, and/or dyspnea-related morbidities (Table 4).[4,9,28,34–36] These findings show that breathlessness in older adults can provide valuable prognostic information on adverse outcomes, independent of dyspnea-related morbidities and impairments, and could be "a good global predictive index of health status in older adults".[35]

The considerable prevalence and burden of breathlessness in older adults and its independent prognostic value, support a systematic search for breathlessness in geriatric health assessments and its inclusion in risk prediction tools for older adults.[1,2,4,9,28] Yet, despite the perceived easiness to assess breathlessness by just 'asking the patient', the best way to assess it in the adult population and in older adults is still a work in progress.

ASSESSMENT OF BREATHLESSNESS IN OLDER ADULTS: EASY AND COMPLEX

Like pain, the assessment of breathlessness relies on the self-report of a "subjective experience of breathing

TABLE 4 Studies on association of breathlessness with adverse outcomes in community-dwelling older adults.

Country, cohort, year	Participants	Dyspnea grade	Adverse outcomes
Belgium, BELFRAIL cohort, 2008–2009[9]	$n = 567$ age ≥80 years	MRC 3–5	*All-cause mortality at 5 years* HR 2.85 (95% CI 1.93–4.20) *First unplanned hospitalization at 3 years* HR 1.72 (1.35–2.19) *New/worsened ADL disability at 2 years* OR 2.49 (1.54–4.04) adjusted for age, sex & smoking status.
USA, Health and Retirement Study, 2008[4]	$n = 3671$ age ≥70 years	Non-exertional[a]	*ADL decline at 5 years* HR 1.43 (95%CI 1.22–1.68) *Mortality at 5 years* HR 1.63 (1.32–2.02) adjusted for age, sex, race and education
Australia, Australian Longitudinal Study of Aging, 1992[34]	$n = 798$ Mean age 76.4 years SD 5.8	MRC ≥2	*Worse self-rated health at baseline* OR 2.02 (95% CI 1.53–2.67) *and at 2 years* OR 1.72 (95% CI 1.28–2.33), adjusted for age, sex, living arrangement, smoking status, and co-morbidities
France, PAQUID cohort, 1988[35]	$n = 2792$ age ≥65 years	MRC 3–5	*Mortality at 8 years* MRC 3: HR 1.4 (95% CI 1.2–1.7); MRC 4: HR 2.01 (1.6–2.5); MRC 5: HR 6.0 (3.7–9.7) versus MRC grade 1, adjusted for age, sex, smoking status, profession
UK, year not reported[28]	$n = 500$ age ≥70 years	MRC 3–5	*Mortality at 10 years* OR 1.94 (95%CI 1.11–3.38) adjusted for age, sex, and dyspnea-related morbidities (left ventricular dysfunction and COPD)
France, PAQUID cohort, 1988–1989[36]	$n = 3646$ Mean age = 75.3 years SD 6.8	MRC 3–5	*Mortality at 13 years* MRC 3: HR 1.42 (95% CI 1.25–1.63); MRC 4–5: HR 1.90 (1.61–2.25) versus MRC 1 adjusted for age, sex, BMI, previous ischemic heart disease, stroke, hypertension, smoking and diabetes

Abbreviations: ADL, activities of daily living; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; MRC, Medical Research Council breathlessness scale; n: number; OR, odds ratio; SD, standard deviation.

[a]"How often do you become short of breath while awake?" Often or sometimes → nonexertional breathlessness.

discomfort" that arises from a complex multi-level interaction of physiological, psychological, social, and environmental factors, and should be assessed across three domains: the sensory-perceptual (intensity and quality of the sensation), the affective distress (unpleasantness and fear/anxiety from the sensation) and the impact/burden (on functional ability and daily activities).[6]

