<u>Association of descriptors of breathlessness with diagnosis and self-reported severity of breathlessness in patients with advanced chronic obstructive pulmonary disease or cancer</u>

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Abstract

Context

Verbal descriptors are important in understanding patients' experience of breathlessness.

Objectives

To examine the association between selection of breathlessness descriptors, diagnosis, self-reported severity of breathlessness and self-reported distress due to breathlessness.

Methods

We studied 132 patients grouped according to their diagnosis advanced COPD (n=69) or advanced cancer (n=63), self-reported severity of breathlessness: mild breathlessness (Numerical rating scale (NRS) ≤3, n=53), moderate breathlessness (4≤NRS≥6, n=59) or severe breathlessness (NRS ≥7, n=20), and distress due to breathlessness: mild distress (NRS ≤3, n=31), moderate distress (4≤NRS≥6, n= 44) or severe distress (NRS ≥7, n=57). Patients selected three breathlessness descriptors. The relationship between descriptors selected and patient groups was evaluated by cluster analysis.

Results

Different combinations of clusters were associated with each diagnostic group; the cluster 'chest tightness' was associated with cancer patients. The association of clusters with patient groups differed depending on their severity of breathlessness and their distress due to breathlessness. The 'air hunger' cluster was associated with patients with moderate or severe breathlessness, the 'chest tightness' cluster was associated with patients with mild breathlessness. The 'air hunger' cluster was associated with patients with severe distress due to breathlessness.

Conclusions

The relationship between clusters and diagnosis is not robust enough to use the descriptors to identify the primary cause of breathlessness. Further work exploring how use of breathlessness descriptors reflects the severity of breathlessness and distress due to breathlessness could enable the descriptors to evaluate patient status and target interventions.

Keywords: dyspnea, COPD, cancer, verbal descriptors, breathlessness

Introduction

Breathlessness is defined by the American Thoracic Society as 'a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity' [1]. It has been reported that patients use different descriptors such as 'tightness' or 'gulping for air' to describe their breathlessness [2]. Simon et al. developed 15 breathlessness descriptors from interviews with healthy volunteers with induced breathlessness and patients who suffered from shortness of breath (Table 1) [3,4]. The method by which breathlessness was induced in healthy volunteers affected which breathlessness descriptors they selected to describe their experience [3], thus it has been hypothesized that breathlessness consists of multiple sensations which are induced by different mechanisms [1,3].

A consensus statement by the National Cancer Research Institute's Palliative Care Breathlessness Sub-Group recommended the routine collection of data on the descriptors of breathlessness in order to further explore the sensations of breathlessness [5]. There is evidence that patients with different diagnosis describe their breathlessness with unique combinations or clusters of breathlessness descriptors [4,6,7].A greater understanding of how the sensation of breathlessness differs between patients from different diagnostic groups could both elucidate the mechanisms behind the sensation of breathlessness and enable identification of the primary cause of breathlessness in patients suffering from multiple conditions. There is also some evidence that the association of clusters of breathlessness descriptors with patient groups may depend on the severity of breathlessness experienced [8,9]. It has further been reported that certain sensations of breathlessness i.e. air hunger are associated with more unpleasantness [10]. Identifying how the sensation of breathlessness differs between patients who experience different severities of breathlessness and distress due to breathlessness could inform the targeting of interventions.

This analysis aimed to identify whether patients' selection of breathlessness descriptors devised by Simon et al. [3,4] is affected by their diagnosis of advanced chronic obstructive pulmonary disease (COPD) or advanced cancer, self-reported severity of breathlessness or self-reported distress due to breathlessness. It further sought to compare the descriptor clusters associated with COPD patients with those reported by similar published studies [4,6,7].

Method

Sample

Data were collected within baseline interviews with 132 patients participating in a Phase III single-blinded fast-track pragmatic randomised controlled trial (RCT) of the Cambridge-Breathlessness Intervention Service (CBIS): a multidisciplinary palliative care service for intractable breathlessness in advanced disease [11]. The sample size was determined by the needs of the RCT, inclusion and exclusion criteria are reported elsewhere [11]. Diagnostic groups were determined by the referring clinician assessment of their primary cause of breathlessness: advanced cancer (n=63) arising from different primary tumors (lung n=30, breast n=12, other n=21) or advanced COPD (n=69). Patients were also classified by their self-reported severity of breathlessness on average in the last 24 hours using a Numerical Rating Scale (NRS) [12]: mild breathlessness (NRS ≤3, n=53), moderate breathlessness (4≤NRS≥6, n=59), or severe breathlessness (NRS ≥7, n=20). They were further classified by

their self-reported distress due to breathlessness [13] using a NRS: mild distress (NRS d distress due to breathlessness (4≤NRS≥6, n= 44), or severe distress (NRS ≥7, n=57).