Individuals with dyspnea use different words to express their breathing difficulty or discomfort (descriptors/language of dyspnea) and these are usually clustered into the main somatic sensations of breathing work/effort, chest tightness, air hunger, or unsatisfied inspiration.[6,7,37] These sensations, that most of the time co-exist, arise from distinctive peripheral sensory receptors/afferent pathways and vary in their levels of intensity, affective distress (fear and/or anxiety), and impact/burden.[6,7,38,39]

The sensations of breathing discomfort arise as an awareness of the neuromechanical uncoupling that is the mismatch between the central respiratory drive to the respiratory muscles and the mechanical/muscular output of the respiratory system assessed through the receptors in the lung parenchyma, airways, respiratory muscles, and chest wall.[6,7] Functional neuroimaging studies have shown that similar to pain, stimulation of respiratory sensations activates a brain network that includes limbic

and paralimbic areas that are responsible for emotional processing, interoception, and cognition.[6,37,40] Two central processing pathways of respiratory sensations are (1) the discriminative pathway through the somatosensory cortex responsible for the sensory-perceptual domain of dyspnea (quality and intensity) and (2) the affective pathway through the limbic system responsible for the affective domain (immediate unpleasantness and the later affective distress).[6,7,37,41]

The current neurocognitive model suggests that a dynamic cortico-limbic network gives shape to the perception of dyspnea by integrating the input of the current respiratory sensation with the brain's expectations about breathlessness that are based on the context cues, past experiences, or learned behaviors for breathlessness, as well as current affect/mood.[6,40] Expectations and affect/emotions play a crucial role in shaping the individual perception and reporting of breathlessness and its impact/burden.[40,41] This important role of the neuropsychological processes in the perception and reporting of breathlessness might explain the common poor correlation of its severity with objective markers of disease or dysfunction.[6,37] The current evolving research and understanding of the neuropsychological processes of dyspnea draw attention to the importance of their assessment and therapeutic targeting, as it can further improve the management of chronic breathlessness.[41–43]

Older adults are generally considered to have a blunted perception of breathlessness as they report less breathlessness than is expected based on their physiologic impairments related to aging and/or comorbidities.[2,7,44] Clinical studies comparing breathlessness ratings between older and younger patients with well-controlled asthma, chronic heart failure, COPD, and interstitial lung disease suggest a reduced reporting of dyspnea in older adults that is also accompanied by an overall more positive self-ratings of health status and health-related quality of life (Supplementary Material S2).[45–47] Yet in laboratory settings, when performing incremental treadmill/cycle exercise testing with standardized ventilatory and/or metabolic loads, healthy older adults report higher ratings of dyspnea intensity (modified Borg scale 0–10) compared with younger ones[38,48,49] except in a small study of healthy cardio-respiratory fit older men (Supplementary Material S2).[50]

These different findings about perception and report of breathlessness in older adults are probably due to: different settings and samples of older adults (clinical vs. nonclinical), assessment of different types of dyspnea (recalled/retrospective vs. at the moment, at rest or after induced effort/activity), and use of unidimensional assessment tools that do not differentiate between sensory and affective dimensions of breathlessness. In a recent study assessing the sensory and affective dimensions of breathlessness during incremental cycle exercise testing of 35 healthy older (68 ± 5 years) and 19 younger (aged 28 ± 8 years) adults, the unpleasantness of breathlessness was rated lower by the older participants at any given level of overall breathlessness intensity, suggesting differences in the affective domain of breathlessness that had not been reported before.[38]

Based on the current status of evidence it is not clear if older adults have a blunted perception of dyspnea. Studies in this area are limited in number and quality of evidence, but their findings draw attention to the need to consider and research the aging-related factors that may influence the perception and report of dyspnea and may impact its assessment in older adults.[2,7,44]

Aging-related factors that may influence perception and reporting of dyspnea

The perception of breathlessness arises from the integration of the somatosensory information, the affective response, and the expectations that are based on previous experiences and context.[6,40,41] Aging-related changes may affect all these inputs but research in this area is very limited.[44]

There is a strong physiological basis for an increase of perception of breathlessness on exertion in older adults. Normal aging-related changes in the respiratory, cardiovascular, and musculoskeletal system reduce ventilatory capacity and exercise performance and increase ventilatory demand (Table 3, Figure 1).[16,19,51] The ventilatory demand is increased in older age because of reduced gas exchange efficiency in the lungs (increased dead space and mismatch of ventilation/perfusion), and it may further increase during effort/activity, especially if there is locomotor muscle inefficiency and reduced cardiac output.[7,19,48,51]

This increased ventilatory demand during exercise, that is characteristic of older age, can no longer be matched by the reduced ventilatory capacity/reserve (due to the aging-related decrease of respiratory muscle strength and lung volume constraints), leading to the sensation of breathlessness.[48,51]

Aging affects respiratory sensitivity and despite an increased ventilatory response to exertion in older adults compared with younger ones, at rest older adults have reduced sensitivity to dyspnea-related stimuli like increased airflow resistance,[52] hypercapnia,[53] and bronchoconstriction.[54] It has been suggested that sensation input from the contraction efforts of respiratory muscles is not affected in older age, and this plays a key role in the increased sensation of exertional breathlessness,

beside the awareness of increased central neural drive because of increased ventilatory demand from gas exchange inefficiency of the aging lungs.[48,51]

The accuracy of the perception of the respiratory sensations is dependent not only on the peripheral pathways, but also on the central neural processing by cognitive-affective neural networks in the brain.

Studies on the central neural processing of dyspnea in older adults are very limited.[44] One recent study comparing respiratory-related evoked potentials during brief airway occlusion suggests an impaired processing of respiratory sensory input in older age as the cognitive-related components had lower amplitude in older adults (11 participants mean age 76 years) compared with younger ones (14 participants mean age 30 years).[55] Age-related cognitive changes may have an impact in the cognitive-affective processing of breathlessness, whereas breathlessness itself may also have a direct impact on the cognitive function.[16,56,57] This potential bidirectional relationship is an area in need of research, especially in older adults who have higher risk and prevalence of cognitive impairment.[16]

Affect/emotions and expectations based on the context and previous experiences of breathlessness play a crucial role in shaping the individual perception, reporting, and the impact/burden of breathlessness, and they may be influenced by aging-related changes.[39–41] Despite the age-related cortical thinning (loss of gray and white matter) and reduced activation, the regulation of the affect/emotions in older adults may remain intact or even improve.[44,58,59] The positivity effect of older age, with decreased attention to negative stimuli/affect and increased memory for positive ones, could have an impact on the affective response to dyspnea and its central processing, especially when assessment refers to recalled breathlessness, but this impact may be dependent on the cognitive reserves of older adults.[44,58] This positivity tendency of older adults and their improved regulation of negative emotions might explain a blunted perception of breathlessness as negative affect can worsen breathlessness and positive affect can improve it.[26,41] Yet, the impact of aging-related cognitive changes on the affective domain of breathlessness in older adults and the potential bidirectional relationship between affect and breathlessness is unknown and needs to be researched.

Older adults with breathlessness from chronic cardiorespiratory morbidities usually have better self-ratings of their health-related quality of life than younger adults, that may be due to a change of their expectations of what is considered 'normal' in older age and higher tolerance for the impact of breathlessness, and these may influence their self-report of breathlessness.[45,47,60,61] Older adults with chronic breathlessness develop coping/adaptive strategies to minimize its burden on daily life, such as avoidance or reduction of dyspnea-triggering activities, and this may lead to reduced self-report or burden despite increased severity.[44,61] Exposure to chronic breathlessness with high affective distress may also lead to sensitization rather than habituation as shown in studies where older adults with COPD compared to those without COPD reported more affective descriptors and impairment/burden of breathlessness or had higher affective domain scores during exercise-induced breathlessness in controlled nonclinical settings.[38,39]

Community-dwelling older adults with dyspnea have higher prevalence of multimorbidity, medication use and/or polypharmacy.[4,16,19,22,62] Comorbidities and polypharmacy may contribute to both the peripheral and central processing of breathlessness and influence its perception and reporting in community-dwelling older adults so their role needs to be further researched.[16,19,62]

Future research on the impact of aging-related changes, especially cognitive-affective ones, on the perception and self-reporting of breathlessness in community-dwelling older adults would help the development of more appropriate tools to assess and address their burden of breathlessness.