Protocol

The Simon et al. 15 descriptors of breathlessness were presented in a random order on separate cards (Table 1)[3,4]. Patients were asked to select any descriptors which described their breathlessness and then select and rank the three descriptors which best described their experience of breathlessness. Patients rated their severity of breathlessness in the last 24 hours on average using a 0-10 NRS anchored at zero with 'not breathlessness at all' and at 10 with 'breathlessness as bad as you can imagine' in response to the question 'How has your breathlessness been over the last 24 hours on average?'[11]. Patients rated their distress due to breathlessness using a 0-10 NRS anchored at zero with 'not distressed at all' and at ten with 'extremely distressed' in response to the question 'How distressed are you by your breathlessness?'[11].

Statistical Analysis

A hierarchical cluster analysis was used to classify the breathlessness descriptors. The Ward algorithm with squared Euclidian distances was used to find homogeneous subgroups of breathlessness descriptors. A dendrogram was constructed to indicate the distance, based on the degree of similarity, of each descriptor to the other descriptors. An optimal number of clusters was selected based on visual inspection of the dendrogram and the number of clusters relative to the total number of descriptors. Simon et al.'s criterion to establish if a patient group was associated with a particular cluster was employed [4]. The criterion was met if the number of times descriptors in the cluster were selected in the top three divided by the product of the total number of descriptors in the cluster and the sample size of the patient group was greater than 0.25 [4]. The clusters associated with the COPD diagnostic group were compared to similar published studies which analysed the association of identical descriptive clusters with patients with COPD using Simon et al.'s criterion [4,6,7].

Results

There was no significant difference in mean age of patients by diagnostic group (COPD: 71.1 years SD=10.3; cancer: 68.4 years SD = 11.7 p = 0.156.) There was a significant difference in sex by diagnostic group, with a greater proportion of males in the advanced COPD group (62% male) compared to the cancer group (40% male) (x^2 (1, N=132)=6.756, p=0.008). The mean severity of breathlessness in the last 24 hours was 4.83 (SD 1.93) for advanced COPD patients and 3.67 (SD 1.82) for patients with advanced cancer. The mean distress due to breathlessness was 6.45 (SD 2.69) for advanced COPD patients and 5.23 (SD 2.73) for advanced cancer patients. The mean number of descriptors selected to describe breathlessness was 9.72 (SD 3.36) for patients with advanced COPD and 8 (SD 3.03) for patients with advanced cancer. Table 2 shows the most frequently selected 'top three' descriptors by diagnostic group.

Cluster analysis identified six clusters of descriptors: 'breathing restrictions', 'enough air', 'out of breath', 'air hunger', 'effort', 'chest tightness' (Figure 1) (Table 3). The clusters 'enough air', 'out of breath', 'air hunger' and 'effort' were associated with both diagnostic groups. The cluster 'chest tightness' was uniquely associated with patients with advanced cancer.

The clusters 'enough air', 'out of breath' and 'effort' were associated with patients with mild, moderate and severe breathlessness. The 'air hunger' cluster was associated with patients with moderate breathlessness (4≤NRS≥6) and patients with severe breathlessness (NRS 7≤) (Table 4). The 'chest tightness' cluster was associated with patients with mild breathlessness (NRS ≤3) (Table 4).

The clusters 'out of breath' and 'effort' were associated with patients with mild (NRS ≤3), moderate (4≤NRS≥6) and severe distress (NRS 7≤). The cluster 'air hunger' was uniquely associated with patients with severe distress (NRS 7≤), the cluster 'enough air' was associated with patients with moderate (4≤NRS≥6) and severe distress (NRS 7≤), the cluster 'chest tightness' was associated with patients with mild distress (NRS ≤3) (Table 4) .

Table 5 compares our findings on the clusters associated with patients with COPD with other published studies [4,6,7]. There was no consensus between the studies on which clusters are associated with COPD (Table 5).