Multidimensional assessment tools

Many tools have been developed to assess breathlessness, but none is a gold standard and most of them have been developed in disease-specific settings (mostly respiratory).[6,63,64] There is a lack of tools that apply to breathless people with different health conditions such as the community-dwelling older adults with multimorbidity and/or multiple age-related impairments, and no tool so far covers all dimensions of breathlessness.[6,63,64]

The most commonly used assessment tools for breathlessness in studies of older adults are the MRC scale, the numerical rating scale, the visual analog scale or the modified 0–10 Borg scale. The MRC scale does not measure breathlessness but rather its functional impact; it is not sensitive to change and not relevant for sedentary/low-mobility older adults as it requires physical activity such as walking up the hill or leaving the house, yet it has been widely used in research studies about breathlessness in older adults with robust findings on its independent prognostic value.[6,63,64] The numerical rating scale, visual analog scale, or modified 0–10 Borg scale have been usually used for the assessment of the overall intensity of breathlessness, and recently also as part of multidimensional assessments of the intensity of different dyspnea sensations, unpleasantness, and affective distress.[6,38,65]

The Multidimension Dyspnea Profile (MDP) and Dyspnea-12 have been developed to capture both the sensory-perceptual and affective distress dimensions of breathlessness.[65] These new tools have been validated in several adult populations with specific diseases or

settings, but only one study has tested and confirmed the internal consistency and concurrent validity of MDP in a sample of 100 community-dwelling older adults (≥75 years old) in Belgium.[65,66]

There is a need for validity and utility studies of the multidimensional tools for breathlessness in older adults outside a particular disease-focused setting, capturing the experience of community-dwelling adults who more likely have breathlessness due to age-related impairments and/or co-existence of chronic diseases, as they may have a different language or set of descriptors compared to those with a specific disease.[9,65,67,68] In a study in Australia, of community-dwelling older adults with and without COPD, the most frequently volunteered descriptors of uncomfortable breathing by COPD participants were affective ones ("frightening" "annoying" "awful"), while non-COPD participants reported more frequently somatic descriptors ("short of breath" and "does not bother me") and behavioral responses (short-term strategies to reduce the sensation such as rest and recover breath or long-term avoidance of activities that provoke breathlessness).[67] In a study in UK of 16 older adults (69–90 years old) with breathlessness who completed the MDP while "thinking aloud", participants wrestled with the meaning of some words and phrases used in the MDP, and this draws attention to the importance and the challenge of incorporating the "*lived experience*" of patients in the assessment for breathlessness.[67,68]

The MDP and Dyspnea-12 provide a more comprehensive assessment of breathlessness that may impact its management, yet even a simple question such as "Have you stopped doing any activities because of breathing difficulty or discomfort?" could be a reasonable approach to proactive search for breathlessness in medical consultations with community-dwelling older adults.[5,7]

The systematic assessment for breathlessness in older adults, no matter what tool is used, requires action to lessen the burden of the identified breathlessness and/or to prevent or reduce the impact of the adverse outcomes associated with it.

INTERVENTIONS FOR BREATHLESSNESS IN OLDER ADULTS: MULTIMODAL

The optimization of the pharmacological treatment of cardio-respiratory diseases in older adults is important, and there are also several evidence-based nonpharmacological interventions available for relief of chronic breathlessness such as neuro-electrical muscle stimulation, chest wall vibration, use of walking aid, breathing training (purse lip and diaphragmatic breathing), mindfulness exercises and relaxation, distraction techniques with music or a hand-held fan in front of one's face, as well as singing.[6,7,69,70] Most of these interventions have been studied in COPD patients and there is lack of evidence on their impact in the multimorbidity setting of community-dwelling older adults.[6,69]

The multifactorial mechanisms of breathlessness require a multimodal approach to its management that targets not only the multiple peripheral pathways but also the central neural processing of breathlessness.[4,6,41–43] Pulmonary rehabilitation that includes exercise training, education, and behavior change components is the cornerstone of the management of chronic breathlessness.[6,71] It takes usually 6–12 weeks with 2–5 sessions per week and can be effectively delivered in ambulatory or inpatient care, community and home-based settings, and as tele-rehabilitation.[71–73] In COPD patients it reduces breathlessness, increases exercise capacity, and improves emotional status, and quality of life.[6,71,73] In 816 outpatients with COPD in UK (mean age 70 years) who were referred for pulmonary rehabilitation, 209 were frail according to Fried phenotype and the majority of the frail participants who completed the pulmonary rehabilitation program (71 out 115) reverted, at least short-term, to prefrail or robust status.[74]

Recently there is a move from the narrow, disease-specific concept of pulmonary rehabilitation into a broader, generic, symptom-based exercise rehabilitation to include patients with other diagnoses such as heart failure who have been shown to gain similar benefit.[75] This approach fits better to the management of breathlessness and is particularly important for community-dwelling adults with multimorbidity and different age-related system impairments.[75]

To our knowledge, only one study has reported the effect of a physical activity intervention on breathlessness in community-dwelling older adults.[29] In this USA study, 1635 adults 70–89 years old who were sedentary & with mobility limitation, were randomized (24–42 months) either in the physical activity or health education group. The results showed no treatment effect of physical activity on respiratory parameters including moderate–severe dyspnea (modified Borg dyspnea scale >2 after 400 m walking test), FEV_1 and maximum inspiratory pressure, despite the positive effect on mobility disability that was the primary focus of the study.[29] The physical activity intervention focused on walking and lower extremity function and these may not address underlying mechanisms of breathlessness in older adults such as the age-related decline of respiratory muscle strength and function.[29]

In a small retrospective study in Taiwan of 95 adults aged ≥65 years who had a 2-week multi-intervention

pulmonary rehabilitation program after coronary artery bypass grafting (including smoking cessation, breathing training, upper and lower extremity exercises, inspiratory muscle training and chest vibration), there was significant improvement in the Borg scale score of dyspnea as well as maximal inspiratory pressure both in patients with and without multimorbidity.[76] Inspiratory muscle training improves inspiratory muscle strength, functional exercise capacity, dyspnea and quality of life based on a meta-analysis of 32 randomized controlled trials in 830 COPD patients.[77] The role of inspiratory muscle training combined with training of ambulatory muscle in the management of breathlessness in community-dwelling older adults needs to be researched based on the important role both respiratory and ambulatory muscles play in the mechanisms of exertional breathlessness.

The effect of pulmonary rehabilitation on the affective domain of breathlessness has been recently investigated in COPD patients.[42,43] Both physical and affective components of dyspnea assessed with the Dyspnea-12 were improved, at short- and long term, by an 8 weeks individualized home- based program that combined physical exercises, education and self-management interventions.[43] Targeting the affective distress domain of breathlessness through multimodal interventions is an important part of its management and needs to be researched in community-dwelling older adults with multimorbidity and multiple age-related impairments.