Discussion

Patients discriminated between six clusters of descriptors of breathlessness: 'breathing restriction', 'enough air', 'out of breath', 'air hunger', 'effort of breathing' and 'chest tightness' (Table 3). This suggests that patients experienced distinct qualitative experiences of breathlessness. This supports the hypothesis that breathlessness consists of multiple sensations which are induced by different mechanisms.

Each diagnostic group was characterised by more than one cluster (Table 3). Clusters 'enough air', 'out of breath', 'air hunger' and 'effort' were associated with both diagnostic groups (Table 3). Different combinations of clusters were associated with the diagnostic groups, the cluster 'chest tightness' was uniquely associated with cancer patients (Table 4). This supports the multiplicity of clusters associated with each diagnostic group, sharing of certain clusters amongst diagnostic groups and uniqueness of the combination of clusters associated with each diagnostic group first reported by Simon et al [4].

The descriptors selected most frequently by patients with advanced COPD replicated the findings of Mahler et al. and Wilcock et al. (Table 2) [6,7]. Mahler et al., Wilcock et al. and Simon et al. analysed the association of some of the same clusters used in this study with COPD patients [4,6,7]. The variation between clusters reported to be associated with COPD across this study, Wilcock et al., Mahler et al. and Simon et al. (Table 5) [4,6,7] could result from differences in sample characteristics such as sample size, language, ethnicity or culture. In particular, in our study the patients were referred to CBIS using the criteria that they were troubled by their breathlessness [11] and so may represent a sub-group of patients with advanced COPD. The lack of a consensus between studies on the association of descriptive clusters with diagnostic groups, and the sharing of clusters amongst diagnostic groups, suggests that the breathlessness descriptors cannot be used to identify the primary cause of breathlessness in patients with multiple conditions.

The association of clusters with patient groups differs depending on their severity of breathlessness: the 'air hunger' cluster was uniquely associated with groups with moderate and severe breathlessness (Table 4). This supports work by Von Leupoldt et al. which demonstrated that the selection of descriptive clusters by COPD patients differed depending on the intensity of exercise they experienced and Smith et al.'s finding that air hunger

descriptors were more frequently selected by dyspnoeic patients after exercise than at rest [8,9]. However, our study is unique in demonstrating that cluster selection is dependent on the severity of self-reported breathlessness rather than the severity of breathlessness induced by exercise. These results suggest that the breathlessness descriptors could be used to evaluate the severity of patients' breathlessness.

In normal subjects the sensation of air hunger occurred when stimuli such as hypercapnia and hypoxia, which intensify the motor drive to breathe, were increased whilst ventilation rate was held constant [14,15,16]. Thus, it has been hypothesized that air hunger occurs due to neuromuscular dissociation, an imbalance between motor drive to breathe and afferent feedback from mechanoreceptors [15,16]. The cluster 'air hunger' was associated with patients with severe distress (Table 4). This supports Banzett et al. findings that healthy subjects were more distressed by laboratory induced air hunger than maximal respiratory work/ effort [10]. Further work to identify the most distressing aspects of breathlessness could help in the selection and targeting of interventions. For example, there is some evidence to suggest that air hunger may be relieved by activation of pulmonary mechanoreceptors through the administration of furosemide [17, 18,19, 20]. Given our finding that air hunger is associated with patients with severe distress (Table 4), future research could target the intervention to this patient group.

Interpretation of our results is limited by the relatively sample size and inability to adjust for potentially significant covariates. There is potential for referral bias given design of the underlying study and sample bias.. In addition, it is difficult to make comparisons to other studies due to methodological heterogeneity. For example, studies use different questionnaires. Amongst the studies using Simon et al.'s 15 descriptors, different clusters have been analysed because different methods have been used to identify clusters and there is no universal agreement on how to determine the appropriate number of clusters. Validated multi-dimensional tools such as the Dyspnoea 12 and the Multidimensional Dyspnoea Profile have reduced the redundancy in descriptors, potentially eliminating the need for cluster analysis [21,22,23]. However, to address questions on the sensations of breathlessness studies need to report results from descriptors describing sensory experience in isolation to those reflecting emotional functioning. The next step would be to conduct a study with a larger sample size using these multi-dimensional tools in order to explore the association of descriptors with distress and severity of breathlessness.