As breathlessness in older adults is not just a symptom of a disease but a multifactorial geriatric condition with a strong association to ambulatory and respiratory sarcopenia and depression/anxiety, there is a need to develop and test the feasibility and outcomes of multi-component/multi-modal interventions that combine lower and upper limb exercises, inspiratory muscle training, health education, medication and symptom management, nutrition, and coping strategies.[4,6,16,24,26,29,42]

IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH

Current research findings support the paradigm shift from breathlessness as a disease symptom to breathlessness as a geriatric condition/syndrome, because it is multi-factorial, crossing the organ/system-based boundaries, including comorbidities and multi-organ/system impairments, it is highly prevalent and with a substantial impact on disability, quality of life, and survival.[16,28]

Based on the current research findings, it is reasonable to search for breathlessness during medical consultations with older adults, because it is prevalent, hidden, distressing, associated with reduced quality of life and adverse outcomes, and there are evidence-based interventions to manage it.[1,2,4] Simple probing questions to start a systematic search for breathlessness in general medical consultations with older adults could be:

- "Have you given up doing something you like because of shortness of breath?" or
- "Have you stopped doing any daily activities because of breathing discomfort or difficulty?" or
- "How often are you short of breath while you are awake?"[4,5,7]

Once breathlessness is identified, a unidimensional 0–10 numerical scale may be applied to provide a rating of its severity and/or distress. Multidimensional tools would provide a more comprehensive assessment of breathlessness and they need to be used and tested in community-dwelling older adults with multi-system age-related impairments and/or multimorbidity.

Upon finding breathlessness in older adults, further steps should be the evaluation and treatment optimization of common cardio-respiratory diseases and their risk factors, as well as an assessment for sarcopenia and increased risk for adverse outcomes.[2,21,23,24] This could lead to interventions that can improve the quality of life of older adults with breathlessness and may also slow down or revert progression towards adverse outcomes such as functional decline, hospitalizations, and death.[2,21,23,24] Clinicians should become familiar with the different evidence-based nonpharmacological interventions for breathlessness, and if available and feasible consider multimodal interventions similar to pulmonary rehabilitation.

Future research on breathlessness in older adults is needed in the following four domains: its potential status as a multifactorial geriatric condition, its perception and report, its use as an independent risk marker for adverse outcomes and its multimodal management. The following research questions need to be addressed:

1. What are the specific contributions and interaction mechanisms of the multiple factors associated with dyspnea in older adults, such as cardio-respiratory comorbidities and age-related impairments, in particular the contribution of sarcopenia?
2. How do cognitive and affective changes of older age influence the experience and reporting of breathlessness in community-dwelling older adults?
3. What is the language of dyspnea in community-dwelling older adults who experience breathlessness because of multiple age-related impairments and/or multimorbidity?
4. Are multidimensional tools such as MDP and Dyspnea-12 fit for use in community-dwelling older

adults? What is their added value over the unidimensional tools most used so far?
5. What is a valid and feasible assessment tool or set of tools to proactive search for breathlessness as an independent prognostic marker in geriatric health assessment of community-dwelling older adults?
6. Is a multimodal rehabilitation program, including inspiratory muscle training, effective and feasible in community-dwelling older adults with breathlessness?
7. Does proactive detection and intervention for breathlessness in geriatric health assessments improve health outcomes (daily functioning, self-reported health, quality of life and survival) in community-dwelling older adults?

In summary, breathlessness is a common, multidimensional, burdensome yet often hidden experience in older adults. It is multifactorial, crossing the borders of system-based impairments and diseases and a general predictor of adverse outcomes. Its proactive search through simple questions could identify higher risk for adverse outcomes and prompt multi-modal interventions that have the potential to improve quality of life and reduce the risk of adverse outcomes in older adults. Further research needs to investigate the complex multi-factorial mechanisms of dyspnea in community-dwelling older adults, the influence of the affective and cognitive changes of older age on the perception and reporting of breathlessness, the best way to assess and use breathlessness to predict risk for adverse outcomes in general geriatric visits, as well as the most appropriate multimodal interventions and their outcomes.

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Both authors have contributed to the conception of the idea and structure of the manuscript, the identification and analysis of reference publications, the drafting of the manuscript and its critical revision. The authors recognize the work of Elizabeth Swain Mb ChB in revising the English language of the submitted manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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None.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Data S1. Age-related physiological changes that may contribute to dyspnea in older adults.

Data S2. Studies comparing perception and report of breathlessness between older and younger adults.

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