<u>Conclusion</u>

The breathlessness descriptors can be used to distinguish between six sensations of breathlessness; 'breathing restriction', 'enough air', 'out of breath', 'air hunger', 'effort' and 'chest tightness'. Many clusters were associated with both diagnostic groups though each diagnostic group was associated with a unique combination of clusters. The relationship between cluster selection and diagnosis is not robust enough to use the descriptors to identify the primary cause of breathlessness. The clusters associated with a patient group varied according to the group's severity of breathlessness and distress due to breathlessness. The cluster 'air hunger' was associated with patients with moderate and severe breathlessness and severe distress due to their breathlessness. How descriptor selection is affected by both patients' distress due to breathlessness and severity of breathlessness should be further explored as one could employ the breathlessness descriptors to evaluate patient status and target interventions.

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Table 1: Descriptors of breathlessness devised by Simon et al. [3,4].

Descriptor number	Descriptors of breathlessness
1	I feel I am suffocating
2	I cannot get enough air
3	I feel out of breath
4	My breath does not go in all the way
5	My breath does not go out all the way
6	My breathing is shallow
7	I feel my breathing is rapid
8	I feel I am breathing more
9	I feel that I am smothering
10	I feel a hunger for more air
11	My breathing requires effort
12	My chest feels tight
13	My breathing is heavy
14	My breathing requires more work
15	My chest feels constricted

Table 2: Descriptors most commonly selected by patients with COPD and advanced cancer as one of the three descriptors which best described patients' breathlessness

	Most frequently selected top three descriptors by diagnostic group	
Diagnosis	Descriptors	% of each diagnostic group selecting the descriptor
Advanced COPD	1. I cannot get enough air 2. I feel out of breath 3. My breathing requires effort	39.1% 39.1% 36.2%
Advanced cancer	1. I feel out of breath 2. I can't get enough air 3. My breathing requires work	54% 36.5% 30.2%

Table 3: Clusters of breathlessness descriptors resulting from hierarchal cluster analysis

Clusters	Descriptors
Cluster 1: Breathing restrictions	1. I feel I am suffocating 4. My breath does not go in all the way 5. My breath does not go out all the way 6. My breathing is shallow 7. I feel my breathing is rapid 8. I feel I am breathing more 9. I feel that I am smothering 13. My breathing is heavy
Cluster 2: Enough air	2. I cannot get enough air
Cluster 3: Out of breath	3. I feel out of breath
Cluster 4: Air hunger	10. I feel a hunger for more air
Cluster 5: Effort	11. My breathing requires effort 14. My breathing requires more work
Cluster 6: Chest tightness	12. My chest feels tight 15. My chest feels constricted

Table 4: Association of clusters with diagnosis, with severity of breathlessness and distress due to breathlessness[1]

Patient group	Cluster 1 Breathing restrictions	Cluster 2 Enough air	Cluster 3 Out of breath	Cluster 4 Air hunger	Cluster 5 Effort	Cluster 6 Chest tightness
Diagnosis of advanced:						
Cancer		*	*	*	*	*
COPD		*	*	*	*	
Severity of breathlessness (NRS):						
Mild (NRS ≤3)		*	*		*	*
Moderate		*	*	*	*	

(4≤NRS≥6)					
Severe (NRS≥7)		*	*	*	*	
Distress due to breathlessness (NRS):					
Mild (NRS≤3)			*		*	*
Moderate (4≤NRS≥6)		*	*		*	
Severe (NRS≥7)		*	*	*	*	

[1] * indicates that the cluster is associated with the patient group.

Table 5 Comparison of descriptive clusters associated with COPD patients across studies[2]

Clusters associated with COPD	BIS Phase III RCT baseline data (n=69)	Wilcock et al. [7] (n=34)	Mahler et al. [6] (n=85)	Simon et al. [4] (n= 16)
Chest tightness	No	Yes	No	No
Air hunger	Yes	Yes	No	NA
Effort	Yes	No	NA	Yes
Out of breath	Yes	No	NA	NA
Enough air	Yes	Yes	NA	NA
Breathing restrictions	No	NA	NA	NA

[1] 'Yes' indicates that the cluster was associated with COPD patients, 'NA' indicates that the cluster was not analysed in the study. For key to clusters see Table 3.

Breathlessness Descriptors